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DOCUMENT DESCRIPTION	DOCUMENT CONTROL NUMBER	DATE RECEIVED
8EHQ-94-13042	89110000172	3/14/11

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8EHQ-94-13042	88940000284	5-27-94

COMMENTS:

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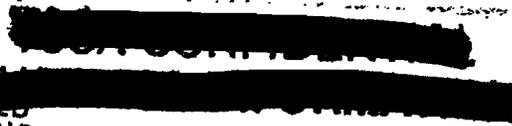
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General Offices/3M

3M Center
St. Paul, Minnesota 55144-1000
612/733 1110

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May 20, 1994

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3M

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CERTIFIED MAIL



88940000284

Document Processing Center (TS-790)
(Attn: Section 8(e) Coordinator)
Office of Toxic Substances
US EPA
401 M Street, SW
Washington, DC 20460

TSCA 8(E) SUBSTANTIAL RISK NOTICE ON: Certain Solvent Mixtures
for Paint Stripping

Dear Sir:

3M has obtained corrosivity indications for two formulations of paint stripper that are under development by our company. Neither has been marketed yet by 3M. However, one formulation is very closely related to paint strippers currently marketed by others. The second formulation is a mixture of relatively common solvents, but not known to exist as such in the marketplace.

3M conducted a skin irritation study in rabbits on a product under development composed primarily of acetone, xylene and methanol for use as an aggressive paint stripper. (See Attachment I for specific composition, Stripper I.) The test showed an unexpected corrosivity response. We feel the results may have implications for comparable paint stripping products sold by other companies that are, to our knowledge, marked as being "irritating" rather than "corrosive." We are concerned that manufacturers may have relied on the properties of the individual components and that they are unaware of the corrosive nature of the mixtures. Of particular concern are currently marketed products that are composed of acetone, toluene and methanol, or ATM-based strippers.

Corrosive results have only been seen in animal testing. We are not aware of any reports of severe irritation or corrosivity from general consumers of ATM products or from our own researchers working with 3M products under development.

3M is also developing a stripper formulation composed of relatively common solvents such as [aromatic petroleum distillate, benzyl alcohol, and methylene chloride] (See Attachment II for specific composition, Stripper II.) A set of irritation tests conducted on this research product showed similar corrosive results.

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8 9 1 1 0 0 0 0 1 7 2

[REDACTED]

(Note: The stripper that 3M does market has been tested under OECD and FHSA protocols and shown to be minimally irritating.)

Test Results for Stripper I/Acetone, Xylene, Methanol Mixture:

OECD Primary Dermal Irritation/Corrosion Study: Application to the skin of rabbits under 4-hour semioccluded conditions resulted in severe erythema and slight to moderate edema reactions. Blanching, possible necrotic areas, subcutaneous hemorrhaging, exfoliation, eschar, and possible scar tissue were also observed. Irritation continued through the Day 14 observation. These results indicate that this material should be considered corrosive. (Attachment III)

Test Results for Stripper II:

OECD Primary Dermal Irritation/Corrosion Study: Application to the skin of rabbits under 4-hour semioccluded conditions resulted in severe erythema and moderate edema reactions. Subcutaneous hemorrhaging, blanching, denuded areas, exfoliation, possible necrotic areas, and possible scar tissue were also observed. Irritation was still present at all test sites on Day 21. (Attachment IV)

DOT/UN Skin Corrosivity Study in Rabbits: Application to the skin of rabbits under 3-minute, 1-hour, and 4-hour semioccluded conditions resulted in corrosion (possible necrotic areas) observed at two sites that received a 3-minute exposure and at all six sites that received either the 1-hour or 4-hour exposure. Subcutaneous hemorrhaging and blanching were also observed. The test material is considered to be corrosive to the skin of rabbits at all three exposure periods. (Attachment V)

Acute Oral Toxicity (LD50) Study in Rats: The material was evaluated for its oral toxicity potential in male and female rats when administered in a single gavage dose at levels ranging from 1,000 to 4,827 mg/kg. Based on observed mortality, the estimated oral LD50 in rats using the Up and Down procedure was determined to be 3,583 mg/kg for males and 3,057 mg/kg for females. While we do not believe them to be significant, the following signs of potential neurotoxicity were observed: excessive salivation, hunched posture, staggered gait, hypersensitivity to touch, prostration, absence of righting reflex. However:

- No lesions were observed in these animals.
- Most of the signs of neurotoxicity disappeared after two days of observation.
- Staggered gait persisted in two animals for five days. These two animals did not die in the study.

Because we do not feel these results are conclusive we are considering whether additional studies are necessary. (Attachment VI)

3M Response

We have modified the MSDS and labels for the two development products to indicate that they are corrosive and are recommending the use of gloves to protect the user.

Please contact Georjean Adams, 3M Corporate Product Responsibility, 612-737-4795, for further information.

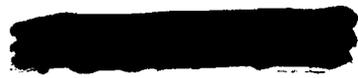
Confidentiality claims: Company identity. Specific formulation information. Substantiation attached. (Attachment VII)

Sincerely,



C. H. Dock
Vice President,
Do-It-Yourself Division

- Attachment I: Stripper I/ATM Analogue Composition
- Attachment II: Stripper II Composition
- Attachment III: Dermal Irritation Stripper I
- Attachment IV: Dermal Irritation Stripper II, OECD
- Attachment V: Skin Corrosivity Stripper II, DOT
- Attachment VI: Acute Oral Stripper II





HAZLETON
WISCONSIN
 POST OFFICE BOX 7545
 MADISON, WI 53707-7545

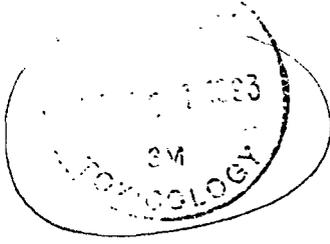
ATTACHMENT IV
 STRIPPER II

[REDACTED]

FINAL REPORT

CONTAINS NO CBI

Mr. Kurt T. Werner
 3M
 Toxicology Services
 Building 220-2E-02
 St. Paul, MN 55144-1000



HWI Number: 30801527

[REDACTED]

Study Title:

Primary Dermal Irritation/Corrosion Study
 of T-5802 (Lanford Stripper) in Rabbits
 (OECD Guidelines)

Signed:

Steven M. Glaza

Steven M. Glaza
 Study Director
 Acute Toxicology

Date

10-27-93

Sample: I-5802

KEY PERSONNEL

Acute Toxicology

Steven M. Glaza
Study Director
Manager

Steven R. Sorenson
Study Coordinator

Patricia Padgham
In-life Supervisor

Rose M. Bridge
Report Supervisor

Laboratory Animal Medicine

Cindy J. Cary, DVM
Diplomate, ACLAM
Supervisor

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Sample: T-5802

OBJECTIVE

The objective of this study was to assess the relative level of primary skin irritation/corrosion of a test material on rabbits under semiocluded conditions.¹

All procedures used in this study are in compliance with the Animal Welfare Act Regulations. In the opinion of the Sponsor and study director, the study did not unnecessarily duplicate any previous work.

TEST MATERIAL

Identification

The test material was identified as T-5802 (Lanford Stripper) and described as a viscous, 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 Hazleton Wisconsin (HWI) Standard Operating Procedure (SOP).

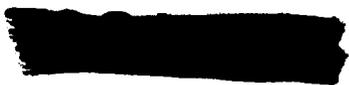
Safety Precautions

The test material handling procedures were according to HWI SOPs and policies.

TEST SYSTEM

Test Animal

Adult albino rabbits of the Hra:(NZW)SPF strain were procured from Hazleton Research Products, Inc. and maintained at the Hazleton Wisconsin facility at 3802 Packers Avenue, Madison, Wisconsin. Animal husbandry and housing at HWI comply with standards outlined in the "Guide for the Care and Use of Laboratory Animals".² The animals were individually housed in screen-bottom cages in temperature- and humidity-controlled quarters, provided access to water *ad libitum* and a measured amount of High Fiber Rabbit Chow® #5326, Purina Mills, Inc., and held for an acclimation period of at least 7 days.



Sample: J-5802

The feed is routinely analyzed by the manufacturer for nutritional components and environmental contaminants. Samples of the water are periodically analyzed by HWI. There were no known contaminants in the feed or water that would have interfered with or affected the results of the study.

One male and two female acclimated animals, weighing from 2,449 to 2,716 g, were selected and maintained during the study in the same manner as for the acclimation period. If variations from the required environmental conditions existed, they were documented and considered to have had no adverse effect on the study outcome. Animals were identified by animal number and corresponding ear tag. On the day before treatment, the back and flanks of each animal were clipped free of hair.

Justification for Species Selection

Historically, the New Zealand White albino rabbit has been the animal of choice for evaluating the effect of chemicals on the skin.

PROCEDURES

Preparation of Test Material

The test material was administered as received.

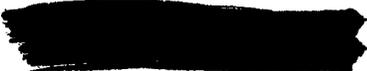
Treatment

The test material was applied to the intact skin on each animal's back (approximate exposure area of 6.25 cm²) in the amount of 0.5 mL. The area of application was covered with a 2.5-cm x 2.5-cm gauze patch secured with paper tape, loosely overwrapped with Saran Wrap®, and secured with Elastoplast® tape to provide a semiocclusive dressing. Collars were not used to restrain the test animals during the 4-hour exposure period.

At the end of the 4-hour exposure period, the patches were removed and the test sites were washed using tap water and disposable paper towels. The test material was removed from the test sites as thoroughly as possible without irritating the skin.

Reason for Route of Administration

Historically, the dermal route has been the route of choice based on the method of Draize.³



Sample: T-5802

Observations

Approximately 30 minutes after removal of the test material, the degree of erythema and edema at each test site was read according to the Draize technique (recorded as the 4-hour score). Subsequent examinations were made at 24, 48, 72, and 96 hours and Days 7, 14, and 21. The untreated skin of each animal was used for comparison.

Animals were weighed just before test material administration and at weekly intervals throughout the study.

Termination

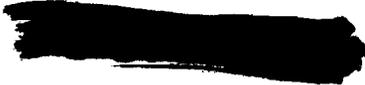
At termination of the experimental phase, all animals were designated to be euthanized and discarded.

Statistical Analyses

No statistical analyses were required by the protocol.

Location of Raw Data, Records, and Final Report

The raw data, records, and a copy of the final report will be retained in the archives of HWI in accordance with HWI SOP.



Sample: T-5802

SUMMARY OF RESULTS

Test Animal: Albino Rabbits - Hra:(NZW)SPF
 Source: Hazleton Research Products, Inc., Kalamazoo, MI
 Date Animals Received: 07/28 and 08/11/93

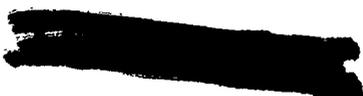
Experimental Start Date: 09/01/93 Experimental Termination Date: 09/22/93

Individual Dermal Irritation Scores

Animal Number	Sex	Erythema								
		Hour					Day			
		4	24	48	72	96	7	14	21	
F48124	M	2	3 ^{a,b}	3 ^{a,b}	3 ^{a,b}	3 ^{a,b}	4 ⁿ	2 ^c	1	
F47926	F	3 ^{a,b}	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	3 ^x	0 ^s	
F47927	F	3 ^{a,b}	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	3 ^x	0 ^s	

Animal Number	Sex	Edema								
		Hour					Day			
		4	24	48	72	96	7	14	21	
F48124	M	3	2	2	2	2	2	2	2	
F47926	F	3	2	2	2	2	2	2	1	
F47927	F	3	3	3	3	3	2	2	1	

- a Subcutaneous hemorrhaging.
- b Blanching.
- c Denuded area.
- n Possible necrotic area.
- s Possible scar tissue.
- x Exfoliation.



Sample: T-5802

Average Primary Dermal Irritation Scores*

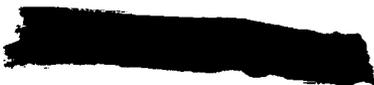
<u>Observation Period</u>	<u>Average Score</u>
1 Hour	5.7
24 Hour	6.0
48 Hour	6.0
72 Hour	6.0
96 Hour	6.0
Day 7	6.0
Day 14	4.7
Day 21	1.7

* The average primary dermal irritation score is the total dermal irritation score for all the animals (erythema and edema) divided by the number of test sites (3) at each observation period.

DISCUSSION

Application of T-5802 to the skin of rabbits under 4-hour semioccluded conditions resulted in severe erythema and moderate edema reactions. Subcutaneous hemorrhaging, blanching, denuded areas, exfoliation, possible necrotic areas, and possible scar tissue were also observed. Irritation was still present at all test sites on Day 21.

REFERENCES

1. "Acute Dermal Irritation/Corrosion," *Organisation for Economic Cooperation and Development's Guidelines for Testing of Chemicals*, Section 404 (adopted May 12, 1981).
 2. NIH Publication No. 86-23 (revised 1985).
 3. Draize, J. H., "Primary Irritation of the Skin," In: *Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics - Dermal Toxicity*, Association of Food and Drug Officials of the U.S., pp. 46-47 (1975).
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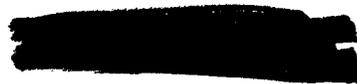
HWI Number: 30801527

Page 8

Sample: T-5802

APPENDIX

Raw Data



HWI: 30801527

PERSONNEL SIGNATURE SHEET
ACUTE TOXICOLOGY

<u>Name</u>	<u>Job Title</u>	<u>Signature</u>	<u>Initials</u>
Rose M. Bridge	Report Supervisor	<u>Rose M. Bridge</u>	RB
Anthony Cass	Lab Animal Technician	<u>Anthony Cass</u>	AC
Cindy J. Cary, DVM	Lab Animal Veterinarian	<u>Cindy J. Cary</u>	CC
Donna J. Clemons, DVM, MS	Lab Animal Veterinarian	<u>Donna Clemons</u>	DC
John A. Disch	Lab Animal Caretaker	<u>John A. Disch</u>	JD
Kari Garfoot	Lab Animal Technician	<u>Kari Garfoot</u>	KG
Steven M. Glaza	Manager	<u>Steven M. Glaza</u>	SG
Kevin Grossman	Lab Animal Caretaker	<u>Kevin Grossman</u>	KG
Ben Haley	Lab Animal Technician	<u>Ben Haley</u>	BH
Jeff Hicks	Lab Animal Technician	<u>Jeff Hicks</u>	JH
Sharen L. Howery	Research Assistant	<u>Sharen L. Howery</u>	SH
Wayne A. Madison	Supervisor	<u>Wayne A. Madison</u>	WAM
Doug McConnell	Lab Animal Technician	<u>Doug B. McConnell</u>	DM
Eileen McConnell	Staff Assistant	<u>Eileen McConnell</u>	EM
Albert Oleson	Lab Animal Caretaker	<u>Albert Oleson</u>	AO
Patricia Padgham	In-life Supervisor	<u>Patricia Padgham</u>	PP
Steven R. Sorenson	Study Coordinator	<u>Steven R. Sorenson</u>	SS
Annette R. Turner	Staff Assistant	<u>Annette R. Turner</u>	AT
Tamra L. Walker	Staff Assistant	<u>Tamra L. Walker</u>	TW
Lana M. Weeden	Staff Assistant	<u>Lana M. Weeden</u>	LW
<u>Charles W. Fritz</u>	<u>Lab Animal Technician</u>	<u>Charles W. Fritz</u>	CF
<u>Matthew Jansson</u>	<u>Lab Animal Technician</u>	<u>Matthew Jansson</u>	MJ
<u>Barbara Daniel</u>	<u>Lab Animal Technician</u>	<u>Barbara Daniel</u>	BD
<u>MARGRIT A. LUND</u>	<u>LAB TECH II</u>	<u>Margrit A. Lund</u>	ML
<u>Tammy L. Slaby</u>	<u>Lab Animal Caretaker</u>	<u>Tammy L. Slaby</u>	TS

