

PFOA

Acute Toxicity - /



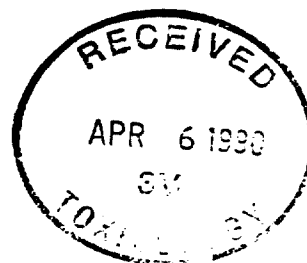
HAZLETON
LABORATORIES AMERICA, INC.
3301 KINSMAN BLVD., P.O. BOX 7545
MADISON, WI 53707 USA

FINAL REPORT

Karen Armstrong
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Toxicology Services
Building 220-2E-02
St. Paul, MN 55144-1000

HLA Number: 91201739

Sample: T-4416



Enclosed: Acute Oral Toxicity Study in Rats (OECD Guidelines)

- o Key Personnel
- o Methodology
- o Summary of Results
- o Individual Pathology Comments
- o References
- o Pathology Report
- o Raw Data/Appendix

Signed: _____

Steven M. Glaza
Study Director
Acute Toxicology

Date

4-2-90



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KEY PERSONNEL

Acute Toxicology

Steven M. Glaza
Study Director
Section Supervisor

Steven R. Sorenson
Study Coordinator

Patricia Padgham
Group Leader

Sharen L. Howery
Report Coordinator

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Deborah L. Keller
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Anatomical Pathology

Thomas E. Palmer, PhD
Anatomical Pathologist

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Group Leader
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Pathology Data



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Sample: T-4416

METHODOLOGY

Objective: To assess the acute oral toxicity produced when a test material is administered by oral gavage to rats.¹

Test Material: T-4416

Physical Description: Clear colorless liquid

Purity and Stability: 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 material will be returned to the Sponsor according to HLA Standard Operating Procedure.

Safety Precautions: Normal handling procedures were used according to HLA Standard Operating Procedure.

Test Animal: Adult albino rats, CrI:CD®BR, were procured, separated by sex, maintained in group cages in temperature- and humidity-controlled quarters, provided continuous access to Rodent Chow® 5001, Purina Mills, Inc., and water, and held for an acclimation period of at least 7 days. Animal husbandry and housing at HLA comply with standards outlined in the "Guide for the Care and Use of Laboratory Animals".² If variations from the prescribed environmental conditions existed, they were documented and considered to have no effect on the study outcome. No contaminants were expected to have been present in the feed or water which would have interfered with or affected the results of the study.

Acclimated animals were chosen at random for the study. Five male and five female rats, weighing from 204 to 299 g, were used for each dose level. The study consisted of three dose levels (0.2, 1.0 and 5.0 g/kg of body weight). 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: Historically, rats have been used as a representative of a rodent species and are preferred by various regulatory agencies.

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

The dose volume of the test material varied for each dose level based upon the bulk density of the material of 1.28 g/mL.



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

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.

Animals were weighed just before test material administration. Surviving animals were weighed again at Day 7 and at termination of the experimental phase or at death (when survival exceeded 1 day).

Pathology: All animals whether dying on test or euthanatized at termination of the experimental phase were subjected to a gross necropsy examination and all abnormalities were recorded. After necropsy, the animals were discarded and no tissues were saved.

Statistical Methods: The LD₅₀ value for males, females and the combined sexes was calculated based upon the observed mortality using a computer program utilizing a modified Behrens-Reed-Muench Cumulant Method.³ No other statistical analysis was performed.

Location of Raw Data and Final Report: The raw data and a copy of the final report will be retained in the archives of HLA.



