

REILLY INDUSTRIES, INC.

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(A)

August 25, 1994

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ATTN: Section 8(e) Coordinator
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Environmental Protection Agency
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Washington, D.C. 20460

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ORIGINAL

Dear Sir or Madam:

This notice is being submitted by Reilly Industries, Inc. (Reilly) pursuant to the requirements of Section 8(e) of the Toxic Substances Control Act.

Reilly manufactures 1-Methylpiperidine, (CAS # 626-67-5) for commercial purposes. In order to understand more about the toxicity of this product, Reilly contracted to have an acute oral toxicity study conducted. The results of this study indicate that the oral LD50 of the compound is between 5.0 and 25.0 mg/kg when tested in Sprague-Dawley albino rats. According to the Section 8(e) Reporting Guide issued in June 1991, lethality findings indicating high toxicity coupled with potential exposure are reportable as a substantial risk. Therefore, Reilly is submitting this notice along with a copy of the study report.

If further information is required regarding this matter, please contact me at 317-248-6427, or Dr. Paul Rivers at 317-248-6425.

Sincerely,

REILLY INDUSTRIES, INC.

Lisa S. Moser
Project Manager,
Corporate Environmental Affairs



8EHQ-94-12975

INIT

LSM:ha

cc: (w/o attachments):
Paul Rivers
Jackie Simmons
Charlie DiGiovanna



88940000217

mm
10/11/94



product safety labs

725 Cranbury Road • East Brunswick, New Jersey 08816-3206 • 908-254-9200 • 800-425-0002 • Fax-908-254-6736

ACUTE ORAL TOXICITY DEFINED LD₅₀

PROTOCOL NO.: P320
AGENCY: EPA/TSCA
STUDY NUMBER: 3027
SPONSOR: REILLY INDUSTRIES, INC.
1500 S. Tibbs Avenue
P.O. Box 41076
Indianapolis, IN 46241-0076
PRODUCT IDENTIFICATION: 1-Methylpiperidine, Lot #30315AC
PRODUCT DESCRIPTION: Clear to light yellow liquid
DATE RECEIVED: March 31, 1994
PSL REFERENCE NO.: E40331-4
DATE OF PROTOCOL APPROVAL: April 22, 1994
DATES OF ADMINISTRATION: May 6, 11, 23, 31 and July 8, 1994
COMPLETION OF IN-LIFE PHASE: July 22, 1994
STUDY TERMINATION DATE: August 11, 1994
NOTEBOOK NO.: 94-15; pages 138-169H

1. PURPOSE:

To determine the Acute Oral Toxicity Defined LD₅₀ of 1-Methylpiperidine, Lot #30315AC. Data from this study may be used as a basis for classification and labeling.

2. SUMMARY:

An Acute Oral Toxicity test was conducted in rats to determine the potential for 1-Methylpiperidine, Lot #30315AC to produce toxicity via the oral route. Based on the results of this test, the single dose Acute Oral Toxicity Defined LD₅₀ of the test substance was determined to be between 5 and 25 mg/kg.

After acclimation to the laboratory, 50 healthy rats were selected for test and equally distributed (5 males and 5 females) into 4 dose groups. Dose levels of 5, 25, 50, 200 and 500 mg/kg of bodyweight were selected for testing. The test substance was administered as

received for the 25, 50, 200 and 500 mg/kg groups. Due to extremely low dose volumes, the 5 mg/kg dose was administered as a 10% w/w solution in distilled water. For each test group, the animals were administered the test substance and observed for signs of gross toxicity and mortality at least once daily for a period up to 21 days. Bodyweights were recorded just prior to administration, on day 7, 14 and 21 (if applicable) or after death. Necropsies were performed on all animals.