HWI No.: 30801527

DERMAL IRRITATION/BODY WEIGHT RECORD (4-HOUR EXPOSURE)

Test Material: T-5802 Pen-Site NA Physical Description: Viscous White liquid / NA / NA
 Dose: 0.5ml with Corning pH Meter No. 05510 Moistened with 0.9% Saline; Mfg/Lot No./Exp. Date: NA / NA / NA
 pH Result: NA Skin Preparation: Intact NA Abraded (with a clipper blade)
 Species/Source Strain/Location: Rabbit/Hrs: (NZ)SPF/MT Date Animals Received: 8-1-93, 7-28-93 Initiated in Room No.: 106
 Technician/Date/Time Animals Clipped: OC / 8-31-93 / 15:35

Animal Number/Sex	8124♂	7926♀	7927♀	7928♀	7929♀	7930♀	7931♀	7932♀	7933♀	7934♀	7935♀	7936♀	7937♀	7938♀	7939♀	7940♀	7941♀	7942♀	7943♀	7944♀	7945♀	7946♀	7947♀	7948♀	7949♀	7950♀
Initial Body Weight (g)	2449	2699	2716																							
Day 7 Body Weight (g)	2549	2934	2829																							

Observations	Technician	Recorded By	Date	Scale Used	Irritation Score
4 Hour Erythema Edema	OC	OC	9-1	CS604465	✓ KN 9-4-93 S.7 ac 9-1-93
24 Hour Erythema Edema	OC	OC	9-2	CS604465	✓ KN 9-4-93 6.0 ac 9-2-93
48 Hour Erythema Edema	OC	OC	9-3		✓ KN 9-4-93 6.0 ac 9-3-93
72 Hour Erythema Edema	KN	KN	9/4		✓ ac 9-8-93 6.0 KN 9-4-93
96 Hour Erythema Edema	KN	KN	9/5		✓ ac 9-8-93 6.0 KN 9-5-93
Day 7 Erythema Edema	OC*	OC	9-8		✓ JH 9/11/93 6.0 ac 9-8-93

Storage conditions of test material: Room Temperature
 NA Not applicable. A Subcutaneous hemorrhage. U Unable to determine pH.
 B Blanching. N Possible necrotic area.
 * Animal(s) shaved prior to dermal observation by technician.
 Animals were weighed and appeared normal before test material administration on the day of dosing. Technician/Date: OC / 9-1-93
 Surviving animals designated for sacrifice and discard. Technician/Date: NA / NA
 (52/12-09-92) Final data review by/Date: JH 12-26-93

HWI No.: 30801527

**Primary Dermal Irritation Scoring Scale
(Draize Technique)**

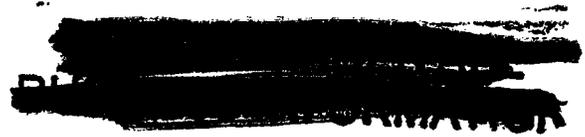
(1) Erythema and Eschar Formation

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	<u>4</u>
Highest possible erythema score	4

(2) Edema Formation

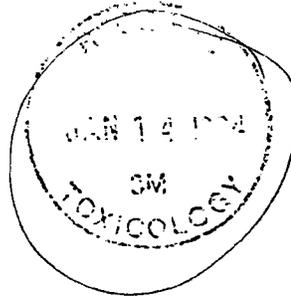
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges are well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised approximately 1 mm and extending beyond area of exposure)	<u>4</u>
Highest possible edema score	4

(S5/01-07-91)

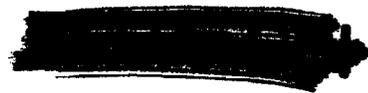


FINAL REPORT

Mr. Kurt T. Werner
3M
Toxicology Services
Building 220-2E-02
St. Paul, MN 55144-1000



HWI Number: 31002766



Study Title:

Skin Corrosivity Study of T-5802 in Rabbits
(DOT/UN Regulations)

Signed:


Steven M. Glaza
Study Director
Acute Toxicology

Date 1-12-94

Sample: J-5802

KEY PERSONNEL

Acute Toxicology

Steven M. Glaza
Study Director
Manager

Steven R. Sorenson
Study Coordinator

Patricia Padgham
In-life Supervisor

Rose M. Bridge
Report Supervisor

Laboratory Animal Medicine

Cindy J. Cary, DVM
Diplomate, ACLAM
Supervisor

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Sample: T-5802

SUMMARY

The primary dermal irritation/corrosion potential of T-5802 was evaluated when applied to the skin of rabbits under 3-minute, 1-hour, and 4-hour semioccluded conditions. Evidence of corrosion (possible necrotic areas) was observed at two sites that received a 3-minute exposure and at all six sites that received either the 1-hour or 4-hour exposure. Subcutaneous hemorrhaging and blanching were also observed. This test material is considered to be corrosive to the skin of rabbits under 3-minute, 1- and 4-hour periods of exposure and would be placed in Packing Group I.¹

OBJECTIVE

The objective of this study was to assess the relative level of primary skin irritation/corrosion of a test material on rabbits under semioccluded conditions.²

All procedures used in this study are in compliance with the Animal Welfare Act Regulations. In the opinion of the Sponsor and the study director, the study did not unnecessarily duplicate any previous work.

TEST MATERIAL

Identification

The test material was identified as T-5802 and described as a white, viscous 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 Hazleton Wisconsin (HWI) Standard Operating Procedure (SOP).

Safety Precautions

The test material handling procedures were according to HWI SOPs and policies.



Sample: T-5802

TEST SYSTEM

Test Animal

Adult albino rabbits of the Hra:(NZW)SPF strain were procured from Hazleton Research Products, Inc. and maintained at the Hazleton Wisconsin facility at 3802 Packers Avenue, Madison, Wisconsin. Animal husbandry and housing at HWI comply with standards outlined in the "Guide for the Care and Use of Laboratory Animals".³ The animals were individually housed in screen-bottom cages in temperature- and humidity-controlled quarters, provided access to water *ad libitum* and a measured amount of Laboratory Rabbit Diet HF® #5326, PMI Feeds, Inc., and held for an acclimation period of at least 7 days. The feed is routinely analyzed by the manufacturer for nutritional components and environmental contaminants. Samples of the water are periodically analyzed by HWI. There were no known contaminants in the feed or water that would have interfered with or affected the results of the study.

Two male and four female acclimated animals, weighing from 2,649 to 2,902 g, were selected and maintained during the study in the same manner as for the acclimation period. If variations from the required temperature and humidity conditions existed, they were documented and considered to have no adverse effect on the study outcome. Animals were identified by animal number and corresponding ear tag. On the day before treatment, the back and flanks of each animal were clipped free of hair.

Justification for Species Selection

Historically, the New Zealand White albino rabbit has been the animal of choice for evaluating the effect of chemicals on the skin.

PROCEDURES

Preparation of Test Material

The test material was administered as received. The pH of the test material was not able to be determined.

Treatment

The undiluted test material was applied to three separate test areas on the intact skin on each animal's back in the amount of 0.5 mL per site. Each area of application was covered with a 1-in. x 1-in. (two single layers thick) gauze patch secured with paper tape, loosely overwrapped with Saran Wrap®, and secured with Elastoplast® tape to provide a semioclusive dressing. The wrappings applied to each test site were independent of the other sites. Each



Sample: T-5802

animal was exposed to the test material for 3-minute, 1-hour, and 4-hour periods of time. Collars were not used to restrain the test animals during the exposure periods.

Reason for Route of Administration

The dermal route is specified in the DOT testing regulations.

Observations

At the end of the 3-minute, 1-hour, or 4-hour exposure periods, one patch from each animal was removed and the treated area was examined for evidence of corrosion. After the initial corrosion examination, the residual test material was removed using tap water and disposable paper towels to prevent further test material exposure. After approximately 30 minutes, the application site was examined for erythema and edema reactions according to the Draize⁴ technique (recorded as the 3-minute, 1-hour, or 4-hour score). Subsequent examinations were made at 24, 48, 72, and 96 hours. The untreated skin of each animal was used for comparison.

Animals were weighed just before test material administration.

Termination

At termination of the experimental phase, all animals were designated to be euthanized and discarded.

Statistical Analyses

No statistical analyses were required by the protocol.

Location of Raw Data, Records, and Final Report

The raw data, records, and a copy of the final report will be retained in the archives of HWI in accordance with HWI SOP.



Sample: T-5802

SUMMARY OF RESULTS

Test Animal: Albino Rabbits - Hra:(NZW)SPF
 Source: Hazleton Research Products, Inc., Kalamazoo, MI
 Date Animals Received: 11/03/93

Experimental Start Date: 12/02/93 Experimental Termination Date: 12/06/93

Individual Dermal Irritation Scores

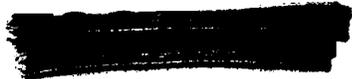
3-Minute Exposure Period

Animal Number	Sex	Erythema					Edema				
		3 Minute	Hour				3 Minute	Hour			
			24	48	72	92		24	48	72	92
F49284	F	2	3 ^a	3 ^a	3 ^a	4 ⁿ	1	2	3	3	3
F49286	M	1	2	2	2	2	1	1	1	1	1
F49287	M	1	2	2	2	2	1	1	1	1	1
F49288	F	2	2	2	2	2	1	1	1	1	1
F49289	F	1	2	2	3	3	1	1	1	2	2
F49290	F	2	3 ^a	3 ^a	3 ^a	4 ⁿ	1	1	1	2	2

1-Hour Exposure Period

Animal Number	Sex	Hour									
		Erythema					Edema				
		1	24	48	72	96	1	24	48	72	96
F49284	F	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	3	3	3	3	3
F49286	M	3 ^a	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	3	3	3	3	3
F49287	M	3 ^a	3 ^{a,b}	4 ⁿ	4 ⁿ	4 ⁿ	3	3	3	3	3
F49288	F	3 ^a	3 ^a	4 ⁿ	4 ⁿ	4 ⁿ	3	3	3	3	3
F49289	F	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	3	3	3	3	3
F49290	F	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	3	3	2	3	3

- a Subcutaneous hemorrhaging.
- b Blanching.
- n Possible necrotic area.



Sample: 7-5802

Individual Dermal Irritation Scores (Continued)

4-Hour Exposure Period

Animal Number	Sex	Hour									
		Erythema					Edema				
		4	24	48	72	96	4	24	48	72	96
F49284	F	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4	3	3	3	3
F49286	M	3 ^{a.b}	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4	4	3	3	3
F49287	M	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	3	3	3	3	3
F49288	F	3 ^{a.b}	3 ^{a.b}	4 ⁿ	4 ⁿ	4 ⁿ	3	3	3	3	3
F49289	F	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4	3	3	3	3
F49290	F	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	4	4	3	3	3

a Subcutaneous hemorrhaging.

b Blanching.

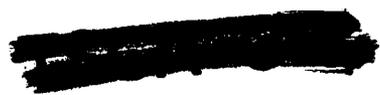
n Possible necrotic area.

Average Primary Dermal Irritation Scores*

Observation Period	Average Score		
	3-Minute Exposure	1-Hour Exposure	4-Hour Exposure
3 Minute	2.5	-	-
1 Hour	-	6.5	-
4 Hour	-	-	7.3
24 Hour	3.5	6.7	7.2
48 Hour	3.7	6.8	7.0
72 Hour	4.2	7.0	7.0
96 Hour	4.5	7.0	7.0

* The average primary dermal irritation score is the total dermal irritation score for all the animals (erythema and edema) divided by the number of test sites for each exposure period (6) at each observation period.

- Not applicable.



Sample: T-5802

DISCUSSION

The primary dermal irritation/corrosion potential of T-5802 was evaluated when applied to the skin of rabbits under 3-minute, 1-hour, and 4-hour semiocluded conditions. Evidence of corrosion (possible necrotic areas) was observed at two sites that received a 3-minute exposure and all six sites that received either the 1-hour or 4-hour exposure. Subcutaneous hemorrhaging and blanching were also observed.

CONCLUSION

Based on the results of this study, this test material, T-5802, is considered to be corrosive to the skin of rabbits under 3-minute, 1- and 4-hour periods of exposure and would be placed into Packing Group 1.

REFERENCES

1. *Code of Federal Regulations*, 49 CFR 173.137 (1992).
2. *Code of Federal Regulations*, 49 CFR 173.136 (1992).
3. NIH Publication No. 86-23 (revised 1985).
4. Draize, J. H., "Primary Irritation of the Skin," In: *Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics - Dermal Toxicity*, Association of Food and Drug Officials of the U.S., pp. 46-47 (1975).