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SUMMARY OF RESULTS

Test Animal: Albino Rats - Cr1:CD®BR
Source: Charles River Laboratories, Inc., Portage MI
Date Animals Received: 12/04/89, 12/18/89 and 01/08/90

Method of Administration: Oral Gavage

Start Date (In-life): 12/28/89

End Date (In-life): 02/16/90

Estimated Oral LD₅₀ : Male - 1.8 g/kg of Body Weight
95% Confidence Limits - 0.7 to 4.9 g/kg

Female - 0.6 g/kg of Body Weight
95% Confidence Limits - 0.2 to 1.5 g/kg

Sexes Combined - 1.0 g/kg of Body Weight
95% Confidence Limits - 0.4 to 2.4 g/kg

Sex	Dose Level (g/kg)	Average Body Weights (g)			Mortality (Number Dead/Number Dosed)
		Initial	Day 7	Terminal	
Male	0.2	290	332	362	0/5
	1.0	272	264	315	1/5
	5.0	274	---	---	5/5
Female	0.2	211	247	254	0/5
	1.0	233	257	268	4/5
	5.0	230	---	---	5/5



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Clinical Signs
(Number of Animals Affected)

<u>Observation</u>	<u>Hour</u>			<u>Day</u>													
	<u>1.0</u>	<u>2.5</u>	<u>4.0</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>	<u>9</u>	<u>10</u>	<u>11</u>	<u>12</u>	<u>13</u>	<u>14</u>
<u>Males (0.2 g/kg)</u>																	
Appeared normal	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
<u>Females (0.2 g/kg)</u>																	
Appeared normal	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
<u>Males (1.0 g/kg)</u>																	
Appeared normal	5	5	5	5	2	1	1	1	2	3	3	3	3	3	3	4	4
Hypoactivity	0	0	0	0	3	2	2	2	2	1	1	1	0	0	0	0	0
Red-stained face	0	0	0	0	1	2	2	2	1	1	1	1	1	1	0	0	0
Yellow-stained urogenital area	0	0	0	0	1	3	3	3	1	1	1	1	1	1	1	0	0
Ataxia	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0
Thin appearance	0	0	0	0	0	0	0	0	1	1	1	1	1	0	0	0	0
Diarrhea	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0
Death	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
<u>Females (1.0 g/kg)</u>																	
Appeared normal	5	5	5	5	1	1	1	1	1	1	1	1	1	1	1	1	1
Hypoactivity	0	0	0	0	2	2	1	0	0	0	0	0	0	0	0	0	0
Red-stained face	0	0	0	0	2	2	1	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
Prostration	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Death	0	0	0	0	1	2	1	0	0	0	0	0	0	0	0	0	0



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Clinical Signs (Continued)
(Number of Animals Affected)

<u>Observation</u>	<u>Hour</u>			<u>Day</u>													
	<u>1.0</u>	<u>2.5</u>	<u>4.0</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>	<u>7</u>	<u>8</u>	<u>9</u>	<u>10</u>	<u>11</u>	<u>12</u>	<u>13</u>	<u>14</u>
<u>Males (5.0 g/kg)</u>																	
Appeared normal	1	0	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Diarrhea	4	4	4	1	-	-	-	-	-	-	-	-	-	-	-	-	-
Hypoactivity	0	4	4	1	-	-	-	-	-	-	-	-	-	-	-	-	-
Red-stained face	0	2	4	1	-	-	-	-	-	-	-	-	-	-	-	-	-
Lacrimation	0	0	1	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Ataxia	0	0	0	1	-	-	-	-	-	-	-	-	-	-	-	-	-
Death	0	0	1	4*	-	-	-	-	-	-	-	-	-	-	-	-	-

* - One animal found dead after the morning observation.

<u>Females (5.0 g/kg)</u>																	
Appeared normal	2	0	0	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Diarrhea	3	3	2	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Hypoactivity	1	3	2	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Lacrimation	0	2	2	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Ataxia	0	1	1	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Red-stained face	0	1	1	0	-	-	-	-	-	-	-	-	-	-	-	-	-
Death	0	2	1	2	-	-	-	-	-	-	-	-	-	-	-	-	-



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INDIVIDUAL PATHOLOGY COMMENTS

Dose Level: 0.2 g/kg of Body Weight

<u>Animal Number</u>	<u>Sex</u>	<u>Test Day</u>		<u>Necropsy Observation</u>
		<u>Died</u>	<u>Sacrificed</u>	
C50366	M	-	14	No visible lesions
C50367	M	-	14	No visible lesions
C50363	M	-	14	No visible lesions
C50369	M	-	14	No visible lesions
C50370	M	-	14	No visible lesions
C50501	F	-	14	No visible lesions
C50502	F	-	14	No visible lesions
C50503	F	-	14	No visible lesions
C50504	F	-	14	No visible lesions
C50500	F	-	14	No visible lesions