The incidence of mortality at each dose level is summarized below:

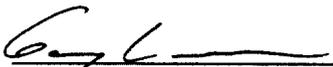
Designated Dose Level	Mortality			
	mg/kg	Males	Females	Total
5		0/5	0/5	0/10
25		4/5	5/5	9/10
50		4/5	5/5	9/10
200		5/5	5/5	10/10
500		5/5	5/5	10/10

Following administration, animals from the 25, 50, 200 and 500 mg/kg dose levels exhibited clinical signs including abnormal posture, unthrifty appearance, abnormal respiration, decreased food consumption and fecal output, facial staining, mouth, ocular and nasal discharge, ano-genital staining, tremors, piloerection and lethargy. Most animals from the 5 mg/kg dose level appeared active and healthy following administration. Gross necropsy of the decedents revealed discoloration of the gastro-intestinal (GI) tract and lungs and/or distension of the GI tract. Overall, gross necropsy findings at terminal sacrifice were generally unremarkable.

1-Methylpiperidine, Lot #30315AC

ACUTE ORAL TOXICITY DEFINED LD₅₀

This study meets the requirements of 40 CFR 792: U.S. EPA Good Laboratory Practice Standards: Toxic Substances Control Act (TSCA) with the following exception: The stability, characterization, identity and verification of the test substance concentration as received and tested are the responsibility of the study sponsor.



Gary Wnorowski, B.A.
Study Director

Aug 11, 1994

Date

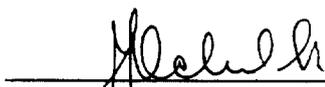
We the undersigned declare that the methods, results and data contained in this report faithfully reflect the procedures and raw data used or collected during the study.



Ralph Shapiro, Ph.D.
Laboratory Director

August 12, 1994

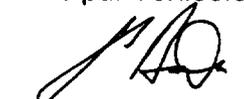
Date



Jacek Ochalski, D.V.M.
Principal Toxicology Technician

Aug. 15, 1994

Date



Jasbir Bawa, B.S.
Assistant Toxicology Technician

Aug 11, 1994

Date



Kenneth Barr
Assistant Toxicology Technician

August 11, 1994

Date

3. MATERIALS:**A. Test Substance:**

The test substance identified as 1-Methylpiperidine, Lot #30315AC, was received on March 31, 1994 and was further identified with PSL Code Number E40331-4. The test substance was a clear to light yellow liquid and was stored at room temperature. For the 25, 50, 200, and 500 mg/kg dose levels, the sample was administered as received. For the 5 mg/kg dose level, the test substance was administered as a 10% w/w solution in distilled water. Documentation of the methods of synthesis, fabrication, or derivation of the test substance is retained by the sponsor.

Characterization of the test substance as provided to Product Safety Labs by the sponsor was:

Composition: 1-Methylpiperidine - 99.6%

pH: 11.30

Solubility: Soluble in water

Stability: Stable

Expiration Date: Not applicable

B. Animals:

3.B.1 Number of Animals: 50

3.B.2 Sex: 25 males and 25 females

3.B.3 Number of Animals/Dose Level: 5 males and 5 females/dose level

3.B.4 Species/Strain: Rat/Sprague-Dawley derived, albino

3.B.5 Age/Bodyweight: Young adult/males 191-258 grams and females 185-227 grams at initiation

3.B.6 Source: Received from Hilltop Lab Animals, Scottdale, PA on April 26, May 3 and 24, and June 28, 1994.

4. METHODS:**A. Husbandry:**

4.A.1 Housing: The animals were singly housed in suspended stainless steel caging with mesh floors which conform to the size recommendations in the Guide for the Care and Use of Laboratory Animals DHEW (NIH) No. 86.23.

Litter paper was placed beneath the cage and was changed at least three times per week.

4.A.2 Room Temperature: 66-79°F

4.A.3 Photoperiod: 12 hour light/dark cycle

4.A.4 Acclimation Period: 7, 10, 11, 16 or 21 days

4.A.5 Food: Purina Rodent Chow #5012

4.A.6 Water: Filtered tap water was supplied by automatic water system ad-libitum.

4.A.7 Contaminants: There were no known contaminants reasonably expected to be found in the food or water which interfered with the results of this study. Results of the analysis of the food and water are kept on file at Product Safety Labs. The dates of the most recent analyses are presented in Appendix A.