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Sample: T-5802

APPENDIX

Raw Data



HWI: 31002766

PERSONNEL SIGNATURE SHEET
ACUTE TOXICOLOGY

<u>Name</u>	<u>Job Title</u>	<u>Signature</u>	<u>Initials</u>
Rose M. Bridge	Report Supervisor	<u>Rose M. Bridge</u>	<u>RB</u>
Anthony Cass	Lab Animal Technician	<u>Anthony Cass</u>	<u>AC</u>
Cindy J. Cary, DVM	Lab Animal Veterinarian	<u>Cindy J. Cary</u>	<u>CC</u>
Donna J. Clemons, DVM, MS	Lab Animal Veterinarian	<u>Donna Clemons</u>	<u>DC</u>
John A. Disch	Lab Animal Caretaker	<u>John A. Disch</u>	<u>JD</u>
Charles W. Fritz	Lab Animal Technician	<u>Charles W. Fritz</u>	<u>CF</u>
Kari Garfoot	Lab Animal Technician	<u>Kari Garfoot</u>	<u>KG</u>
Steven M. Glaza	Manager	<u>Steven M. Glaza</u>	<u>SG</u>
Kevin Grossman	Lab Animal Caretaker	<u>Kevin Grossman</u>	<u>KG</u>
Jeff Hicks	Lab Animal Technician	<u>Jeff Hicks</u>	<u>JH</u>
Sharen L. Howery	Research Assistant	<u>Sharen L. Howery</u>	<u>SH</u>
Wayne A. Madison	Supervisor	<u>Wayne A. Madison</u>	<u>WAM</u>
Doug McConnell	Lab Animal Technician	<u>Douglas B. McConnell</u>	<u>DM</u>
Eileen McConnell	Staff Assistant	<u>Eileen McConnell</u>	<u>EM</u>
Bud McDonald	Study Coordinator	<u>Bud McDonald</u>	<u>BM</u>
Albert Oleson	Lab Animal Caretaker	<u>Albert Oleson</u>	<u>AO</u>
Patricia Padgham	In-life Supervisor	<u>Patricia Padgham</u>	<u>PP</u>
Steven R. Sorenson	Study Coordinator	<u>Steven R. Sorenson</u>	<u>SRS</u>
Annette R. Turner	Staff Assistant	<u>Annette R. Turner</u>	<u>AT</u>
Tamra L. Walker	Staff Assistant	<u>Tamra L. Walker</u>	<u>TW</u>
Lana M. Weeden	Staff Assistant	<u>Lana M. Weeden</u>	<u>LW</u>
<u>Kathleen M. Weber</u>	<u>Lab Animal Caretaker</u>	<u>Kathleen M. Weber</u>	<u>KW</u>
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____

DERMAL IRRITATION/BODY WEIGHT RECORD

Test Material: 1-5802 Physical Description: White Viscous Liquid
 Dose: 0.5 ml Per Intact Site pH Result: 11 with Corning pH Meter No. 05510 Initiated in Room No. 103
 Species/Source Strain/Location: Rabbit/Hra: (NZU)SPF/NI Date Received: 11-3-93 Tech/Date/Time Animals Clipped: QC/12-1-93/13:55

Animal Number/Sex	F4	9284 ♀			9286 ♂			9287 ♂			9288 ♀			9289 ♀			9290 ♀			Technician	Date	Scale used:	A&D
		Site	a	b	c	Site	a	b	c	Site	a	b	c	Site	a	b	c	Site	a				
Initial Body Weight (g)		2861			2649			2877			2902			2722			2821		QC	12-2	CS604465		
Day 7 Body Weight (g)																							
Observation Period		Site			Site			Site			Site			Site			Site			Mean Scores			
		a	b	c	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c	
3 Min.	Erythema	2	NA	NA	1	NA	NA	1	NA	NA	2	NA	NA	1	NA	NA	2	NA	NA				
	Edema	1	NA	NA	1	NA	NA	1	NA	NA	1	NA	NA	1	NA	NA	1	NA	NA			2.5 NA NA	
1 Hour	Erythema	NA	4M	NA	NA	3A	NA	NA	3A	NA	NA	4M	NA	4M	NA	4M	NA	NA	QC	12-2	NA NA	NA NA	
	Edema	NA	3	NA	NA	3	NA	NA	3	NA	NA	3	NA	3	NA	3	NA	NA	QC	12-2	NA 6.5	NA NA	
4 Hour	Erythema	NA	NA	4M	NA	3AB	NA	NA	4M	NA	NA	4M	NA	4M	NA	4M	NA	4M	QC	12-2	NA NA	7.3	
	Edema	NA	4	NA	NA	4	NA	NA	4	NA	NA	4	NA	4	NA	4	NA	4	QC	12-2	NA NA	7.3	
24 Hour	Erythema	3A	4M	4M	2	4M	4M	2	3AB	4M	2	3A	4M	2	4M	3A	4M	4M	QC	12-3	3.5	6.7 7.2	
	Edema	2	3	3	1	3	3	1	3	3	1	3	3	1	3	1	3	4	QC	12-3	3.5	6.7 7.2	
48 Hour	Erythema	3A	4M	4M	2	4M	4M	2	4M	4M	2	4M	4M	2	4M	3A	4M	4M	JH	12-4	3.7	6.8 7.0	
	Edema	3	3	3	1	3	3	1	3	3	1	3	3	1	3	1	3	3	JH	12-4	3.7	6.8 7.0	

* Animal(s) shaved prior to dermal observation by technician.

NA Not applicable. N Possible necrotic area.
 A Subcutaneous hemorrhage. B Blanching.

Storage conditions of test material: Room temperature
 Temperature of test material prior to dosing: NA

Head
 a b
 c
 Tail

Animals were weighed and appeared normal before test material administration on day of dosing. Tech/Date: QC/12-2-93
 Surviving animals designated for sacrifice and discard. Tech/Date: NA/NA

(S3/04-01-91) Final data review by/Date: JH/12-7-93

DERMAL IRRITATION/BODY WEIGHT RECORD

Test Material: T-5802

Animal Number	F4	9284			9286			9287			9288			9289			9290			Technician	1993 Date	Scale used: A&D
		a	b	c	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c			
Day 14 Body Weight (g)																						
Day 21 Body Weight (g)																						
Observation Period																						
72 Hour	Erythema	3A	4N	4N	2	4N	4N	2	4N	4N	2	4N	4N	3	4N	4N	3A	4N	4N	JH	12/5	
	Edema	3	3	3	1	3	3	1	3	3	1	3	3	2	3	3	2	3	3			AC 12-6-93 JH/12-5-93
96 Hour	Erythema	4N	4N	4N	2	4N	4N	2	4N	4N	2	4N	4N	3	4N	4N	4N	4N	4N			
	Edema	3	3	3	1	3	3	1	3	3	1	3	3	2	3	3	2	3	3	AC	12-6	KS 12-7-93 AC 12-6-93
Day 7	Erythema																					
	Edema																					
Day 14	Erythema																					
	Edema																					
Day 21	Erythema																					
	Edema																					

* Animal(s) shaved prior to dermal observation by technician.

NA Not applicable. N Possible necrotic area.
A Subcutaneous hemorrhage. B Blanching.

Head
a b
c
Tail

Surviving animals designated for sacrifice and discard. Tech/Date: AC/12-16-93

(S3/04-01-91)

Final data review by/Date: 12/12-7-93



HWI No.: 31002766

SKIN CORROSIVITY RECORD
SITE A

Observation Period: 3 minute

No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F <u>NA</u>	F <u>NA</u>
F <u>↓</u>	F <u>↓</u>
F <u>↓</u>	F <u>↓</u>

Tech./Date: GC / 12-2-93

Observation Period: 24 hours

No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F <u>NA</u>	F <u>NA</u>
F <u>↓</u>	F <u>↓</u>
F <u>↓</u>	F <u>↓</u>

Tech./Date: GC / 12-3-93

Observation Period: 48 hours

No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F <u>NA</u>	F <u>NA</u>
F <u>↓</u>	F <u>↓</u>
F <u>↓</u>	F <u>↓</u>

Tech./Date: JH / 12-4-93

Observation Period: 72 hours

No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F <u>NA</u>	F <u>NA</u>
F <u>↓</u>	F <u>↓</u>
F <u>↓</u>	F <u>↓</u>

Tech./Date: JH / 12-5-93

NA Not applicable.

Final data review by/Date: IC / 12-7-93

HWI No.: 31002766

SKIN CORROSIVITY RECORD
SITE b

Observation Period: 1 hour

~~NA~~ No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F49284 F NA
F49289 F 1
F49290 F ↓

Tech./Date: ac 112-2-93

Observation Period: 24 hours

~~NA~~ No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F49284 F49290
F49286 F NA
F49289 F NA

Tech./Date: ac 112-3-93

Observation Period: 48 hours

~~NA~~ No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F4 9284 F4 9288
F4 9286 F4 9289
F4 9287 F4 9290

Tech./Date: JH 112-4-93

Observation Period: 72 hours

~~NA~~ No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F4 9284 F4 9288
F4 9286 F4 9289
F4 9287 F4 9290

Tech./Date: JH 112-5-93

NA Not applicable.

Final data review by/Date: KL 112-7-93

HWI No.: 31002766

SKIN CORROSION RECORD
SITE C

Observation Period: 4 hours

~~NA~~ No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

<u>F49284</u>	<u>F49290</u>
<u>F49287</u>	<u>F NA</u>
<u>F49289</u>	<u>F NA</u>

Tech./Date: ac 112-2-93

Observation Period: 24 hours

~~NA~~ No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

<u>F49284</u>	<u>F49289</u>
<u>F49286</u>	<u>F49290</u>
<u>F49287</u>	<u>F NA</u>

Tech./Date: ac 112-3-93

Observation Period: 48 hours

~~NA~~ No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

<u>F49284</u>	<u>F49288</u>
<u>F49286</u>	<u>F49289</u>
<u>F49287</u>	<u>F49290</u>

Tech./Date: JH 112-4-93

Observation Period: 72 hours

~~NA~~ No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

<u>F49284</u>	<u>F49288</u>
<u>F49286</u>	<u>F49289</u>
<u>F49287</u>	<u>F49290</u>

Tech./Date: JH 112-5-93

NA Not applicable.

Final data review by/Date: KJ 112-7-93

HWI No.: 31002766

SKIN CORROSION RECORD
SITE a

Observation Period: 96 hours

NA No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F <u>49284</u>	F <u>NA</u>
F <u>49290</u>	F <u>↓</u>
F <u>NA</u>	F <u>↓</u>

Tech./Date: ac / 12-6-93

Observation Period: _____

No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F _____	F _____
F _____	F _____
F _____	F _____

Tech./Date: _____ / _____

Observation Period: _____

No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F _____	F _____
F _____	F _____
F _____	F _____

Tech./Date: _____ / _____

Observation Period: _____

No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F _____	F _____
F _____	F _____
F _____	F _____

Tech./Date: _____ / _____

NA Not applicable.

Final data review by/Date: KJ / 12-7-93

HWI No.: 310027166

SKIN CORROSIVITY RECORD
SITE b

Observation Period: 96 hours

- NA No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F49284 F49288
F49286 F49289
F49287 F49290 Tech./Date: ac / 12-6-93

~~Observation Period: _____~~

- ~~No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.~~

~~F _____ F _____
F _____ F _____
F _____ F _____ Tech./Date: _____ / _____~~

~~Observation Period: _____~~

- ~~No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.~~

~~F _____ F _____
F _____ F _____
F _____ F _____ Tech./Date: _____ / _____~~

~~Observation Period: _____~~

- ~~No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.~~

~~F _____ F _____
F _____ F _____
F _____ F _____ Tech./Date: _____ / _____~~

NA Not applicable.

Final data review by/Date: KG / 12-7-93

HWI No.: 31002766

SKIN CORROSIVITY RECORD
SITE C

Observation Period: 96 hours

NA No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F49284 F49288
F49286 F49289
F49287 F49290 Tech./Date: QC / 12-6-93

Observation Period: _____

No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F _____ F _____
F _____ F _____
F _____ F _____ Tech./Date: _____ / _____

Observation Period: _____

No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F _____ F _____
F _____ F _____
F _____ F _____ Tech./Date: _____ / _____

Observation Period: _____

No signs of corrosivity were seen in any animal.
 Signs of corrosivity were seen in the following animals.

F _____ F _____
F _____ F _____
F _____ F _____ Tech./Date: _____ / _____

NA Not applicable.

Final data review by/Date: KG / 12-7-93

Attachment 1

Primary Dermal Irritation Scoring Scale
(Draize Technique)

(1) Erythema and Eschar Formation

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	<u>4</u>
Highest possible erythema score	4

(2) Edema Formation

No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges are well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised approximately 1 mm and extending beyond area of exposure)	<u>4</u>

Highest possible edema score 4

Corrosion will be considered to have resulted if the substance in contact with the rabbit skin has caused destruction or irreversible alteration of the tissue. Tissue destruction is considered to have occurred if, at any of the readings, there is ulceration or necrosis. Tissue destruction does not include merely sloughing of the epidermis, or erythema, edema, or fissuring.

Sample: T-5802

KEY PERSONNEL

Acute Toxicology

Steven M. Glaza
Study Director
Manager

Steven R. Sorenson
Study Coordinator

Patricia Padgham
In-life Supervisor

Rose M. Bridge
Report 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

Anne Mosher
Supervisor
Pathology Data

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Sample: T-5802

SUMMARY

The test material, T-5802, was evaluated for its acute oral toxicity potential in male and female rats when administered as a single gavage dose at levels ranging from 1,000 to 4,827 mg/kg. Based on the observed mortality, the estimated oral LD₅₀ in rats using the Up and Down procedure was determined to be 3,583 mg/kg for males and 3,057 mg/kg for females. Clinical signs of toxicity included red-stained face, miosis, staggered gait, hypoactivity, excessive salivation, hunched posture, hypersensitive to touch, lacrimation, yellow- or dark-stained urogenital area, tachypnea, prostration, dark-staining around the eyes, hypothermic to touch, absence of righting reflex, few feces, bradypnea, and death. All surviving animals exhibited body weight gain throughout the study and returned to a normal appearance by Day 6. The gross necropsy examinations did not reveal any definitive test material-related findings other than a strong chemical odor in the gastrointestinal tract of the animals dying during the study.

OBJECTIVE

The objective of this study was to estimate the lethality (LD₅₀ value) and acute oral toxicity induced by a test material administered by oral gavage to a small number of rats.¹

TEST MATERIAL

Identification

The test material was identified as T-5802 and described as a white, viscous 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 Hazleton Wisconsin (HWI) Standard Operating Procedure (SOP).

Safety Precautions

The test material handling procedures were according to HWI SOPs and policies.

Sample: T-5802

TEST SYSTEM

Test Animal

Young adult albino rats of the CrI:CD®(SD)BR strain were procured from Charles River Laboratories, Inc. and maintained at the Hazleton Wisconsin facility at 3802 Packers Avenue, Madison, Wisconsin. Animal husbandry and housing at HWI comply with standards outlined in the "Guide for the Care and Use of Laboratory Animals".² The animals were separated by sex, housed 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. The feed is routinely analyzed by the manufacturer for nutritional components and environmental contaminants. Samples of the water are periodically analyzed by HWI. There were no known contaminants in the feed or water that would have interfered with or affected the results of the study.

Twenty acclimated rats (approximately 8 weeks of age), weighing from 226 to 310 g, were selected and maintained during the study in the same manner as for the acclimation period with the exception that the animals were individually housed. Animals were identified by animal number and corresponding ear tag. Food and water were available *ad libitum* throughout the study, except for approximately 17 to 20 hours before test material administration when food, but not water, was withheld. The animals were returned to *ad libitum* feeding after test material administration. If variations from the required temperature and humidity conditions existed, they were documented and considered to have had no adverse effect on the study outcome.

Justification for Species Selection

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

PROCEDURES

Preparation and Administration of Test Material

The undiluted test material was administered by gavage using a bulk density determination of 0.99 to 1.00 g/mL to determine the dose volume for each dose level. An individual dose was calculated for each animal based on its fasted body weight.

Selection of Dose Levels

One male and one female animal was administered an initial dose of 1,000 mg/kg of body weight. This dose level was selected based upon the Sponsor's approximate LD₅₀ estimate. Testing utilizing the up and down procedure was then conducted. One male and/or one female rat were used for each dose level.

Sample: (F-5802)

If an animal died at a particular dose level the dose for the next animal of that sex was decreased. If an animal survived at a particular dose level, the dose for the next animal of that sex was increased. For each sex, the next dose was either increased or decreased depending upon the fate of the previous animal. After reversal of the initial outcome, i.e., a decreasing dose pattern was required to be increased by a survival, an additional four animals were treated and the procedure was then stopped.

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 and mortality checks were conducted at approximately 1, 2.5, and 4 hours after test material administration and daily thereafter for 14 days.

Body weights were determined on Day -1 (prefasted) and before test material administration (Day 0). Additional body weights were determined for animals at Day 7, at termination of the experimental phase (Day 14), or at death when survival exceeded 1 day.

Pathology

At termination of the experimental phase, all surviving animals were euthanized. All animals dying during the study or euthanized at termination 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

Calculation of the LD₅₀ value for males and females was determined using the HWI statistics library UPDOWN program.³ No other statistical analyses were required by the protocol.