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INDIVIDUAL PATHOLOGY COMMENTS (continued)

Dose Level: 1.0 g/kg of Body Weight

<u>Animal Number</u>	<u>Sex</u>	<u>Test Day</u>		<u>Necropsy Observation</u>
		<u>Died</u>	<u>Sacrificed</u>	
C49861	M	-	14	No visible lesions
C49862	M	-	14	No visible lesions
C49863	M	-	14	No visible lesions
C49864	M	2	-	Stomach, Glandular Mucosa: diffusely red
C49860	M	-	14	No visible lesions
C49921	F	3	-	Stomach, Glandular Mucosa: diffusely red
C49917	F	2	-	No visible lesions
C49918	F	4	-	Perinasal Discharge: red Stomach, Glandular Mucosa: multiple dark areas, up to 2 x 4 mm
C49919	F	3	-	Stomach, Glandular Mucosa: diffusely red
C49920	F	-	14	No visible lesions



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INDIVIDUAL PATHOLOGY COMMENTS (continued)

Dose Level: 5.0 g/kg of Body Weight

<u>Animal Number</u>	<u>Sex</u>	<u>Test Day</u>		<u>Necropsy Observation</u>
		<u>Died</u>	<u>Sacrificed</u>	
C49191	M	1	-	No visible lesions
C49192	M	1	-	No visible lesions
C49193	M	1	-	Stomach, Glandular Mucosa; multiple brown areas, up to 3 x 1 mm
C49194	M	0	-	Stomach, Glandular Mucosa: diffusely dark red
C49490	M	1	-	No visible lesions
C49131	F	0	-	Stomach contents: clear white fluid
C49132	F	1	-	Stomach, Glandular Mucosa: multiple brown areas, up to 4 x 2 mm
C49128	F	0	-	Stomach Contents: clear white fluid
C49129	F	0	-	Stomach Contents: clear white fluid
C49130	F	1	-	No visible lesions



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REFERENCES

1. "Acute Oral Toxicity," *Organisation for Economic Cooperation and Development's Guidelines for Testing of Chemicals*, Section 401 (adopted May 12, 1981).
2. NIH Publication No. 86-23 (revised 1985).
3. Thakur, A. K. and Fezio, W. L., "A Computer Program for Estimating LD₅₀ and its Confidence Limits Using a Modified Behrens-Reed-Muench Cumulant Method," *Drug and Chemical Toxicology*, 4(3):297-305 (1981).



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PATHOLOGY REPORT

There were 10 rats (5 males, 5 females) from each of 3 dose levels (0.2, 1.0, and 5.0 g/kg) necropsied. The animals that died on test (DOT) were refrigerated and necropsied within 24 hours, usually the same day. All surviving animals were euthanatized and necropsied at the termination of the study. The dose level, day of death, and gross observations recorded for each animal are on page 8 through 10 of this report.

All animals in the 5.0 g/kg dose group died on test. At necropsy, the only changes observed were in the animals that died on test. The most frequently recorded observations pertained to the content and coloration changes in the mucosa of the stomach. These findings possibly represent test material mixed with ingesta, postmortem change, or both. All remaining observations in the DOTs were considered postmortem change, incidental, and unrelated to the test material. There were no visible lesions in the sacrificed animals.