B. Identification:

4.B.1 Cage: Each cage was identified with a cage card indicating at least the study number and identification and sex of the animals.

4.B.2 Animal: A number was allocated to each rat on receipt and a stainless steel ear tag bearing this number was attached to the rat. This number, together with the sequential animal number assigned to study 3027, constituted unique identification.

5. PROCEDURE:

A. Preparation and Selection of Animals:

On the day before dosing, each group of animals was fasted for approximately 20-24 hours by removing feed from their cages. After the fasting period, the rats were examined for health and weighed (initial). Ten (5 males and 5 females) healthy rats were selected for each dose level.

B. Dose Calculations:

Individual doses were calculated based on the initial bodyweights, taking into account the specific gravity of the test substance, and for the 5 mg/kg dose level, the concentration of the test solution.

C. Dosing:

Each animal received the appropriate amount of the test substance (5, 25, 50, 200 or 500 mg/kg) by oral intubation using a stainless steel ball-tipped gavage needle attached

to an appropriate syringe. After administration, each animal was returned to its designated cage. Feed was replaced approximately 3-4 hours after dosing.

D. Bodyweights:

Individual weights of the animals were recorded just prior to test substance administration (initial), on days 7, 14, 17 and/or 21 (if applicable) or after death.

E. Cage-Side Observations:

The animals were observed for signs of gross toxicity, behavioral changes and mortality at least once daily for a period up to 21 days. Observations included gross evaluation of skin and fur, eyes and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, somatomotor activity and behavior pattern. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea, sleep and coma.

F. Necropsy:

Surviving rats were euthanized via CO₂ inhalation on days 14 or 21. A gross necropsy was performed on all decedents and survivors. Tissues and organs of the thoracic and abdominal cavities were examined.

6. STUDY CONDUCT:

This study was conducted at Product Safety Labs, 725 Cranbury Road, East Brunswick, NJ 08816, to comply with the Good Laboratory Practices as defined in 40 CFR 792: U.S. EPA Good Laboratory Practice Standards: Toxic Substances Control Act (TSCA) and in accordance with Health Effects Testing Guidelines, Subpart B: Acute Oral Toxicity, 40 CFR 798.1175.

7. QUALITY ASSURANCE:

Procedure audits were made by Quality Assurance during the study. The draft final report was audited for agreement with the raw data records and for compliance with the protocol, Product Safety Labs Standard Operating Procedures and appropriate Good Laboratory Practices Regulations. Dates of inspections and reporting are presented in the Quality Assurance Statement.

8. DEVIATIONS FROM FINAL PROTOCOL: None

9. RECORDS TO BE MAINTAINED:

A copy of this signed report, together with the protocol and all raw data generated at Product Safety Labs, is retained in the Product Safety Labs Archives.

10. RESULTS:**5 mg/kg (10% w/w solution in distilled water)**

All animals survived and gained weight during the study. Two males exhibited a hunched posture and/or piloerection within 3 hours of test substance administration, but recovered by day 3. All animals appeared active and healthy for the remainder of the 14-day observation period. Gross necropsy findings at terminal sacrifice were generally unremarkable. Apart from red lung discoloration consistent with euthanasia by CO₂ inhalation, all tissues and organs appeared normal.

25 mg/kg (as received)

Ninety percent mortality occurred within 11 days of test substance administration. Toxic signs prior to death included abnormal posture, unthrifty appearance, irregular respiration, gasping, facial staining, mouth and nasal discharge, rales, abdominal distention, piloerection and lethargy. The surviving rat, a male, exhibited similar clinical signs as well as reduced fecal output and ano-genital staining. In order to assess reversal of toxicity in this animal, the observation period was extended to 21 days when this animal appeared normal. Although the surviving rat lost weight from day 7 to 14, it gained bodyweight over the entire 21-day observation period. Gross necropsy of the decedents revealed discoloration of the gastrointestinal (GI) tract and lungs, gaseous distension of the GI tract and/or edema of the lungs. Gross necropsy findings at terminal sacrifice of the survivor were generally unremarkable. Apart from red lung discoloration consistent with euthanasia by CO₂ inhalation, all tissues and organs appeared normal.