Location of Raw Data, Records, and Final Report

The raw data, records, and a copy of the final report will be retained in the archives of HWI in accordance with HWI SOP.



Sample: T-5802

SUMMARY OF RESULTS

Test Animal: Albino Rats - CrI:CD®(SD)BR
 Source: Charles River Laboratories, Inc., Portage, MI
 Date Animals Received: 12/03, 12/06, 12/27/93, and 01/03/94

Experimental Start Date: 12/14/93 Experimental Termination Date: 03/16/94

Estimated Oral LD₅₀ :

Male - 3,583 mg/kg of Body Weight
 95% Confidence Limits - 2,655 to 4,837 mg/kg of Body Weight
 Female - 3,057 mg/kg of Body Weight
 95% Confidence Limits - 2,287 to 4,086 mg/kg of Body Weight

Mortality Summary - Up and Down Procedure
 (Number of Deaths)

Dose Level (mg/kg)	Hours 0 - 4	Days							Total (Number Dead/ Number Dosed)	
		1	2	3	4	5	6	7-14		
<u>Male - Up and Down Procedure</u>										
1,000	0	0	0	0	0	0	0	0	0	0/1
1,300	0	0	0	0	0	0	0	0	0	0/1
1,690	0	0	0	0	0	0	0	0	0	0/1
2,197	0	0	0	0	0	0	0	0	0	0/1
2,856	0	0	0	0	0	0	0	0	0	0/2
3,713	0	0	2	0	0	0	0	0	0	2/3
4,827	0	1	-	-	-	-	-	-	-	1/1
<u>Female - Up and Down Procedure</u>										
1,000	0	0	0	0	0	0	0	0	0	0/1
1,300	0	0	0	0	0	0	0	0	0	0/1
1,690	0	0	0	0	0	0	0	0	0	0/1
2,197	0	0	0	0	0	0	0	0	0	0/2
2,856	0	0	0	1	0	0	0	0	0	1/3
3,713	0	0	2	-	-	-	-	-	-	2/2

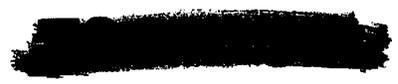
- Not applicable.



Sample: T-5802

Up and Down Dosing Sequence

<u>Animal Number</u>	<u>Dose Level (mg/kg)</u>	<u>Date Dosed</u>	<u>Results</u>
<u>Male</u>			
C25537	1,000	12/14/93	Survived to termination
C25551	1,300	12/16/93	Survived to termination
C25558	1,690	12/21/93	Survived to termination
C25579	2,197	12/23/93	Survived to termination
C25559	2,856	12/28/93	Survived to termination
C26583	3,713	01/05/94	Found dead
C26582	2,856	01/07/94	Survived to termination
C26556	3,713	01/12/94	Survived to termination
C27209	4,827	01/18/94	Found dead
C27211	3,713	01/21/94	Found dead
<u>Female</u>			
C25598	1,000	12/14/93	Survived to termination
C25629	1,300	12/16/93	Survived to termination
C25613	1,690	12/21/93	Survived to termination
C25683	2,197	12/23/93	Survived to termination
C25595	2,856	12/28/93	Survived to termination
C26600	3,713	01/05/94	Found dead
C26608	2,856	01/07/94	Found dead
C26599	2,197	01/12/94	Survived to termination
C27260	2,856	01/18/94	Survived to termination
C27256	3,713	01/21/94	Found dead



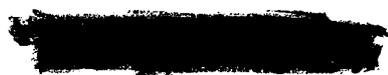
Sample: ~~T-5802~~

Individual Body Weights (g)
(By Order of Dosing)

<u>Animal Number</u>	<u>Dose Level (mg/kg)</u>	<u>Prefasted</u>	<u>Day 0</u>	<u>Day 7</u>	<u>Day 14</u>
<u>Males</u>					
C25537	1,000	249	229	302	350
C25551	1,300	288	263	341	393
C25558	1,690	299	271	348	409
C25579	2,197	280	256	308	354
C25559	2,856	310	278	332	386
C26583	3,713	280	256	(229) ²	-
C26582	2,856	296	268	347	395
C26556	3,713	296	269	321	391
C27209	4,827	296	270	(246) ¹	-
C27211	3,713	294	270	(245) ²	-
<u>Females</u>					
C25598	1,000	248	227	264	281
C25629	1,300	246	222	260	278
C25613	1,690	265	243	286	294
C25683	2,197	236	218	252	260
C25595	2,856	265	245	277	298
C26600	3,713	247	228	(209) ²	-
C26608	2,856	245	228	(209) ³	-
C26599	2,197	271	252	281	299
C27260	2,856	226	209	242	250
C27256	3,713	262	240	(218) ²	-

() Value in parentheses is the body weight at the time the animal was found dead. Superscript number indicates day of death.

- Not applicable.

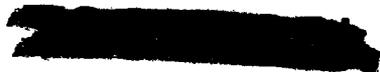


Sample: T-5802

Individual Clinical Signs

Animal Number	Observation	Hour			Day					
		1.0	2.5	4.0	1	2	3	4	5	6 through 14
<u>Male (1,000 mg/kg)</u>										
C25537	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓
<u>Female (1,000 mg/kg)</u>										
C25598	Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓
<u>Male (1,300 mg/kg)</u>										
C25551	Appeared normal	✓	-	-	✓	✓	✓	✓	✓	✓
	Red-stained face	-	✓	✓	-	-	-	-	-	-
<u>Female (1,300 mg/kg)</u>										
C25629	Appeared normal	✓	-	-	✓	✓	✓	✓	✓	✓
	Hypoactivity	-	✓	✓	-	-	-	-	-	-
<u>Male (1,690 mg/kg)</u>										
C25558	Appeared normal	✓	-	✓	✓	✓	✓	✓	✓	✓
	Miosis	-	✓	-	-	-	-	-	-	-
	Staggered gait	-	✓	-	-	-	-	-	-	-
<u>Female (1,690 mg/kg)</u>										
C25613	Appeared normal	✓	-	-	✓	✓	✓	✓	✓	✓
	Staggered gait	-	✓	✓	-	-	-	-	-	-
	Hypoactivity	-	-	✓	-	-	-	-	-	-

✓ Condition existed.
 - Condition not evident.



Sample: T-5802

Individual Clinical Signs (Continued)

Animal Number	Observation	Hour			Day					
		1.0	2.5	4.0	1	2	3	4	5	6 through 14
<u>Male (2,197 mg/kg)</u>										
C25579	Appeared normal	-	-	-	-	-	-	-	-	✓
	Miosis	✓	✓	✓	-	-	-	-	-	-
	Excessive salivation	✓	✓	-	-	-	-	-	-	-
	Hunched posture	✓	✓	✓	-	-	-	-	-	-
	Staggered gait	-	✓	✓	✓	✓	✓	✓	✓	-
	Hypoactivity	-	✓	✓	✓	✓	-	-	-	-
<u>Female (2,197 mg/kg)</u>										
C25683	Appeared normal	-	-	-	-	-	-	-	-	✓
	Hunched posture	✓	✓	✓	✓	✓	-	-	-	-
	Hypoactivity	✓	✓	✓	✓	✓	-	-	-	-
	Hypersensitivity to touch	-	✓	-	-	-	-	-	-	-
	Staggered gait	-	✓	✓	✓	✓	✓	✓	✓	-
	Lacrimation	-	-	✓	-	-	-	-	-	-
<u>Males (2,856 mg/kg)</u>										
C25559	Appeared normal	-	-	-	-	-	✓	✓	✓	✓
	Lacrimation	✓	-	-	-	-	-	-	-	-
	Miosis	✓	✓	✓	-	-	-	-	-	-
	Excessive salivation	✓	-	-	-	-	-	-	-	-
	Staggered gait	✓	✓	✓	✓	✓	-	-	-	-
	Hypoactivity	-	✓	✓	✓	-	-	-	-	-
	Hunched posture	-	-	✓	✓	-	-	-	-	-
	Red-stained face	-	-	-	✓	✓	-	-	-	-
C26582	Appeared normal	-	-	-	-	-	✓	✓	✓	✓
	Red-stained face	✓	✓	✓	✓	✓	-	-	-	-
	Staggered gait	✓	✓	✓	-	-	-	-	-	-
	Hunched posture	✓	✓	✓	-	-	-	-	-	-
C27260	Appeared normal	-	-	-	-	✓	✓	✓	✓	✓
	Staggered gait	✓	✓	✓	✓	-	-	-	-	-
	Hunched posture	-	-	✓	✓	-	-	-	-	-
	Hypoactivity	-	-	✓	✓	-	-	-	-	-
	Red-stained face	-	-	-	✓	-	-	-	-	-

✓ Condition existed.
 - Condition not evident.

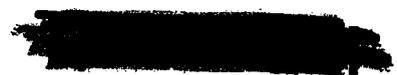


Sample: T-5802

Individual Clinical Signs (Continued)

Animal Number	Observation	Hour			Day					
		1.0	2.5	4.0	1	2	3	4	5	6 through 14
<u>Females (2.856 mg/kg)</u>										
C25595	Appeared normal	-	-	-	-	-	-	-	-	✓
	Staggered gait	✓	✓	✓	✓	✓	-	-	-	-
	Miosis	-	✓	✓	-	-	-	-	-	-
	Hypoactivity	-	-	✓	✓	-	-	-	-	-
	Red-stained face	-	-	-	✓	✓	-	-	-	-
	Yellow-stained urogenital area	-	-	-	✓	✓	✓	✓	✓	-
C26608	Staggered gait	✓	✓	✓	-	-				
	Hunched posture	-	✓	✓	-	-				
	Hypoactivity	-	✓	✓	-	-				
	Excessive salivation	-	-	✓	-	-				
	Hypothermic to touch	-	-	-	✓	✓				
	Prostration	-	-	-	✓	✓				
	Dark-stained urogenital area	-	-	-	✓	✓				
	Bradypnea	-	-	-	✓	✓				
	Found dead	-	-	-	-	-	✓			
C27260	Appeared normal	-	-	-	-	✓	✓	✓	✓	✓
	Staggered gait	✓	✓	✓	✓	-	-	-	-	-
	Hunched posture	-	-	✓	✓	-	-	-	-	-
	Hypoactivity	-	-	✓	✓	-	-	-	-	-
	Red-stained face	-	-	-	✓	-	-	-	-	-

✓ Condition existed.
 - Condition not evident.



Sample: T-5802

Individual Clinical Signs (Continued)

Animal Number	Observation	Hour			Day					
		1.0	2.5	4.0	1	2	3	4	5	6 through 14

Males (3,713 mg/kg)

C26583	Staggered gait	✓	✓	✓	-						
	Hunched posture	✓	✓	✓	-						
	Tachypnea	✓	✓	-	-						
	Hypoactivity	-	✓	✓	✓						
	Prostration	-	-	-	✓						
	Dark-staining around the eyes	-	-	-	✓						
	Lacrimation	-	-	-	✓						
	Found dead	-	-	-	-	✓					
C26556	Appeared normal	-	-	-	-	-	-	-	-	-	✓
	Excessive salivation	✓	-	-	-	-	-	-	-	-	-
	Hypoactivity	✓	✓	✓	✓	✓	✓	✓	✓	✓	-
	Staggered gait	✓	✓	✓	-	✓	-	-	-	-	-
	Red-stained face	-	-	✓	✓	✓	-	-	-	-	-
	Absence of righting reflex	-	-	-	✓	-	-	-	-	-	-
C27211	Excessive salivation	✓	-	-	-						
	Staggered gait	✓	✓	✓	-						
	Hypoactivity	✓	✓	✓	-						
	Prostration	-	-	-	✓						
	Hypothermic to touch	-	-	-	✓						
	Few feces	-	-	-	✓						
	Bradypnea	-	-	-	✓						
Found dead	-	-	-	-	✓						

✓ Condition existed.
 - Condition not evident.



Sample: T-5802

Individual Clinical Signs (Continued)

Animal Number	Observation	Hour			Day					
		1.0	2.5	4.0	1	2	3	4	5	6 through 14

Females (3.713 mg/kg)

C26600	Staggered gait	✓	✓	✓	-						
	Tachypnea	✓	-	-	-						
	Hypoactivity	-	✓	✓	✓						
	Hunched posture	-	✓	✓	-						
	Red-stained face	-	-	✓	✓						
	Prostration	-	-	-	✓						
	Found dead	-	-	-	-					✓	
C27256	Staggered gait	✓	✓	✓	-						
	Hypoactivity	-	✓	✓	-						
	Prostration	-	-	-	✓						
	Hypothermic to touch	-	-	-	✓						
	Bradypnea	-	-	-	✓						
	Few feces	-	-	-	✓						
	Found dead	-	-	-	-					✓	

Male (4.827 mg/kg)

C27209	Excessive salivation	✓	✓	-	-						
	Staggered gait	✓	✓	✓	-						
	Hunched posture	-	-	✓	-						
	Hypoactivity	-	-	✓	-						
	Found dead	-	-	-	✓						

- ✓ Condition existed.
- Condition not evident.

~~XXXXXXXXXX~~

Sample: T-5802

Individual Pathology Comments

<u>Animal Number</u>	<u>Sex</u>	<u>Test Day</u>		<u>Necropsy Observation</u>
		<u>Died</u>	<u>Sacrificed</u>	
<u>Dose Level: 1,000 mg/kg of Body Weight</u>				
C25537	M	-	14	No visible lesions.
C25598	F	-	14	No visible lesions.
<u>Dose Level: 1,300 mg/kg of Body Weight</u>				
C25551	M	-	14	No visible lesions.
C25629	F	-	14	No visible lesions.
<u>Dose Level: 1,690 mg/kg of Body Weight</u>				
C25558	M	-	14	No visible lesions.
C25613	F	-	14	No visible lesions.
<u>Dose Level: 2,197 mg/kg of Body Weight</u>				
C25579	M	-	14	No visible lesions.
C25683	F	-	14	No visible lesions.
C26599	F	-	14	No visible lesions.
<u>Dose Level: 2,856 mg/kg of Body Weight</u>				
C26582	M	-	14	No visible lesions.
C25559	M	-	14	No visible lesions.
C25595	F	-	14	No visible lesions.
C26608	F	3	-	The stomach contained a dark-red semifluid material.
C27260	F	-	14	No visible lesions.

Sample: F-5802~~XXXXXXXXXX~~

Individual Pathology Comments

<u>Animal Number</u>	<u>Sex</u>	<u>Test Day</u>		<u>Necropsy Observation</u>
		<u>Died</u>	<u>Sacrificed</u>	
<u>Dose Level: 3,713 mg/kg of Body Weight</u>				
C26556	M	-	14	No visible lesions.
C27211	M	2	-	The glandular mucosa of the stomach has multiple, dark-red areas up to 1 mm in diameter.
C26583	M	2	-	The stomach has multiple, dark-red areas on the glandular mucosa up to 4 x 3 mm. The gastrointestinal tract contents appear normal but has a strong chemical odor.
C27256	F	2	-	The stomach has multiple, dark-red areas on the glandular mucosa, up to 1 mm in diameter.
C26600	F	2	-	The stomach has multiple dark red areas on the glandular mucosa, up to 5 x 3 mm. The gastrointestinal tract contents appears normal but has a strong chemical odor.
<u>Dose Level: 4,827 mg/kg of Body Weight</u>				
C27209	M	1	-	There is a brown oral discharge. The stomach contains a yellow semifluid.