Thomas E. Palmer, PhD
Pathologist

4-3-90
Date

(91201739.cjr)

HLA: 91201739PERSONNEL SIGNATURE SHEET
ACUTE TOXICOLOGY

<u>Name</u>	<u>Job Title</u>	<u>Signature</u>	<u>Initials</u>
Becky Beckwith	Lab Animal Technician	<u>Becky Beckwith</u>	<u>B/B</u>
Ann Bursaw	Sr. Clerk	<u>Ann Bursaw</u>	<u>AnnB</u>
Anthony Cass	Lab Animal Assistant	<u>Anthony Cass</u>	<u>AC</u>
Cindy J. Cary, DVM	Lab Animal Veterinarian	<u>Cindy J. Cary</u>	<u>CK</u>
Kari Gassen	Sr. Lab Animal Assistant	<u>Kari Gassen</u>	<u>KG</u>
Steven M. Glaza	Section Supervisor	<u>Steven M. Glaza</u>	<u>SG</u>
Ben Haley	Sr. Lab Animal Assistant	<u>Ben Haley</u>	<u>BH</u>
Jeff Hicks	Lab Animal Technician	<u>Jeff Hicks</u>	<u>JH</u>
Sharen L. Howery	Research Assistant	<u>Sharen L. Howery</u>	<u>SLH</u>
Jim Jirschele	Lab Animal Assistant	<u>Jim Jirschele</u>	<u>JJ</u>
Wayne Madison	Senior Section Supervisor	<u>Wayne A. Madison</u>	<u>WAM</u>
Bud McDonald	Sr. Lab Animal Assistant	<u>Bud McDonald</u>	<u>BMC</u>
Eileen McConnell	Administrative Clerk	<u>Eileen McConnell</u>	<u>EMC</u>
Henry Mikula	Lab Animal Assistant	<u>Henry Mikula</u>	<u>H M</u>
Albert Oleson	Sr. Lab Animal Assistant	<u>Albert Oleson</u>	<u>AO</u>
Patricia Padgham	Group Leader	<u>Patricia Padgham</u>	<u>TP</u>
Jane Polnow	Lab Animal Technician	<u>Jane Polnow</u>	<u>JP</u>
Steven R. Sorenson	Study Coordinator	<u>Steven R. Sorenson</u>	<u>SRS</u>
Dawn Thieding	Clerk	<u>Dawn Thieding</u>	<u>DT</u>
Annette R. Turner	Sr. Clerk	<u>Annette R. Turner</u>	<u>AT</u>
<u>KEN BRIDGES</u>	<u>SO. LAB ANIMAL ASST.</u>	<u>Ken Bridges</u>	<u>KB</u>

(09/11/89)

000827

HLA: 91201739

DOSE ADMINISTRATION/BODY WEIGHT/MORTALITY RECORD

Study Title: Acute Oral ToxicityTest Material: T-4416Vehicle: NABulk Density: 1.28 (g/mL) Species/Strain: Albino Rat/Sprague-Dawley Source: Charles River Date Received: 1-8-90Dose Level: 0.2 (g/kg) Fasted Date/Time/Technician 2-1-90/3:05 p.m./BH Room No. 102Route of Administration: Oral Gavage

Dose Volume <u>0.16</u> (mL/kg)	Sex: <u>(Male/Female)</u>					Dose Time: <u>9:50 AM</u>	Technician	1990 Date	Scale Used KTron
Animal No. <u>C5-</u>	<u>0366</u>	<u>0367</u>	<u>0363</u>	<u>0369</u>	<u>0370</u>	/	<u>BH</u>	<u>2/2</u>	<u>NA</u>
Prefasted Body Weight (g)	<u>NA</u>								
Fasted Body Weight (g)	<u>284</u>	<u>282</u>	<u>299</u>	<u>291</u>	<u>294</u>		<u>BH</u>	<u>2/2</u>	<u>5228</u>
Actual Dose (mL)	<u>0.05</u>	<u>0.05</u>	<u>0.05</u>	<u>0.05</u>	<u>0.05</u>		<u>BH</u>	<u>2/2</u>	Verified by: <u>W 2-2-90</u>
Day 7 Body Weight (g)	<u>329</u>	<u>324</u>	<u>351</u>	<u>328</u>	<u>327</u>		<u>BH</u>	<u>2/4</u>	<u>5228</u>
Day 14 Body Weight (g)	<u>356</u>	<u>353</u>	<u>386</u>	<u>358</u>	<u>358</u>		<u>BH</u>	<u>2/16</u>	<u>5228</u>
Dead Body Weight (g)									