50 mg/kg (as received)

Ninety percent mortality occurred within 9 days of test substance administration. Toxic signs prior to death included hunched posture, irregular respiration, facial staining, mouth, ocular and nasal discharge, gasping, decreased food consumption and fecal output, piloerection and lethargy. The surviving rat, a male, exhibited similar clinical signs through day 14. In order to assess reversal of toxicity in this animal, the observation period was extended to 21 days. Although the surviving rat lost weight initially, it gained bodyweight over the entire 21-day observation period. Gross necropsy of the decedents revealed discoloration of the gastrointestinal (GI) tract and lungs and/or gaseous distension of the GI tract. Gross necropsy of the survivor revealed that the left lobe of the lung was enlarged, pale in color and filled with a light green semi-solid.

200 mg/kg (as received)

All animals died within 9 days of test substance administration. Toxic signs prior to death included abnormal posture, unthrifty appearance, irregular respiration, gasping, facial staining, mouth, ocular and nasal discharge, ano-genital staining, tremors, piloerection and lethargy. Gross necropsy of the decedents revealed discoloration of the gastrointestinal (GI) tract and lungs and/or gaseous distension of the GI tract. In one female, the stomach was attached to the abdominal peritoneum by an anomalous section of connective tissue.

500 mg/kg (as received)

All animals died within 8 days of test substance administration. Toxic signs prior to death included abnormal posture, irregular respiration, gasping, rales, decreased food consumption and fecal output, facial staining, mouth and ocular discharge, ano-genital staining, tremors,

piloerection and lethargy. Gross necropsy of the decedents revealed discoloration of the gastro-intestinal (GI) tract and lungs and/or distension of the GI tract.

- A. **Summary of Mortality Data:** See Table 1
- B. **Bodyweight, Dosage and Mortality:** See Tables 2, 5, 8, 11 and 14
- C. **Individual Cage-Side Observations:** See Tables 3, 6, 9, 12 and 15
- D. **Individual Necropsy Observations:** See Tables 4, 7, 10, 13 and 16

11. CONCLUSION:

The Acute Oral Toxicity Defined LD_{50} of 1-Methylpiperidine, Lot #30315AC can not be determined by Probit Analysis. However, based on the observed mortality at the two lowest levels, it can be concluded that the Acute Oral Toxicity LD_{50} of the test substance is between 5 and 25 mg/kg.

TABLE - 1

SUMMARY OF MORTALITY DATA

Designated Dose Level	Mortality		
	mg/kg	Males	Females
5	0/5	0/5	0/10
25	4/5	5/5	9/10
50	4/5	5/5	9/10
200	5/5	5/5	10/10
500	5/5	5/5	10/10

TABLE - 2

BODYWEIGHT AND DOSAGE

DOSE LEVEL: 5 mg/kg

Animal No.	Sex	Bodyweight (g)			Actual Dose ¹	
		Initial	Day 7	Day 14	mg/kg	ml
4234	M	207	291	329	4.7	0.01
4235	M	213	293	331	4.6	0.01
4236	M	210	286	323	4.7	0.01
4237	M	201	272	312	4.9	0.01
4238	M	215	289	322	4.6	0.01
4239	F	217	257	269	4.5	0.01
4240	F	211	243	257	4.6	0.01
4241	F	216	267	284	4.5	0.01
4242	F	203	250	263	4.8	0.01
4243	F	207	245	252	4.7	0.01

¹ Administered as 10% w/w solution in distilled water. Specific Gravity 0.981 g/ml.