Sample: T-5802

DISCUSSION

The acute oral toxicity of T-5802 was evaluated in male and female rats when administered as a single gavage dose at levels ranging from 1,000 to 4,827 mg/kg of body weight. Based on the observed mortality, the estimated oral LD₅₀ in rats using the Up and Down procedure was determined to be 3,583 mg/kg for males and 3,057 mg/kg for females. Clinical signs of toxicity included red-stained face, miosis, staggered gait, hypoactivity, excessive salivation, hunched posture, hypersensitive to touch, lacrimation, yellow- or dark- stained urogenital area, tachypnea, prostration, dark-staining around the eyes, hypothermic to touch, absence of righting reflex, few feces, bradypnea, and death. All surviving animals exhibited body weight gain throughout the study and returned to a normal appearance by Day 6 after treatment. Page 17 contains a pathology report by the study pathologist.

Deviation from the Protocol:

The animals for the 1,690 mg/kg dose level were fasted for approximately 21 hours instead of 17 to 20 hours as stated in the protocol. This deviation is not considered to have had an adverse effect on the study outcome.

REFERENCES

1. Bruce, R. D., An Up-and-Down Procedure for Acute Toxicity Testing, *Fundam. Appl. Toxicol.* 5, 151-157, (1985).
2. NIH Publication No. 86-23 (revised 1985).
3. Thakur, A. K., "Program Updown, HP/3000 Conversion," HLA Statistics Library, Hazleton Laboratories America, Inc. (1986).

HWI Number: 31102212

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Sample: T-5802

PATHOLOGY REPORT

Variable numbers of male and female rats from dose levels of 1,000, 1,300, 1,690, 2,197, 2,856, 3,713, and 4,827 mg/kg were necropsied. Some animals given the highest doses died on test (DOT) and the remaining animals were euthanized 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 precede this report.

At necropsy, the only findings were in the DOTs and most of these pertained to the contents and coloration changes in the gastrointestinal tract. The stomach in some animals contained dark red or yellow semifluid material and the glandular mucosa in others had dark red areas of variable size. All changes were considered incidental or possibly related to postmortem change. The gastrointestinal tract in some of these DOTs appeared normal but had a strong chemical odor which possibly represented test material. There were no visible lesions in any of the animals surviving to study termination.


Thomas E. Palmer, PhD
Pathologist

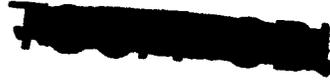
3-16-94
Date

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HWI Number: 31102212

Page 18

Sample: T-5802



APPENDIX

Raw Data

HWI: 31102212

PERSONNEL SIGNATURE SHEET
ACUTE TOXICOLOGY

<u>Name</u>	<u>Job Title</u>	<u>Signature</u>	<u>Initials</u>
Rose M. Bridge	Report Supervisor	<u>Rose M. Bridge</u>	<u>RB</u>
Anthony Cass	Lab Animal Technician	<u>Anthony Cass</u>	<u>AC</u>
Cindy J. Cary, DVM	Lab Animal Veterinarian	<u>Cindy J. Cary</u>	<u>CC</u>
Donna J. Clemons, DVM, MS	Lab Animal Veterinarian	<u>Donna Clemons</u>	<u>DC</u>
John A. Disch	Lab Animal Caretaker	<u>John A. Disch</u>	<u>JD</u>
Charles W. Fritz	Lab Animal Technician	<u>Charles W. Fritz</u>	<u>CF</u>
Kari Garfoot	Lab Animal Technician	<u>Kari Garfoot</u>	<u>KG</u>
Steven M. Glaza	Manager	<u>Steven M. Glaza</u>	<u>SG</u>
Kevin Grossman	Lab Animal Caretaker	<u>Kevin Grossman</u>	<u>KG</u>
Jeff Hicks	Lab Animal Technician	<u>Jeff Hicks</u>	<u>JH</u>
Sharen L. Howery	Research Assistant	<u>Sharen L. Howery</u>	<u>SH</u>
Wayne A. Madison	Supervisor	<u>Wayne A. Madison</u>	<u>WAM</u>
Doug McConnell	Lab Animal Technician	<u>Douglas B. McConnell</u>	<u>DM</u>
Eileen McConnell	Staff Assistant	<u>Eileen McConnell</u>	<u>EM</u>
Bud McDonald	Study Coordinator	<u>Bud McDonald</u>	<u>BM</u>
Albert Oleson	Lab Animal Caretaker	<u>Albert Oleson</u>	<u>AO</u>
Patricia Padgham	In-life Supervisor	<u>Patricia Padgham</u>	<u>PP</u>
Steven R. Sorenson	Study Coordinator	<u>Steven R. Sorenson</u>	<u>SRS</u>
Annette R. Turner	Staff Assistant	<u>Annette R. Turner</u>	<u>AT</u>
Tamra L. Walker	Staff Assistant	<u>Tamra L. Walker</u>	<u>TW</u>
Lana M. Weeden	Staff Assistant	<u>Lana M. Weeden</u>	<u>LW</u>
<u>Heather M. Weber</u>	<u>Lab Animal Caretaker</u>	<u>Heather M. Weber</u>	<u>HW</u>
_____	_____	_____	_____
_____	_____	_____	_____
_____	_____	_____	_____

~~TOP SECRET~~

HWI No.: 31102212

DOSING SEQUENCE

Study Type: Acute Oral Toxicity (Up and Down Procedure)

Test Material: T-5802

Sex: Male / Female

Dose Level (mg/kg)	Dose Level Approved	Date Dosed 1993	Animal Number	Dose Results (Tech/Date)	Terminal Results (Tech/Date)
1000	✓ SG 12-13-93	12-14	C25537	Not moribund C7121593	A C7 12-28-93
1300	✓ SG 12-15-93	12-16	5551	Not moribund C7122093	A C7 12-30-93
1690	✓ SG 12-20-93	12-21	5558	Not moribund C7122293	A C7 1-4-94
2197	✓ SG 12-22-93	12-23	5579	Not moribund C7122793	A C7 1-6-94
2856	✓ SG 12-27-93	12-28	5559	Not moribund C71494	A C7 1-11-94
3713	✓ JRS 1-4-94	1-5-94	6583	Dead C717-94	B C7 1-7-94
2856	✓ SG 1-7-94	1-7-94	6582	Not moribund C7111-94	A C7 1-21-94
3713	✓ SG 1-12-94	1-12-94	6556	Not moribund C7118-94	A C7 1-26-94
4827	✓ SG 1-18-94	1-18-94	7209	Dead 1-19-94 ②	B C7 1-19-94
3713	✓ JRS 1-21-94	1-21-94	7211	DEAD 1-23-94 1-23-94	B K7 1-23-94
STOP					

① DENTAL ERROR SG 12-15-93 ② I inadvertently did not initial and date when entry was made on 1-19-94. C7 2-11-94

A Survived to termination. Submitted for terminal necropsy.
B Died on test. Submitted for terminal necropsy.

✓ Dose level approved

(015/09-20-93)

Final data review by/Date: K7 12-11-94

HWI No.: 31102212

DOSING SEQUENCE

Study Type: Acute Oral Toxicity (Up and Down Procedure)

Test Material: T-5802

Sex: Male / Female

Dose Level (mg/kg)	Dose Level Approved	Date Dosed 1993	Animal Number	Dose Results (Tech/Date)	Terminal Results (Tech/Date)
1000	✓ SG 12-13-93	12-14	C255990	Not moribund C7 12-15-93	A C7 12-28-93
1300	✓ SG 12-15-93	12-16	5629	Not moribund C7 12-20-93	A C7 12-30-93
1690	✓ SG 12-20-93	12-21	5613	Not moribund C7 12-22-93	A C7 1-4-94
2197	✓ SG 12-22-93	12-23	5683	Not moribund C7 12-27-93	A C7 1-6-94
2856	✓ SG 12-24-93	12-28	5595	Not moribund C7 1-4-94	A C7 1-11-94
3713	✓ SG 1-4-94	1-5-94	6600	Dead C7 1-7-94	B C7 1-7-94
2856	✓ SG 1-7-94	1-7-94	6608	Dead C7 1-10-94	B C7 1-10-94
2197	✓ SG 1-12-94	1-12-94	6599	Not moribund C7 1-18-94	A C7 1-26-94
2856	✓ SG 1-18-94	1-18-94	7260	Not moribund C7 1-21-94	A C7 2-1-94
3713	✓ SG 1-21-94	1-21-94	7256	DEAD [Ⓢ] K ₁ 1-23-94 1-23-94	B K ₁ 1-23-94
STOP					

Ⓢ Animal was replaced with C25598 prior to dosing. 12-14-93

- A Survived to termination. Submitted for terminal necropsy.
- B Died on test. Submitted for terminal necropsy.

Ⓢ INITIALS NOT NEEDED. K₁ 1-23-94

✓ Dose level approved

(015/09-20-93)

Final data review by/Date: K₁ 12-11-94

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure) Route of Administration: Oral Gavage
 Test Material: 7-5802 Vehicle: NA
 Dose Level: 1000 (mg/kg) Dose Volume: 1.0 (mL/kg)
 Species/Source Strain: Rat/Crl:CD8R Date Received: 12-6-93 Initiated in Room Number: 102
 Fasted Date/Time/Tech: 12-13-93 / 16:30 / C7 Syringe used/Size: Disposable / 1 -cc
 Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. X 16 gauge

Sex: Male Dose Time/Tech: From 9:22 To 9:22 / NO

Animal Number	C2-	Dose	Volume	Time/Tech	1993 Date	Technician	Scale used	A&D
Prefasted Body Weight (g)					12-13	C7	C0221330	
Fasted Body Weight (g)					12-14	NO	C0221330	Verified by
Actual Dose (mL)					12-14	NO	SRI 12.14.93	
Day 7 Body Weight (g)					12-21	C7	C0221330	
Day 14 Body Weight (g)					12-28	C7	C0221330	

Sex: Female Dose Time/Tech: From 9:23 To 9:24 / NO

Animal Number	C2-	Dose	Volume	Time/Tech	1993 Date	Technician	Scale used	A&D
Prefasted Body Weight (g)					12-13	C7	C0221330	
Fasted Body Weight (g)					12-14	NO	C0221330	Verified by
Actual Dose (mL)					12-14	NO	SRI 12.14.93	
Day 7 Body Weight (g)					12-21	C7	C0221330	
Day 14 Body Weight (g)					12-28	C7	C0221330	

NA Not applicable. C25599 had soft stool at the time of weighing (Fasted body weight).
 This animal was returned to stock and replaced with C25598 which had originally been fasted for another study. The prefasted body weight was transcribed from the data sheet J. Dose Administration.
 Body Weight Record for 31001658 Final data review by/Date: JH / 12-31-82

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure) Route of Administration: Oral Gavage
 Test Material: E5797 Vehicle: distilled water
 Dose Level: 3140 (mg/kg) Dose Volume: NA (mL/kg) Initiated In Room Number: 102
 Species/Source Strain: Rat/Crl:CD[®]BR Date Received: 12-6-93 Syringe used/Size: Disposable NA -cc
 Fasted Date/Time/Tech: 12-13-93 / 6:30 / C7 Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. X NA gauge

Sex: Male Dose Time/Tech: From NA To NA / NA 1993

Animal Number	C2-	Dose Time/Tech: From NA To NA / NA	1993	Technician	Date	Scale used: A&D
Prefasted Body Weight (g)	5539	/	/	C7	12-13	C0221330
Fasted Body Weight (g)	253	Animal not used and returned to stock.	/	/	/	Verified by
Actual Dose (mL)						
Day 7 Body Weight (g)		ND	/	/	/	
Day 14 Body Weight (g)		12-14-93	/	/	/	

Sex: Female Dose Time/Tech: From NA To NA / NA 1993

Animal Number	C2-	Dose Time/Tech: From NA To NA / NA	1993	Technician	Date	Scale used: A&D
Prefasted Body Weight (g)	5598 ^⓪	/	/	C7	12-13	C0221330
Fasted Body Weight (g)	248	/	/	/	/	Verified by
Actual Dose (mL)						
Day 7 Body Weight (g)		/	/	/	/	
Day 14 Body Weight (g)		/	/	/	/	

NA Not applicable. ⓪ C25598 was used on study 31102212. Fasted body weight was transcribe error recording error NA 12.14.93

Final data review by/Date: JH 1 12-31-93



HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 1000 (mg/kg)

Animal Number/Sex: C2 5537 1♂		Hours			Study Day														
Observations	Pre-dose	1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
/																			
Time	NA	10:22	11:50	13:22	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Technician	NP	NP	NP	K	C7	C7	C7	JH	JH	C7	C7	C7	C7	K	K	K	C7	C7	
Date 1993	12/14	12/14	12/14	12/14	12/14	12/15	12/16	12/17	12/18	12/19	12/20	12/21	12/22	12/23	12/24	12/25	12/26	12/27	12/28

① Illegible entry. C712-20-93

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: JH 1 12/31/93

(08/09-20-93)



HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 1000 (mg/kg)

Animal Number/Sex: C2 5598 1♀																			
Observations	Pre-dose	Hours			Study Day														
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Appeared normal	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
/																			
Time	NA	10:22	12:51	13:22	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Technician	NP	NP	NP	K	C7	C7	C7	JH	JH	C7	C7	C7	C7	KL	KL	KL	C7	C7	
Date 1993	12/14	12/14	12/14	12/14	12/15	12/16	12/17	12/18	12/19	12/20	12/21	12/22	12/23	12/24	12/25	12/26	12/27	12/28	

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: JH 1 12-31-93

(08/09-20-93)

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure) Route of Administration: Oral Gavage
 Test Material: 7-5802 Vehicle: NA
 Dose Level: 1300 (mg/kg) Dose Volume: 1.31 (mL/kg)
 Species/Source Strain: Rat/Crl:CD08R Date Received: 12-6-93 Initiated in Room Number: 102
 Fasted Date/Time/Tech: 12-5-93 / 16:20 / C7 Syringe used/Size: Disposable / 1 -cc
 Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. X 16 gauge

Sex: Male Dose Time/Tech: From 11:21 To 11:22 / C7

Animal Number	C2-	Dose Time/Tech	From	To	1993	Date	Technician	Scale used: A&D
Prefasted Body Weight (g)		5551	05548			12-75	C7	C0221330
Fasted Body Weight (g)		288	270			12-16	C7	C0221330
Actual Dose (mL)		263				12-16	C7	Verified by NO 12-16-93
Day 7 Body Weight (g)		0.34				12-23	C7	C0221330
Day 14 Body Weight (g)		341				12-30	C7	C0221330

Sex: Female Dose Time/Tech: From 11:22 To 11:23 / C7

Animal Number	C2-	Dose Time/Tech	From	To	1993	Date	Technician	Scale used: A&D
Prefasted Body Weight (g)		5629	05622			12-15	C7	C0221330
Fasted Body Weight (g)		246	242			12-16	C7	C0221330
Actual Dose (mL)		222				12-16	C7	Verified by NO 12-16-93
Day 7 Body Weight (g)		0.29				12-23	C7	C0221330
Day 14 Body Weight (g)		260				12-30	C7	C0221330