Dose Volume <u>0.16</u> (mL/kg)	Sex: <u>(Male/Female)</u>					Dose Time: <u>9:52 AM</u>	Technician	1990 Date	Scale Used KTron
Animal No. <u>C5-</u>	<u>0501</u>	<u>0502</u>	<u>0503</u>	<u>0504</u>	<u>0500</u>	/	<u>BH</u>	<u>2/2</u>	<u>NA</u>
Prefasted Body Weight (g)	<u>NA</u>								
Fasted Body Weight (g)	<u>218</u>	<u>204</u>	<u>209</u>	<u>217</u>	<u>206</u>		<u>BH</u>	<u>2/2</u>	<u>5228</u>
Actual Dose (mL)	<u>0.03</u>	<u>0.03</u>	<u>0.03</u>	<u>0.03</u>	<u>0.03</u>		<u>BH</u>	<u>2/2</u>	Verified by: <u>W 2-2-90</u>
Day 7 Body Weight (g)	<u>258</u>	<u>243</u>	<u>241</u>	<u>256</u>	<u>238</u>		<u>BH</u>	<u>2/9</u>	<u>5228</u>
Day 14 Body Weight (g)	<u>270</u>	<u>246</u>	<u>241</u>	<u>266</u>	<u>247</u>		<u>BH</u>	<u>2/16</u>	<u>5228</u>
Dead Body Weight (g)									

MORTALITY (NO. DIED/NO. DOSED)

Dose Level (g/kg)	Sex	Hours 0-2	Study Day														Total
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	
0.2	♂	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
0.2	♀	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
Tech.		<u>BH</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>	<u>7/2</u>
Time		<u>NA</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>	<u>8:51</u>
Date 1990		<u>2/2</u>	<u>2/3</u>	<u>2/3</u>	<u>2/4</u>	<u>2/4</u>	<u>2/5</u>	<u>2/5</u>	<u>2/6</u>	<u>2/6</u>	<u>2/7</u>	<u>2/8</u>	<u>2/8</u>	<u>2/9</u>	<u>2/10</u>	<u>2/10</u>	<u>2/16</u>

NA - Not Applicable

Reviewed By JH Date 2-22-90

000828

HLA: 91201739

OBSERVATIONS (Individual)

Dose level: 0.2 g/kgTest material: T-4416Male/female

Animal Number	Observations	Pre-dose	Hours			Study Day													
			1	2.5	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
CS-0366	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CS-0367	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CS-0363	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CS-0369	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CS-0370	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Deaths		NA	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Collected by		3/1	3/1	3/1	3/1	3/1	3/1	3/1	3/1	3/1	3/1	3/1	3/1	3/1	3/1	3/1	3/1	3/1	3/1
Date 1990		2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2

- Surviving animals submitted for terminal necropsy.

Technician AWDate 2-16-90

- Surviving animals designated for sacrifice and discard.

Technician NADate NA

✓ Indicates condition exists

S1 Slight.

- Condition not evident.

* Found dead, P.M. check.

NA Not applicable

Reviewed by: JADate: 2-22-90

000829

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HLA: 91201739

OBSERVATIONS (Individual)

Dose level: 0.2 g/kg

Test material: T-4416

Male Female

Animal Number	Observations	Pre-dose	Hours			Study Day													
			1	2.5	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
CS-0501	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CS-0502	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CS-0503	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CS-0504	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
CS-0500	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Deaths		NA	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Collected by		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Date 1990		2/2	2/2	2/2	2/2	2/3	2/4	2/5	2/6	2/7	2/8	2/9	2/10	2/11	2/12	2/13	2/14	2/15	2/16

- Surviving animals submitted for terminal necropsy.

Technician BH

Date 2-16-90

- Surviving animals designated for sacrifice and discard.

Technician NA

Date NA

✓ Indicates condition exists

S1 Slight.

- Condition not evident.

* Found dead, P.M. check.