TABLE - 3INDIVIDUAL CAGE-SIDE OBSERVATIONSDOSE LEVEL: 5 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>MALES</u>		
4234	Active and healthy Piloerection	0(1 hr), 2-14 0(3-22 hr)
4235, 4237, 4238	Active and healthy	0-14
4236	Active and healthy Piloerection, hunched posture	0(1 hr), 3-14 0(3 hr)-2
<u>FEMALES</u>		
4239-4243	Active and healthy	0-14

TABLE - 4

INDIVIDUAL NECROPSY OBSERVATIONS

DOSE LEVEL: 5 mg/kg

<u>Animal Number</u>	<u>Tissue</u>	<u>Findings</u>
<u>MALES</u>		
4234-4238	Lungs	Moderately red ¹
<u>FEMALES</u>		
4239-4243	Lungs	Moderately red ¹

¹ Customarily seen with CO₂ inhalation, euthanasia procedure.

TABLE - 5

BODYWEIGHT, DOSAGE AND MORTALITY

DOSE LEVEL: 25 mg/kg

Animal No.	Sex	Bodyweight (g)				Actual Dose ¹		Mortality	
		Initial	Day 7	Day 14	Day 21	mg/kg	ml	Day	Weight
3734	M	211	-	-	-	23	0.006	3	162
3735	M	210	224	217	251	23	0.006	E	-
3736	M	193	152	-	-	25	0.006	11	123
3737	M	191	128	-	-	25	0.006	11	118
3738	M	201	-	-	-	24	0.006	2	165
3739	F	197	-	-	-	25	0.006	7	116
3740	F	185	164	-	-	26	0.006	10	142
3741	F	205	-	-	-	24	0.006	6	140
3742	F	213	-	-	-	23	0.006	3	174
3743	F	201	-	-	-	24	0.006	3	169

E - Euthanized on day 21 via CO₂ inhalation after weighing

¹ Administered as received. Specific Gravity - 0.805 g/ml.

TABLE - 6

INDIVIDUAL CAGE-SIDE OBSERVATIONS

DOSE LEVEL: 25 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>MALES</u>		
3734	Hunched posture, mouth discharge	0 (1 hr)-3
	Gasping	0 (1-3 hr), 2-3
	Lethargic, nasal discharge	0 (19 hr)-3
	Distended abdomen, piloerection	2-3
	Reduced fecal volume	3
	Dead	3 PM
3735	Active and healthy	0 (1, 19 hr), 4-11, 21
	Hunched posture	0 (3 hr), 16-19
	Nasal discharge	24 hr
	Piloerection	2-3
	Reduced fecal volume	12-16
	Ano-genital staining	13
	Unthrifty	20
3736	Irregular respiration	0 (1-19 hr), 3-5, 8-9
	Piloerection	0 (19 hr)-7, 9-10
	Nasal discharge	0 (19 hr), 2
	Unthrifty	2-10
	Facial staining, lethargic	10
	Dead	11
3737	Active and healthy	0 (1-3 hr)
	Piloerection	0 (19 hr)-2, 9-10
	Nasal discharge	24 hr-5
	Dry rales	3-8
	Unthrifty	4-10
	Reduced fecal volume	5-9
	Hunched posture	6-10
	Lethargic	7-10
	Facial staining	10
	Dead	11
3738	Irregular respiration, hunched posture	0 (1 hr)-24 hr
	Lethargic, piloerection, nasal discharge	0 (19 hr)-24 hr
	Dead	2

TABLE - 6 (cont.)