NA Not applicable. Unused animals returned to stock. C7 12-16-93

Final data review by/Date: TH 12-31-93

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HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 1300 (mg/kg)

Animal Number/Sex: C2 5551 1♂		Hours			Study Day														
Observations	Pre-dose	1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Appeared normal	✓	✓	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Red stained face			✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
/																			
Time	NA	12:20	13:51	15:21	3 AM	NA													
Technician	C7	C7	C7	C7	JH	JH	JH	C7	C7	C7	C7	LS	LS	LS	C7	C7	C7	C7	
Date 1993	12/16	12/16	12/16	12/16	12/17	12/18	12/19	12/20	12/21	12/22	12/23	12/24	12/25	12/26	12/27	12/28	12/29	12/30	

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

① ENTRIES MADE IN HRWG COLUMN.
 JH 12-18-93
 ② Inadvertently not signed for on 12-17-93.
 Late entries made on 12-20-93. C7 12-20-93

(08/09-20-93)

Final data review by/Date: JH 1 12-31-93

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HWI No.: 31102212

OBSERVATIONS

Test material: X-5802

Dose level: 1300 (mg/kg)

Animal Number/Sex: C2 5629 1♀		Hours			Study Day														
Observations	Pre-dose	1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Appeared normal	✓	✓	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
<i>Hyporeactive</i>			✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
/																			
Time	NA	12:21	13:52	15:22	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Technician	C7	C7	C7	C7	C7	JH	JH	C7	C7	C7	C7	K7	K7	K7	C7	C7	C7	C7	
Date 1993	12/16	12/16	12/16	12/16	12/17	12/18	12/19	12/20	12/21	12/22	12/23	12/24	12/25	12/26	12/27	12/28	12/29	12/30	

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: JH 1 12/31/93

(08/09-20-93)

HWI No.: 31102212

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure) Route of Administration: Oral Gavage
 Test Material: (1-5802) Vehicle: NA
 Dose Level: 1690 (mg/kg) Dose Volume: 1.71 (mL/kg) Initiated in Room Number: 102
 Species/Source Strain: Rat/Crl:CDPBR Date Received: 12-6-93
 Fasted Date/Time/Tech: 12-20-93 / 16:00 / CF Syringe used/Size: Disposable / 1 -cc
 Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. x 16 gauge

Sex: Male Dose Time/Tech: From 13:24 To 13:25 / CF

Animal Number	C2-	Dose	Time/Tech	1993 Date	Technician	Scale used: A&D
		5558	288	12-20	CF	C0221330
		299	271	12-21	CF	C0221330
		0.46	348	12-21	CF	Verified by JH 12-21-93
		409		12-28	CF	C0221330
				1-4	CF	C0221330

Sex: Female Dose Time/Tech: From 13:25 To 13:26 / CF

Animal Number	C2-	Dose	Time/Tech	1993 Date	Technician	Scale used: A&D
		5613	254	12-20	CF	C0221330
		265	243	12-21	CF	C0221330
		0.42	286	12-21	CF	Verified by JH 12-21-93
		294		12-28	CF	C0221330
				1-4	CF	C0221330

NA Not applicable. ① Illegible entry, C712-21-93
 ② Unused animals returned to stock, C712-21-93

Final data review by/Date: KJ 11-8-94

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HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 1690 (mg/kg)

Animal Number/Sex: C2 5558 1♂																		
Observations	Pre-dose	Hours			Study Day													
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Appeared normal	✓	✓	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Miosis			✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Staggered gait			✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Time	NA	14:24	15:54	17:24	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Technician	C7	C7	C7	C7	C7	C7	K6	K6	K6	C7	C7	C7	C7	JH	JH	JH	C7	C7
Date	1993/94	12/21	12/21	12/21	12/21	12/22	12/23	12/24	12/25	12/26	12/27	12/28	12/29	12/30	1/1	1/2	1/3	1/4

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: K2 11-8-94

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HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 1690 (mg/kg)

Animal Number/Sex: C2 5613 1♀																				
Observations	Pre-dose	Hours			Study Day															
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14		
Appeared normal	✓	✓	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Staggered gait			✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Hypoactive				✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Time	NA	14:25	15:55	17:25	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Technician	C7	C7	C7	C7	C7	C7	K	K	K	C7	C7	C7	C7	TH	TH	TH	C7	C7	C7	
Date	1993/99	12/21	12/21	12/21	12/21	12/22	12/23	12/24	12/25	12/26	12/27	12/28	12/29	12/30	1/1	1/2	1/3	1/4	1/4	1/4

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

(08/09-20-93)

Final data review by/Date: K5/1-8-94

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure) Route of Administration: Oral Gavage
 Test Material: 21915802 Vehicle: NA
 Dose Level: 2191 (mg/kg) Dose Volume: 2.22 (mL/kg)
 Species/Source Strain: Rat/Crl:CD®BR Date Received: 12-6-93 12-3-93 Initiated in Room Number: 102
 Fasted Date/Time/Tech: 12-22-93 / 16:30 / CF Syringe used/Size: Disposable / 1 -cc
 Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. x 1/6 gauge

Sex: Male Dose Time/Tech: From 10:44 To 10:45 / CF

Animal Number	C2-	Dose Time/Tech	From	To	1993 Date	Technician	Scale used: A&D
Prefasted Body Weight (g)	280	5579	05559		12-22	CF	C0221330
Fasted Body Weight (g)	256				12-23	CF	C0221330 Verified by M 12-23-93
Actual Dose (mL)	0.57				12-23	CF	
Day 7 Body Weight (g)	308				12-30	CF	C0221330
Day 14 Body Weight (g)	354				1-6-94	CF	C0221330

Sex: Female Dose Time/Tech: From 10:47 To 10:48 / CF

Animal Number	C2-	Dose Time/Tech	From	To	1993 Date	Technician	Scale used: A&D
Prefasted Body Weight (g)	236	5683	05628		12-22	CF	C0221330
Fasted Body Weight (g)	218				12-23	CF	C0221330 Verified by M 12-23-93
Actual Dose (mL)	0.48				12-23	CF	
Day 7 Body Weight (g)	252				12-30	CF	C0221330
Day 14 Body Weight (g)	260				1-6-94	CF	C0221330

NA Not applicable. Unused animals returned to stock. CF 12-23-93

Final data review by/Date: KG 11-8-94

HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 2197 (mg/kg)

Animal Number/Sex: C2 5579 1♂																		
Observations	Pre-dose	Hours			Study Day													
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Appeared normal	✓	-	-	-	-	-	-	-	-	-	✓	✓	✓	✓	✓	✓	✓	✓
Miosis	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Excessive Salivation	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hunched posture	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Staggered gait	✓	✓	✓	✓	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-
Hypoactive	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Time	NA	11:45	13:15	14:45	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Technician	C7	C7	C7	C7	K6	K6	K6	C7	C7	C7	C7	JH	JH	JH	C7	C7	C7	C7
Date	1993/4/23	12/23	12/23	12/23	12/24	12/25	12/26	12/27	12/28	12/29	12/30	1/1	1/2	1/3	1/4	1/5	1/6	

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: K6 11-8-94

HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 2197 (mg/kg)

Animal Number/Sex: C2 <u>5683</u> <u>1♀</u>		Hours			Study Day													
Observations	Pre-dose	1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Appeared normal	✓	-	-	-	-	-	-	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓
Hunched posture	✓	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-
Hypnactive	✓	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-
Hypersensitive to touch	✓	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-
Staggered gait	✓	✓	✓	✓	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-
Lacrimation	✓	✓	✓	✓	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-
Time	NA	11:46	13:16	14:46	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Technician	C7	C7	C7	C7	K5	K5	K5	C7	C7	C7	C7	JH	JH	JH	C7	C7	C7	C7
Date	1993/94	12/23	12/23	12/23	12/24	12/25	12/26	12/27	12/28	12/29	12/30	12/31	1/1	1/2	1/3	1/4	1/5	1/6

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: K5 / 1-8-94

(08/09-20-93)

HMI No.: 3102222

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure) Vehicle: NA Route of Administration: Oral Gavage
 Test Material: 2197 (T-5802) Dose Volume: 2.20 (mL/kg) Initiated in Room Number: 102
 Dose Level: 2197 (mg/kg) Date Received: 12-27-93 Disposable / / -cc
 Species/Source Strain: Rat/Cr1:CD98R Syringe used/Size: 3 in. x 1/6 gauge
 Fasted Date/Time/Tech: 1-11-94 / 5:00 / C7
 Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. x 1/6 gauge

Sex: Male Dose Time/Tech: From _____ To _____

Animal Number	C2-	Technician	Date	Scale used: A&D
Prefasted Body Weight (g)				
Fasted Body Weight (g)				Verified by
Actual Dose (mL)				
Day 7 Body Weight (g)				
Day 14 Body Weight (g)				

Sex: Female Dose Time/Tech: From 8:33 To 8:33 / C7 1994

Animal Number	C2-	Technician	Date	Scale used: A&D
Prefasted Body Weight (g)	<u>6599</u>	<u>C7</u>	<u>1-11</u>	<u>C022/330</u>
Fasted Body Weight (g)	<u>271</u>	<u>C7</u>	<u>1-12</u>	<u>C022/330</u>
Actual Dose (mL)	<u>252</u>	<u>C7</u>	<u>1-12</u>	Verified by <u>NP 1-12-94</u>
Day 7 Body Weight (g)	<u>0.55</u>	<u>C7</u>	<u>1-19</u>	<u>C022/330</u>
Day 14 Body Weight (g)	<u>281</u>	<u>C7</u>	<u>1-26</u>	<u>C022/330</u>

NA Not applicable. Unused animal returned to stock on 1-12-94, inadvertently not documented until 1-14-94. C7 1-14-94

Final data review by/Date: Ka 12-11-94

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HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 2197 (mg/kg)

Animal Number/Sex: C2 6599 1♀																			
Observations	Pre-dose	Hours			Study Day														
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Appeared normal	✓	✓	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Staggered gait			✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Time	NA	9:32	11:02	12:31	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Technician	C7	C7	C7	C7	C7	C7	JH	JH	K5	C7	C7	C7	C7	K5	K5	C7	C7	C7	
Date	1994	1/12	1/12	1/12	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

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: JH 1 130-94

(08/09-20-93)

HMI No.: 31102212

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure) Route of Administration: Oral Gavage
 Test Material: 5-5802 Vehicle: NA
 Dose Level: 2.856 (mg/kg) Dose Volume: 2.87 (mL/kg)
 Species/Source Strain: Rat/Cri:COBR Date Received: 12-6-93
 Fasted Date/Time/Tech: 12-27-93 / 15:45 / C7 Syringe used/Size: Disposable / 1 -cc
 Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. X 1/6 gauge

Sex: Male Dose Time/Tech: From 9:51 To 9:51 / C7

Animal Number	C2-	Dose Time/Tech	From	To	Tech	1993 Date	Scale used	A&D
Prefasted Body Weight (g)	5559				C7	12-27	C0221330	
Fasted Body Weight (g)	310				C7	12-28	C0221330	Verified by
Actual Dose (mL)	0.80				C7	12-28	NO	12-28-93
Day 7 Body Weight (g)	332				C7	1-4-94	C0221330	
Day 14 Body Weight (g)	386				C7	1-11-94	C0221330	

Sex: Female Dose Time/Tech: From 9:53 To 9:54 / C7

Animal Number	C2-	Dose Time/Tech	From	To	Tech	1993 Date	Scale used	A&D
Prefasted Body Weight (g)	5595				C7	12-27	C0221330	
Fasted Body Weight (g)	265				C7	12-28	C0221330	Verified by
Actual Dose (mL)	0.71				C7	12-28	NO	12-28-93
Day 7 Body Weight (g)	277				C7	1-4-94	C0221330	
Day 14 Body Weight (g)	298				C7	1-11-94	C0221330	

NA Not applicable. Unused animal returned to stock on 12-28-93, Inadvertently not documented until 12-30-93, C7 12-30-93

Final data review by/Date: JH / 1-15-94

(09/09-20-93)

HWI No.: 31102212

OBSERVATIONS

Test material: F-5802

Dose level: 2856 (mg/kg)

Animal Number/Sex: C2 5559 1♂																			
Observations	Pre-dose	Hours			Study Day														
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Appeared normal	✓	-	-	-	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Lacrimation	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Miosis	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Excessive Salivation	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Staggered gait	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hypnactive		✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hunched posture			✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Red stained face				✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Time	NA	10:53	12:53	13:53	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Technician	C7	C7	C7	C7	C7	JH	JH	JH	C7	C7	C7	C7	C7	C7	K9	K9	C7	C7	
Date	1993/94	12/28	12/28	12/28	12/28	12/29	12/30	1/1	1/1	1/3	1/4	1/5	1/6	1/7	1/8	1/9	1/10	1/11	

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: JH 11-15-94

(08/09-20-93)



HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 2856 (mg/kg)

Animal Number/Sex: C2 5595 1♀																			
Observations	Pre-dose	Hours			Study Day														
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Appeared normal	✓	-	-	-	-	-	-	-	-	-	✓	✓	✓	✓	✓	✓	✓	✓	
Staggered gait	✓	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	
Miosis	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Hypoactive	✓	-	-	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	
Red stained face	✓	-	-	-	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	
Yellow stained urogenital area	✓	-	-	-	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	
Time	NA	10:54	12:24	13:54	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
Technician	C7	C7	C7	C7	C7	C7	JH	JH	JH	C7	C7	C7	C7	C7	C7	K5	K5	C7	C7
Date	1993/94	12/28	12/28	12/28	12/28	12/29	12/30	1/1	1/1	1/3	1/4	1/5	1/6	1/7	1/10	1/9	1/10	1/11	

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: JH 1 1-15-94

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure) Route of Administration: Oral Gavage
 Test Material: U-5802 Vehicle: NA
 Dose Level: 2856 (mg/kg) Dose Volume: 2.89 (mL/kg)
 Species/Source Strain: Rat/Crl:CD08R Date Received: 12-27-93 Initiated in Room Number: 102
 Fasted Date/Time/Tech: 1-6-94 / 16:45 / C7 Syringe used/Size: Disposable / 1 -cc
 Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. X 1/6 gauge

Sex: Male Dose Time/Tech: From 11:42 To 11:43 / C7

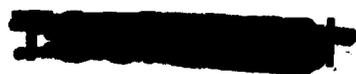
Animal Number	C2-	Dose	Volume	Weight (g)	Technician	Date	Scale used: A&D
		6582	0.6584	294	C7	1-6	C0221330
		296			C7	1-7	C0221330
		268			C7	1-7	Verified by SL 1-7-94
		0.77			C7	1-14	C5604465
		347			C7	1-21	C0221330
		395			C7		

Sex: Female Dose Time/Tech: From 11:44 To 11:44 / C7

Animal Number	C2-	Dose	Volume	Weight (g)	Technician	Date	Scale used: A&D
		6608	0.6610	244	C7	1-6	C0221330
		245			C7	1-7	C0221330
		228			C7	1-7	Verified by SL 1-7-94
		0.66			C7	1-10	C0221330
		209			C7		

NA Not applicable. Unused animals returned to stock. C7 1-7-94
Form change. C7 1-10-94