NA Not applicable

Reviewed by: SH

Date: 2-22-90

000830

HLA: 91201739

DOSE ADMINISTRATION/BODY WEIGHT/MORTA. (RECORD

Study Title: Acute Oral ToxicityTest Material: T-4416Vehicle: NABulk Density: 1.28 (g/mL) Species/Strain: Albino Rat/Sprague-Dawley Source: Charles River Date Received: 12-18-89Dose Level: 1.0 (g/kg) Fasted Date/Time/Technician: 1-8-90/3:30 p.m./BJH Room No. 102Route of Administration: Oral Gavage

Dose Volume (mL/kg)	Sex: (Male/Female)	Dose Time: 9:25am	Technician	1990 Date	Scale Used KTron
Animal No.	9861 9862 9863 9864 9860		BJH	1/9	NA
Prefasted Body Weight (g)	NA				
Fasted Body Weight (g)	267 272 279 271 273		BJH	1/9	5228
Actual Dose (mL)	0.21 0.21 0.22 0.21 0.21		BJH	1/9	Verified by: JRS 1-9-90
Day 7 Body Weight (g)	294 294 292 Dead 175 ^{nm}		BJH	1/16	5228
Day 14 Body Weight (g)	329 333 336 1-11-90 260		BJH	1/23	5228
Dead Body Weight (g)		226			

Dose Volume (mL/kg)	Sex: (Male/Female)	Dose Time: 9:28am	Technician	1990 Date	Scale Used KTron
Animal No.	9921 9917 9918 9919 9920		BJH	1/9	NA
Prefasted Body Weight (g)	NA				
Fasted Body Weight (g)	235 268 220 215 229		BJH	1/9	5228
Actual Dose (mL)	0.18 0.21 0.17 0.17 0.18		BJH	1/9	Verified by: JRS 1-9-90
Day 7 Body Weight (g)	Dead Dead Dead Dead 257		BJH	1/16	5228
Day 14 Body Weight (g)	1-12-90 219 1-11-90 225 1-13-90 221 1-12-90 234 268		BJH	1/23	5228
Dead Body Weight (g)	203 224 190 183				

MORTALITY (NO. DIED/NO. DOSED)

Dose level (g/kg)		Sex	Hours 0 - 4	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		
1.0		♂	0/5	0/5	0/5	0/5	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	NA	1/5	
1.0		♀	0/5	0/5	0/5	1/5	0/5	1/5	1/5	0/5	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	NA	4/5
Tech.			NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Time			NA	8:15	2:45	8:25	3:15	8:30	3:00	7:45	12:45	7:15	12:15	8:15	1:30	8:00	3:15	7:45	3:00	8:10	3:30	8:25	3:30	8:25	12:35	8:35	12:40	7:10	2:55	8:10	NA	NA	
Date 1990			1/9	1/10	1/10	1/11	1/11	1/12	1/12	1/13	1/13	1/14	1/14	1/15	1/15	1/16	1/16	1/17	1/17	1/18	1/18	1/19	1/19	1/20	1/20	1/21	1/21	1/22	1/22	1/23	NA	1/23	

NA - Not Applicable

Reviewed By BJH Date 2-22-90

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HLA: 91201739

OBSERVATIONS (Individual)

Dose level: 1.0 g/kg

Test material: T-4416

Male/Female		Pre-dose	Hours				Study Day													
Animal Number	Observations		1	2.5	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
C4-9861	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
C4-9862	Appeared Normal	✓	✓	✓	✓	✓	✓	-	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	
	Yellow stained urogenital area							✓	✓	✓	-	-	-	-	-	-	-	-	-	
C4-9863	Appeared Normal	✓	✓	✓	✓	✓	-	-	-	-	-	✓	✓	✓	✓	✓	✓	✓	✓	
	Hypoactive						✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	
	Red stained face							✓	✓	✓	-	-	-	-	-	-	-	-	-	
	Yellow stained urogenital area							✓	✓	✓	-	-	-	-	-	-	-	-	-	
C4-9864	Appeared Normal	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	
	Hypoactive						✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	
	Red stained face							✓	✓	✓	-	-	-	-	-	-	-	-	-	
	Dead							*												
C4-9860	Appeared Normal	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	✓	✓	
	Hypoactive						✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	-	-	
	Yellow stained urogenital area						✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	-	-	
	Red stained face							✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	-	-	
	Ataxia										✓	✓	✓	✓	-	-	-	-	-	
	Appears thin										✓	✓	✓	✓	-	-	-	-	-	
	Diarrhea										✓	✓	✓	✓	-	-	-	-	-	
	Deaths	NA	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Collected by		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Date 1990		1/9	1/9	1/9	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	

- Surviving animals submitted for terminal necropsy.
Technician NA

Date 1-23-90

- Surviving animals designated for sacrifice and discard.
Technician NA

Date NA

✓ Indicates condition exists
S1 Slight.
- Condition not evident.
* Found dead, P.M. check.

NA Not applicable
Reviewed by: NA
Date: 2-22-90

000832

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HLA: 91201739

OBSERVATIONS (Individual)

Dose level: 1.0 g/kg

Test material: T-4416

Animal Number	Observations	Pre-dose	Hours			Study Day													
			1	2.5	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
C4-9921	Appeared Normal	✓	✓	✓	✓	✓	-	-											
	Hypoactive					✓	-	-											
	Red stained face					✓	-	-											
	Dead							✓											
C4-9917	Appeared Normal	✓	✓	✓	✓	✓	-	-											
	Dead						✓	-											
C4-9918	Appeared Normal	✓	✓	✓	✓	✓	-	-											
	Hypoactive						✓	✓	✓										
	Red stained face							✓	✓										
	PROSTRATE								✓										
C4-9919	Appeared Normal	✓	✓	✓	✓	✓	-	-											
	Red stained face						✓	✓											
	Hypoactive							✓											
	Ataxia							✓											
C4-9920	Appeared Normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Deaths		NA	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0	0	0
Collected by		SH	SH	SH	SH	SH	SH	SH	SH	SH	SH	SH	SH	SH	SH	SH	SH	SH	SH
Date 1990		1/9	1/9	1/9	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

- Surviving animals submitted for terminal necropsy.
Technician SH

Date 1-23-90

- Surviving animals designated for sacrifice and discard.
Technician NA

Date NA

✓ Indicates condition exists
S1 Slight.
- Condition not evident.
* Found dead, P.M. check.
NA Not applicable
Reviewed by: JH
Date: 2-22-90

000833

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HLA: 91201739

DOSE ADMINISTRATION/BODY WEIGHT/MORTALITY RECORD

Study Title: Acute Oral ToxicityTest Material: T-4416Vehicle: NABulk Density: 1.28 (g/mL) Species/Strain: Albino Rat/Sprague-Dawley Source: Charles River Date Received: 12-4-89Dose Level: 5.0 (g/kg) Fasted Date/Time/Technician: 12-27-89/12:45 p.m./BH Room No. 102Route of Administration: Oral Gavage

Dose Volume	3.91 (mL/kg)	Sex: (Male/Female)	Dose Time: 10:10 AM	Technician	Date	Scale Used	KTron
Animal No.	C4-9191	9192	9193	9194	9190		
Prefasted Body Weight (g)	NA						
Fasted Body Weight (g)	258	285	259	272	294		
Actual Dose (mL)	1.0	1.1	1.0	1.1	1.1		
Day 7 Body Weight (g)	Dead	Dead	Dead	Dead	Dead		
Day 14 Body Weight (g)	12-24-89	12-29-89	12-29-89	12-28-89	12-27-89		
Dead Body Weight (g)	244	277	248	BH	275		

Dose Volume	3.91 (mL/kg)	Sex: Male/Female	Dose Time: 10:12 AM	Technician	Date	Scale Used	KTron
Animal No.	C4-9131	9132	9128	9129	9130		
Prefasted Body Weight (g)	NA						
Fasted Body Weight (g)	240	226	229	236	218		
Actual Dose (mL)	0.94	0.88	0.90	0.92	0.85		
Day 7 Body Weight (g)	Dead	Dead	Dead	Dead	Dead		
Day 14 Body Weight (g)	12-28-89	12-29-89	12-28-89	12-28-89	12-29-89		
Dead Body Weight (g)	219	218	219	219	204		