Final data review by/Date: JH 1/30/94



HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 2856 (mg/kg)

Animal Number/Sex: C2 6582 1 ♂																			
Observations	Pre-dose	Hours			Study Day														
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Appeared normal	✓	-	-	-	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Red stained face		✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-
Staggered gait		✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hunched posture		✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
INAPPROPRIATE TOUCHING INAPPROPRIATE ①					⊗	⊗													
PROSTRATED ②					⊗	⊗													
FACE STAINED UROGENITAL AREA ③					⊗	⊗													
Time	NA	12:45	14:13	15:43	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Technician	C7	C7	C7	C7	K	K	C7	C7	C7	C7	C7	JH	JH	KG	C7	C7	C7	C7	C7
Date 1994	7/7	7/7	7/7	7/7	7/10	7/11	7/10	7/11	7/12	7/13	7/14	7/15	7/16	7/17	7/18	7/19	7/20	7/21	7/21

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

① WRONG WORD USED. KN 1-8-94
 ② INADVERTENTLY RECORDED FOR WRONG ANIMAL NUMBER. THE ONLY OBSERVATION NOTED FOR C26582 IS RED STAINED FACE. KN 1-8-94

(08/09-20-93)

Final data review by/Date: JH 1 130-94

HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 2856 (mg/kg)

Animal Number/Sex: C2 6608 1♀		Study Day																	
Observations	Pre-dose	Hours																	
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Appeared normal	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Staggered gait	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hunched posture	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hypoactive	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Excessive Salivation	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HYPOTHERMIC TO TOUCH	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PROSTRATE	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
DARK STAINED UROGENITAL AREA	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
BRADYPNEA	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dead	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Time	NA	12:49	14:14	15:45	NA	NA	NA	16:58											
Technician	C7	C7	C7	C7	K	L	C7												
Date 1994	1/7	1/7	1/7	1/7	1/8	1/9	1/10												

Entered wrong time - C71-7-94

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: JH 1 1-15-94

HWI No.: 31102212

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure)

Route of Administration: Oral Gavage

Vehicle: NA

Test Material: ~~F-5802~~ (mg/kg) Dose Volume: 2.86 (mL/kg)

Species/Source Strain: Rat/Cr1:CD8BR Date Received: 1-3-94

Fasted Date/Time/Tech: 1-17-94 / 15:10 / KJ Syringe used/Size: Disposable / 1 -cc

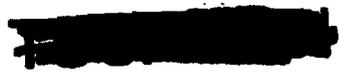
Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. x 1/6 gauge

Sex:	Male	Dose Time/Tech:	From	To	Technician	Date	Scale used:	A&D
Animal Number		C2-						
Prefasted Body Weight (g)								
Fasted Body Weight (g)								Verified by
Actual Dose (mL)								
Day 7 Body Weight (g)								
Day 14 Body Weight (g)								

Sex:	Female	Dose Time/Tech:	From	To	Technician	Date	Scale used:	A&D
Animal Number		C2-	72600	07257		1/17		C0221330
Prefasted Body Weight (g)			2250	243	KJ	1/17		C0221330
Fasted Body Weight (g)			209		C7	1/18		Verified by
Actual Dose (mL)			0.60		C7	1/18		JH 1-18-94
Day 7 Body Weight (g)			242		C7	1/25		C0221330
Day 14 Body Weight (g)			250		C7	2/1		C0221330

NA Not applicable. ^⓪ Unused animal returned to stock. C71-78-94

Final data review by/Date: KJ 12-11-94



HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 2856 (mg/kg)

Animal Number/Sex: C2 7260 1♀																		
Observations	Pre-dose	Hours			Study Day													
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Appeared normal	✓	-	-	-	-	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Staggered gait	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-
Hunched posture				✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-
Hypoactive				✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-
Red Stained face				✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-
Time	NA	11:03	12:34	14:04	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Technician	C7	C7	C7	C7	C7	C7	C7	KG	KG	C7	C7	C7	C7	C7	JH	JH	C7	C7
Date 1994	1/18	1/18	1/18	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

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: KG 12-11-94

HMI No.: 3102212

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure)
 Test Material: X-5802 Vehicle: NA Route of Administration: Oral Gavage
 Dose Level: 373 (mg/kg) Dose Volume: 3.71 (mL/kg)
 Species/Source Strain: Rat/Crl:CD¹B¹R Date Received: 12-27-93 Initiated in Room Number: 102
 Fasted Date/Time/Tech: 1-4-94 / C7 Syringe used/Size: Disposable / 1 -cc
 Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. x 16 gauge

Sex: Male Dose Time/Tech: From 10:22 To 10:23 / C7

Animal Number	C2-	Dose	Time/Tech	From	To	1994 Date	Technician	Scale used: A&D
		6583		06586		1-4	C7	C0221330
		280		279		1-5	C7	C0221330
		256				1-5	C7	Verified by SS 1-5-94
		095				1-7	C7	C0221330
Day 7		229						
Day 14								

Sex: Female Dose Time/Tech: From 10:24 To 10:25 / C7

Animal Number	C2-	Dose	Time/Tech	From	To	1994 Date	Technician	Scale used: A&D
		6600		06598		1-4	C7	C0221330
		247		240		1-5	C7	C0221330
		228				1-5	C7	Verified by SS 1-5-94
		0.85				1-7	C7	C0221330
Day 7		209						
Day 14								

NA Not applicable. ① Unused animals returned to stock. C71-5-94
 ② Form changes. C71-7-94

Final data review by/Date: C71-8-94

HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 3713 (mg/kg)

Animal Number/Sex: C2 6583 1♂		Study Day																	
Observations	Pre-dose	Hours																	
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Appeared normal	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Staggered gait		✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hunched posture		✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tachypnea		✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hypoactive			✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Prostrate					✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dark staining around eyes					✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Lacrimation					✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dead (7:13†)							✓	-	-	-	-	-	-	-	-	-	-	-	-
Time	NA	11:22	12:51	14:24	NA	NA													
Technician	C7	C7	C7	C7	C7	C7													
Date ①-1993-1994	Y5	Y5	Y5	Y5	Y6	Y7													

① Form change. C7 1-4-94

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

† Animal found dead at AM check, time is approximate. Inadvertently not documented until 1-10-94. C7 1-10-94

Final data review by/Date: JH 1 1-15-94

HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 3713 (mg/kg)

Animal Number/Sex: C2 6600 1♀		Study Day																	
Observations	Pre-dose	Hours																	
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Appeared normal	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Staggered gait		✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tachypnea		✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hypoactive			✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hunched posture			✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Red stained face				✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Prostrate					✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dead (7:13 ^{PM})						✓	-	-	-	-	-	-	-	-	-	-	-	-	-
Time	NA	11:23	11:55	12:25	NA	NA													
Technician	C7	C7	C7	C7	C7	C7													
Date	0-1993-1994	1/5	1/5	1/5	1/5	1/6	1/7												

① Form change. C71-4-94 ② Wrong footnote number. C71-5-94 wrong year C71-5-94
 NA Not applicable. ③ Wrong time. C71-5-94 Correct time is 12:55. C71-5-94
 ✓ Indicates condition exists.
 - Not evident.
 * Found dead, P.M. check.
 † Animal found dead at AM check, time is approximate. Inadvertently not documented until 1-10-94. C71-10-94

Final data review by/Date: JH 1 1-15-94

HWI No.: 31022212

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure) Route of Administration: Oral Gavage
 Test Material: (S-5802) Vehicle: NA
 Dose Level: 373 (mg/kg) Dose Volume: 3.71 (mL/kg)
 Species/Source Strain: Rat/Crl:CD₀₁B Date Received: 12-27-93 Initiated in Room Number: 102
 Fasted Date/Time/Tech: 1-11-94 / 15:00 / C7 Syringe used/Size: Disposable / 1 -cc
 Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. x 16 gauge

Sex: Male Dose Time/Tech: From 8:32 To 8:32 / C7

Animal Number	C2-	6556	6558	Technician	Date	Scale used: A&D
Prefasted Body Weight (g)		276	288	C7	1-11	C0221330
Fasted Body Weight (g)		269		C7	1-12	C0221330 Verified by
Actual Dose (mL)		1.0		C7	1-12	NP 1-12-94
Day 7 Body Weight (g)		321		C7	1-19	C0221330
Day 14 Body Weight (g)		391		C7	1-26	C0221330

Sex: Female Dose Time/Tech: From / To

Animal Number	C2-			Technician	Date	Scale used: A&D
Prefasted Body Weight (g)						
Fasted Body Weight (g)						
Actual Dose (mL)						Verified by
Day 7 Body Weight (g)						
Day 14 Body Weight (g)						

NA Not applicable. Unused animal returned to stock on 1-12-94, inadvertently not documented until 1-14-94. C71-14-94

Final data review by/Date: JH / 1-30-94

~~XXXXXXXXXX~~

HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 3713 (mg/kg)

Animal Number/Sex: C2 6556 1♂																		
Observations	Pre-dose	Hours			Study Day													
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Appeared normal	✓	-	-	-	-	-	-	-	-	-	✓	✓	✓	✓	✓	✓	✓	✓
Excessive salivation		✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hypoactive		✓	✓	✓	✓	✓	✓	✓	✓	-	-	-	-	-	-	-	-	-
Staggered gait		✓	✓	✓	-	✓	-	-	-	-	-	-	-	-	-	-	-	-
Red stained face				✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-
Righting reflex absent					✓	*	-	-	-	-	-	-	-	-	-	-	-	-
Time	NA	9:31	11:01	12:30	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Technician	C7	C7	C7	C7	C7	C7	JH	JH	LS	C7	C7	C7	C7	LS	LS	C7	C7	C7
Date 1994	1/12	1/12	1/12	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 Stray mark. C71-14-94

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: JH 1 1-30-94

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure) Route of Administration: Oral Gavage
 Test Material: X-5802 Vehicle: NA
 Dose Level: 3713 (mg/kg) Dose Volume: 3.71 (mL/kg) Initiated in Room Number: 102
 Species/Source Strain: Rat/Crl:CD[®]BR Date Received: 1-3-94 Disposable 1143-cc
 Fasted Date/Time/Tech: 1-20-94 / C7 Syringe used/Size: 3 in. x 16 gauge
 Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. x 16 gauge

Sex: Male Dose Time/Tech: From 11:31 To 11:31 / C7

Animal Number	C2-	Dose Time/Tech	From	To	Technician	Date	Scale used: A&D
Prefasted Body Weight (g)		7211		7210	C7	1-20	C0221330
Fasted Body Weight (g)		294		299	C7	1-21	C0221330 Verified by JH 1-21-94
Actual Dose (mL)		270		1.0	C7	1-21	JH 1-21-94
DEAD Day 7 Body Weight (g)		1.0					
Day 14 Body Weight (g)		245			K	1/23	C0221330

Sex: Female Dose Time/Tech: From 11:32 To 11:33 / C7

Animal Number	C2-	Dose Time/Tech	From	To	Technician	Date	Scale used: A&D
Prefasted Body Weight (g)		7256		7257	C7	1-20	C0221330
Fasted Body Weight (g)		262		251	C7	1-21	C0221330 Verified by JH 1-21-94
Actual Dose (mL)		240		0.89	C7	1-21	JH 1-21-94
DEAD Day 7 Body Weight (g)		0.89					
Day 14 Body Weight (g)		2.18			K	1/23	C0221330

NA Not applicable. ① Wrong time: C7 1-21-94
 ② Unused animals returned to Stock, C7 1-21-94
 ③ FORM CHANGES KN 1-23-94

Final data review by/Date: JH 1-20-94

HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 3713 (mg/kg)

Animal Number/Sex: C2 7211 1♂		Study Day																	
Observations	Pre-dose	Hours																	
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Appeared normal	✓	-	-	-	-	-													
Excessive Salivation	✓	-	-	-	-	-													
Staggered gait	✓	✓	✓	✓	-	-													
Hypoactive	✓	✓	✓	✓	-	-													
PROSTRATE HYPOTHERMIC TO TOUCH					✓	-													
FEW FELES					✓	-													
BRADYPNEA					✓	-													
DEAD (L:38)							✓												
Time	NA	9:23	14:03	15:33	NA	NA													
Technician	C7	C7	C7	C7	K5	K5													
Date 1994	1/21	1/21	1/21	1/21	1/22	1/23													

① To clarify, time is 12:32. C7 1-21-94

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: JH 1 1-30-94

(08/09-20-93)

~~XXXXXXXXXX~~

HWI No.: 31102212

OBSERVATIONS

Test material: T-5802

Dose level: 3713 (mg/kg)

Observations	Pre-dose	Hours			Study Day														
		1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Animal Number/Sex: C2 <u>7256 P ♂ ♀</u>																			
Appeared normal	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Staggered gait		✓	✓	✓	-	-													
Hypoaactive			✓	✓	-	-													
PROSTRATE HYPOTHERMIC TO TOUCH					✓	-													
BRADYPNEA					✓	-													
FEW FEES FEW FEWES ^②					✓	-													
DEAD (6:42)							✓												
Time	NA	13:33	14:03	15:33	NA	NA													
Technician	C7	C7	C7	C7	KG	KG													
Date 1994	1/21	1/21	1/21	1/21	1/22	1/23													

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.
- ① Wrong sex. C71-20-94
- ② SPELLING ERROR. KG 1-22-94

Final data review by/Date: JH 1/30-94

(08/09-20-93)

DOSE ADMINISTRATION/BODY WEIGHT RECORD

Study Type: Acute Oral Toxicity (Up and Down Procedure)
 Test Material: (V-5802)
 Dose Level: 482.7 (mg/kg) Dose Volume: 4.83 (mL/kg)
 Species/Source Strain: Rat/Crl:CD08R Date Received: 1-3-94
 Fasted Date/Time/Tech: 1-17-94 11:15:10 Syringe used/Size: Disposable 10/3-cc
 Gavage method used/Size: Ball-tipped stainless steel gavage needle / 3 in. x 16 gauge
 Vehicle: NA Route of Administration: Oral Gavage
 Initiated in Room Number: 102

Sex: Male Dose Time/Tech: From 10:01 To 10:01 / C7

Animal Number	C2-	Dose Time/Tech	From	To	1994	Technician	Date	Scale used: A&D
Prefasted Body Weight (g)			7209			K9	1/17	C0221330
Fasted Body Weight (g)			285			C7	1/18	C0221330
Actual Dose (mL)			1.3			C7	1/18	Verified by JH 1-18-94
Day 7 Body Weight (g)								
Day 14 Body Weight (g)			246			C7	1/19	C0221330

Sex: Female Dose Time/Tech: From / To

Animal Number	C2-	Dose Time/Tech	From	To	1994	Technician	Date	Scale used: A&D
Prefasted Body Weight (g)								
Fasted Body Weight (g)								
Actual Dose (mL)								Verified by
Day 7 Body Weight (g)								
Day 14 Body Weight (g)								

NA Not applicable.
 ① Wrong syringe size. C7 1-18-94
 ② Unused animal returned to stock. C7 1-18-94
 ③ Form change. C7 1-19-94

Final data review by/Date: JH 1-18-94



HWI No.: 31102242

NOTED
FALLING
COPIES COLLECTED

OBSERVATIONS

Test material: T-5802

Dose level: 4827 (mg/kg)

Animal Number/Sex: C2 7209 1♂		Hours			Study Day													
Observations	Pre-dose	1.0	2.5	4.0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Appeared normal	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Excessive Salivation		✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Staggered gait		✓	✓	✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hunched posture																		
Hypnactive				✓	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dead (7:48)					✓	-	-	-	-	-	-	-	-	-	-	-	-	-
Time	NA	11:01	12:33	14:01	NA													
Technician	C7	C7	C7	C7	C7													
Date 1994	1/18	1/18	1/18	1/18	1/19													

- NA Not applicable.
- ✓ Indicates condition exists.
- Not evident.
- * Found dead, P.M. check.