Entry error.
BH 12-28-89① C49194 was found
dead at P.M. check
BH 12-28-89③ Last animal found
dead at 10 AM.
BH 12-29-89

MORTALITY (NO. DIED/NO. DOSED)

Dose Level (g/kg)	Sex	Hours 0-4	Study Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
5.0	♂	18/5	3/5	1/5														5/5
5.0	♀	23/5	2/5	NA														5/5
tech.		BH	BH	BH														BH
Time		NA	7:15	10:25														NA
Date 1989		12/28	12/29	12/29														12/29

NA - Not Applicable

Reviewed By JH Date 2-22-90

000834

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HLA: 91201739

OBSERVATIONS (Individual)

Dose level: 5.0 g/kg

Test material: T-4416

Animal Number	Observations	Pre-dose	Hours			Study Day													
			1	2.5	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
C4- 9191	Male/Female																		
	Appeared Normal	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Hypoactive			✓	✓	✓													
	Diarrhea				✓	✓													
	Red stained face				✓	✓													
C4- 9192	Ataxia				✓	✓													
	Dead					①													
	Appeared Normal	✓	-	-	-	-													
	Diarrhea		✓	✓	✓	-													
	Red stained face				✓	-													
C4- 9193	Dead					✓													
	Appeared Normal	✓	-	-	-	-													
	Diarrhea		✓	✓	✓	-													
	Hypoactive			✓	✓	-													
	Red stained face			✓	✓	-													
C4- 9194	Lacrimation				✓	-													
	Dead					✓													
	Appeared Normal	✓	-	-	-	-													
	Diarrhea		✓	✓	✓	-													
	Hypoactive			✓	✓	-													
C4- 9190	Dead				*														
	Appeared Normal	✓	-	-	-	-													
	Diarrhea		✓	✓	✓	-													
	Hypoactive			✓	✓	-													
	Red stained face			✓	✓	-													
C4- 9190	Dead				✓														
	Deaths	NA	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Collected by	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Date 1989/90	12/18	12/21	12/24	12/26	12/27	12/28	12/29	12/30	12/31	1	2	3	4	5	6	7	8	9

① Found dead at 10 AM.
NA 12-29-89

- Surviving animals
submitted for terminal
necropsy.
Technician NA

Date NA

- Surviving animals
designated for sacrifice
and discard.
Technician NA

Date NA

✓ Indicates condition
exists
S1 Slight.
- Condition not evident.
* Found dead, P.M. check.
NA Not applicable
Reviewed by: JH
Date: 2-22-90

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HLA: 91201739

OBSERVATIONS (Individual)

Dose level: 5.0 g/kg

Test material: T-4416

Male/Female

Animal Number	Observations	Pre-dose	Hours			Study Day													
			1	2.5	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14
C4-9131	Appeared Normal	✓	-	-	-														
	Diarrhea		✓	✓	-														
	Hypoactive			✓	-														
	Dead				✓														
C4-9132	Appeared Normal	✓	-	-	-														
	Diarrhea		✓	✓	-														
	Hypoactive			✓	✓														
	Lacrimation			✓	✓														
	Ataxia			✓	✓														
C4-9128	Appeared Normal	✓	-	-	-														
	Diarrhea		✓	-	-														
	Hypoactive		✓	-	-														
C4-9129	Appeared Normal	✓	✓	-	-														
	Dead			✓	-														
C4-9130	Appeared Normal	✓	✓	-	-														
	Diarrhea			✓	✓														
	Hypoactive			✓	✓														
	Lacrimation			✓	✓														
	Red stained face			✓	✓														
Deaths	Collected by	NA	NA	2	1	2													
	Date 1989/90	12/28	1/28	1/28	1/28	1/28													

- Surviving animals submitted for terminal necropsy.

Technician NA

Date NA

- Surviving animals designated for sacrifice and discard.

Technician NA

Date NA

✓ Indicates condition exists

SI Slight.

- Condition not evident.

* Found dead, P.M. check.

NA Not applicable

Reviewed by: JH

Date: 2-22-90

000836