Final data review by/Date: JH 1 1-30-94

~~TOP SECRET~~
~~CONFIDENTIAL~~
~~BUSINESS INFORMATION~~

~~CONFIDENTIAL~~

Attachment VII

3M §8(E) MAY 20, 1994
Support Information for Confidentiality Claims

MAY 27 AM 8:01

RECEIVED
OPPT CBIC

1. Period of Time

3M identity should be held confidential until the products are marketed. (Current plans anticipate fall 1994 introduction.)

Percent composition should be held confidential indefinitely for both products. 3M competition in this market is not sophisticated in all cases and is not likely to be able to determine specific percent composition without significant effort.

Specific chemical composition for Stripper II should be held confidential indefinitely for all intentional components present at levels of less than 1%. A significant R & D effort (5 person years) has been spent to develop this patentable formulation. Once the product is introduced to the market, we will be issuing an MSDS which will contain chemical composition information for components above 1% (but will continue to mask precise percentages).

2. EPA prior determinations: None

3. Disclosure to others:

Formulation information has been disclosed to manufacturing plants that will be making the final products. These facilities are required to sign a confidentiality agreement with 3M to ensure protection of the information.

4. Use and Procedure Restrictions:

3M has multiple procedures to protect proprietary information including: employee technical agreements, restricted markings and distribution of materials, and security controlled access to buildings.

5. Public Information:

MSDS will only reveal chemical identities for Stripper I and identities above 1% for Stripper II; percentages will be given in broad ranges. Neither product is marketed yet, so that MSDS are not available to the public.

Advertising/promotional materials do/will not reveal formulation information.

6. Substantial Harm:

Disclosure of this information would enable competitors, who might not otherwise have the capability to conduct sophisticated analytical testing to obtain our formulations. Revealing the claimed information now would jeopardize our market launch/positioning of these products in a market and could cause our competitors to place 3M at a price or promotional disadvantage prior to introduction. Significant research investment and potential sales would be at risk.

7. Disclosure of §14(b) information:

Revealing the chemical composition of Stripper II would reveal the process by which this unique mixture of components performs its function.

Claims are specifically made on proportions of the mixtures.

Confidentiality of company identity is not related to, nor necessary to interpret, the effects of the substance on health or the environment.

~~CONFIDENTIAL~~

ATTACHMENT I
COMPOSITION OF STRIPPER T-5876
(ATM Analogue)

~~CONFIDENTIAL~~
~~CONFIDENTIAL~~

INGREDIENT	C.A.S. NO.	PERCENT
ACETONE.....	67-64-1	~ 45
XYLENE.....	1330-20-7	~ 26.6
METHYL ALCOHOL.....	67-56-1	~ 17.97
ETHYLBENZENE.....	100-41-4	~ 5.65
CLAY-TREATED PARAFFIN WAXES.....	64742-43-4	~ 3.2
HYDROXYPROPYL METHYL CELLULOSE.....	9004-65-3	~ 1.37
WATER.....	7732-18-5	~ .12
SODIUM CHLORIDE.....	7647-14-5	~ .019
BENZENE.....	71-43-2	< .0135
TOLUENE.....	108-88-3	< .3

~~CONFIDENTIAL~~



HAZLETON
WISCONSIN
 POST OFFICE BOX 7545
 MADISON, WI 53707-7545

ATTACHMENT III
STRIPPER I

© CORNING Laboratory Services Company

FINAL REPORT

[REDACTED]

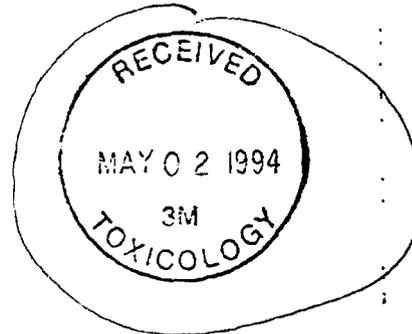
Mr. Kurt T. Werner
 3M
 Toxicology Services
 Building 220-2E-02
 St. Paul, MN 55144-1000

HWI Number: 40201133

[REDACTED]

Study Title:

Primary Dermal Irritation/Corrosion
 Study of T-5876 in Rabbits
 (OECD Guidelines)



Signed:

Steven M. Glaza

Steven M. Glaza
 Study Director
 Acute Toxicology

Date

4-29-94

HWI Number: 40201133

Page 2

Sample: T-5876

KEY PERSONNEL

Acute Toxicology

Steven M. Glaza
Study Director
Manager

Steven R. Sorenson
Study Coordinator

Patricia Padgham
In-life Supervisor

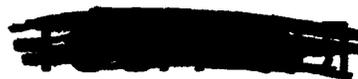
Rose M. Bridge
Report Supervisor

Laboratory Animal Medicine

Cindy J. Cary, DVM
Diplomate, ACLAM
Supervisor

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Sample: T-5876

SUMMARY OF RESULTS

Test Animal: Albino Rabbits - Hra:(NZW)SPF
 Source: HRP, Inc., Kalamazoo, MI
 Date Animals Received: 03/09/94

Experimental Start Date: 03/16/94 Experimental Termination Date: 03/31/94

Individual Dermal Irritation Scores

Animal Number	Sex	Erythema						Edema							
		Hour					Day	Hour					Day		
		4	24	48	72	96	7	14	4	24	48	72	96	7	14
F50253	M	2 ^b	4 ⁿ	4 ⁿ	4 ⁿ	4 ⁿ	2 ^x	0 ^s	2	2	2	2	2	2	1
F50254	M	2 ^b	3 ^{a,b}	4 ⁿ	4 ⁿ	4 ⁿ	4 ^e	2 ^x	2	3	3	2	2	2	2
F50255	M	2 ^b	3 ^{a,b}	3 ^{a,b}	4 ⁿ	4 ⁿ	4 ⁿ	0 ^s	2	3	3	3	2	2	1

- a Subcutaneous hemorrhaging.
- b Blanching.
- e Eschar.
- n Possible necrotic area.
- s Possible scar tissue.
- x Exfoliation.

Average Primary Dermal Irritation Scores*

Observation Period	Average Score
4 Hour	4.0
24 Hour	6.0
48 Hour	6.3
72 Hour	6.3
96 Hour	6.0
Day 7	5.3
Day 14	2.0

* The average primary dermal irritation score is the total dermal irritation score for all the animals (erythema and edema) divided by the number of test sites (3) at each observation period.



HWI Number: 40201133

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Sample: T-5876

APPENDIX

Raw Data

~~XXXXXXXXXX~~

~~XXXXXXXXXX~~

HWI: 40201133

PERSONNEL SIGNATURE SHEET
ACUTE TOXICOLOGY

<u>Name</u>	<u>Job Title</u>	<u>Signature</u>	<u>Initials</u>
Rose M. Bridge	Report Supervisor	<u>Rose M. Bridge</u>	<u>RB</u>
Anthony Cass	Lab Animal Technician	<u>Anthony Cass</u>	<u>AC</u>
Cindy J. Cary, DVM	Lab Animal Veterinarian	<u>Cindy J. Cary</u>	<u>YC</u>
Donna J. Clemons, DVM, MS	Lab Animal Veterinarian	<u>Donna Clemons</u>	<u>DC</u>
John A. Disch	Lab Animal Caretaker	<u>John A. Disch</u>	<u>JD</u>
Charles W. Fritz	Lab Animal Technician	<u>Charles W. Fritz</u>	<u>CF</u>
Kari Garfoot	Lab Animal Technician	<u>Kari Garfoot</u>	<u>KG</u>
Steven M. Glaza	Manager	<u>Steven M. Glaza</u>	<u>SG</u>
Kevin Grossman	Lab Animal Caretaker	<u>Kevin Grossman</u>	<u>KG</u>
Jeff Hicks	Lab Animal Technician	<u>Jeff Hicks</u>	<u>JH</u>
Sharen L. Howery	Research Assistant	<u>Sharen L. Howery</u>	<u>SH</u>
Wayne A. Madison	Supervisor	<u>Wayne A. Madison</u>	<u>wam</u>
Doug McConnell	Lab Animal Technician	<u>Douglas B. McConnell</u>	<u>DM</u>
Eileen McConnell	Staff Assistant	<u>Eileen McConnell</u>	<u>EM</u>
Bud McDonald	Study Coordinator	<u>Bud McDonald</u>	<u>BM</u>
Albert Oleson	Lab Animal Caretaker	<u>Albert Oleson</u>	<u>AO</u>
Patricia Padgham	In-life Supervisor	<u>Patricia Padgham</u>	<u>PP</u>
Steven R. Sorenson	Study Coordinator	<u>Steven R. Sorenson</u>	<u>SRS</u>
Annette R. Turner	Staff Assistant	<u>Annette R. Turner</u>	<u>AT</u>
Tamra L. Walker	Staff Assistant	<u>Tamra L. Walker</u>	<u>TW</u>
Lana M. Weeden	Staff Assistant	<u>Lana M. Weeden</u>	<u>LW</u>
Heather M. Weber	Lab Animal Caretaker	<u>Heather M. Weber</u>	<u>HW</u>
Janice Griffiths	Lab Animal Caretaker	<u>Janice Griffiths</u>	<u>JG</u>
Nikolai Larbakasfier	Lab Animal Caretaker	<u>Nikolai Larbakasfier</u>	<u>NL</u>
Pamela J. Klith	Lab Animal Caretaker	<u>Pamela J. Klith</u>	<u>P.J.K</u>
Carol Koch (62/10-06-93)	Lab Animal Technician	<u>Carol Koch</u>	<u>CK</u>

HWI No.: 40201133

DERMAL IRRITATION/BODY WEIGHT RECORD (4-HOUR EXPOSURE)

Test Material: T-5871 Physical Description: CLOUDY WHITE VISCOUS LIQUID
 Dose: 0.5mL Per Site NA Moistened with 0.9% Saline; Hfg/Lot No./Exp. Date: NA / NA / NA
 pH Result: LL with Corning pH Meter No. 05510 Skin Preparation: Intact Abraded (with a clipper blade)
 Species/Source Strain/Location: Rabbit/Hrs: (NZM)SPE/ALL Date Animal(s) Received: 3-9-94 Initiated in Room No.: 104
 Technician/Date/Time Animal(s) Clipped: KJ 13-15-94/ 14:15

Animal Number/Sex	ES	0253	0254	0255				Technician	Recorded By	Date	Scale Used	A: D
Initial Body Weight (g)	2202	2200	2245					KJ	KJ	3/16	CS604465	
Day 7 Body Weight (g)	2329	2254	2460					ac	ac	3-23	CS604465	
Observations												
4 Hour	Erythema	2B	2B	2B								
	Edema	2	2	2						3/16		ac 3-23-94 40K3-17-94
24 Hour	Erythema	4N	3AB	3AB								
	Edema	2	3	3						3/17		ac 3-23-94 40K3-17-94
48 Hour	Erythema	4N	4N	3AB								
	Edema	2	3	3						3/18		ac 3-23-94 43K3-18-94
72 Hour	Erythema	4N	4N	4N								
	Edema	2	2	3						3/19		ac 3-23-94 43K3-19-94
96 Hour	Erythema	4N	4N	4N								
	Edema	2	2	2						3/20		CF 3-25-94 60ac 3-23-94
Day 7	Erythema	2 ^x	4E	4N								
	Edema	2	2	2				ac*	ac	3-23		CF 3-25-94 53ac 3-23-94

Storage conditions of test material: ROOM TEMPERATURE

- NA Not applicable.
- B Blanching.
- X-ekfoliation
- * Animal(s) shaved prior to dermal observation by technician.
- A Subcutaneous hemorrhage.
- N Possible necrotic area.
- U Unable to determine pH.

Animals were weighed and appeared normal before test material administration on the day of dosing. Technician/Date: KJ 13-16-94
 Surviving animals designated for sacrifice and discard. Technician/Date: NR 1 NR
 Final data review by/Date: JA 13-24-94



HWI No.: 40201133

'DERMAL IRRITATION/BODY WEIGHT RECORD (4-HOUR EXPOSURE)
(CONTINUED)

Test Material: I-5876

Animal Number	FS	0253	0254	0255	Technician	Recorded By	Date	Scale Used
Day 14 Body Weight (g)	2602	2424	2570		ac	ac	3-30	CS604465
Day 21 Body Weight (g)								
Day 28 Body Weight (g)								

Observations

Day	Erythema	Edema	Erythema	Edema	Erythema	Edema	Erythema	Edema	Irritation Score
Day 14	0 ^s	1	2 ^x	2	0 ^s	1			✓ ac 4-1-94 2.0563-30-94
Day 21									
Day 28									

NA Not applicable.
 A Subcutaneous hemorrhage.
 B Blanching.
 N Possible necrotic area.
 S-Possible scar tissue
 * Animal(s) shaved prior to dermal observation by technician.

Surviving animals designated for sacrifice and discard. Technician/Date: ac 12-31-94

(S4/12-09-92)

Final data review by/Date: ka/4-4-94

HWI No.: 40201133

Test Material Administration Record
(Dermal Irritation Studies)

All animals on this study received their dose and were wrapped as indicated below for the period of time shown.

DOSING APPARATUS

3 -cc plastic disposable syringe
 NA -cc glass syringe
 Weigh boat
 Other: NA

PATCHES

2.5 cm X 2.5 cm gauze patch
 5.0 cm X 5.0 cm gauze patch
 Other: NA

WRAPS

Saran Wrap®
 Dental Dam®
 Other: NA

TAPES

Paper tape
 Elastoplast® tape
 Other: NA

Wrapped to provide a semi-occlusive dressing.
 Wrapped to provide an occlusive dressing.

COLLARS

Collars were applied for the exposure period.
 Collars were not applied.

Approximate area of exposure is: 2.5 cm x 2.5 cm

Time of treatment
as described above: From 11:20 to 11:24 Tech./Date: KG 13-16-94

Time of bandage removal
as described below: From 15:20 to 15:23 Tech./Date: KG 13-16-94

Test material was removed with tap water and disposable paper towels.
 Test material was removed with liquid Ivory® soap mixed with warm tap water. The test sites were then thoroughly rinsed with clean tap water and dried with disposable paper towels.

Time of first observation: 15:48 Tech./Date: KG 13-16-94

NA Not applicable.

(S11/01-27-94)

Final data review by/Date: JH 1 3-26-94

HWI No.: 40201133

Primary Dermal Irritation Scoring Scale
(Draize Technique)

(1) Erythema and Eschar Formation

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	<u>4</u>

Highest possible erythema score 4

TSCA CBI

(2) Edema Formation

No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges are well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised approximately 1 mm and extending beyond area of exposure)	<u>4</u>

Highest possible edema score 4

(S5/01-07-91)