INDIVIDUAL CAGE-SIDE OBSERVATIONS

DOSE LEVEL: 25 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>FEMALES</u>		
3739	Hunched posture	0 (1 hr)-24 hr
	Lethargic	0 (3 hr)-24 hr
	Irregular respiration	0 (19 hr)-24 hr
	Piloerection	0 (19 hr)-6
	Nasal discharge	24 hr-2
	Reduced fecal volume	3,5
	Rales	3-6
	Red stain in litter pan	4-5
	Unthrifty	5
	Dead	7
3740	Active and healthy	0 (1 hr)
	Irregular respiration	0 (3 hr)-10
	Facial staining	0 (19 hr)-4
	Unthrifty	3
	Reduced fecal volume	3-9
	Piloerection, lethargic	9-10
	Dead	10(3:00 PM)
3741	Active and healthy	0 (1 hr), 24 hr
	Hunched posture	0 (3-19 hr)
	Irregular respiration	0 (19 hr), 3-5
	Piloerection	2-5
	Reduced fecal volume, unthrifty	3-5
	Gasping, lethargic, facial staining	5
	Dead	6
3742	Irregular respiration	0 (1 hr)-3
	Hunched posture, mouth discharge, lethargic	0 (3 hr)-3
	Nasal discharge, gasping	0 (19 hr)-3
	Reduced fecal volume	3
	Dead	3 (2:55 PM)
3743	Hunched posture, irregular respiration, mouth discharge	0 (1 hr)-3
	Lethargic, piloerection	0 (19 hr)-3
	Prostrate, reduced fecal volume	3
	Dead	3 (2:55 PM)

TABLE - 7

INDIVIDUAL NECROPSY OBSERVATIONS

DOSE LEVEL: 25 mg/kg

<u>Animal Number</u>	<u>Tissue</u>	<u>Findings</u>
<u>MALES</u>		
3734	Lungs GI Tract	Extremely red, edematous Gaseous distention, yellow/tan
3735	Lungs	Moderately red ¹
3736	Lungs GI Tract	Red Discolored
3737	Lungs GI Tract	Mottled red Discolored
3738	Lungs GI Tract	Mottled red Red, gaseous distention
<u>FEMALES</u>		
3739, 3740	Lungs GI Tract	Mottled red Discolored
3741	Lungs GI Tract	Moderately red Discolored
3742	Lungs GI Tract	Extremely red, edematous Gaseous distention, yellow/dark red
3743	Lungs GI Tract Eyes	Moderately red, edematous Red Corneal opacity

¹ Customarily seen with CO₂ inhalation, euthanasia procedure.

TABLE - 8

BODYWEIGHT, DOSAGE AND MORTALITY

DOSE LEVEL: 50 mg/kg

Animal No.	Sex	Bodyweight (g)					Actual Dose ¹		Mortality	
		Initial	Day 7	Day 14	Day 17	Day 21	mg/kg	ml	Day	Weight
3634	M	227	-	-	-	-	35	0.01	2	184
3635	M	233	-	-	-	-	35	0.01	4	173
3636	M	250	-	-	-	-	64	0.02	2	222
3637	M	248	170	-	-	-	32	0.01	9	160
3638	M	247	228	239	256	271	33	0.01	E	-
3639	F	216	-	-	-	-	37	0.01	2	191
3640	F	202	-	-	-	-	40	0.01	7	151
3641	F	204	-	-	-	-	39	0.01	2	175
3642	F	193	-	-	-	-	42	0.01	7	131
3643	F	217	-	-	-	-	37	0.01	2	191

E - Euthanized on day 21 via CO₂ inhalation after weighing

¹ Administered as received. Specific Gravity - 0.805 g/ml.

TABLE - 9

INDIVIDUAL CAGE-SIDE OBSERVATIONSDOSE LEVEL: 50 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>MALES</u>		
3634	Gasping	0 (1 hr)-24 hr
	Hunched posture	0 (1 hr)-2
	Lethargic	0 (3 hr)-2
	Mouth discharge	0 (3-5 hr)
	Ano-genital staining	24 hr
	Facial staining, irregular respiration	24 hr-2
	Reduced fecal volume	2
	Dead	2 PM
3635	Active and healthy	0 (1 hr)
	Hunched posture, irregular respiration	0 (3 hr)-3
	Ano-genital staining	24 hr
	Facial staining	24 hr-3
	Piloerection, reduced fecal volume	2-3
	Dead	4
3636	Hunched posture	0 (1 hr)-24 hr
	Irregular respiration	0 (3 hr)-24 hr
	Lethargic	0 (5 hr)-24 hr
	Dead	2
3637	Active and healthy	0 (1 hr)
	Lethargic	0 (3 hr)-24 hr, 3-8
	Hunched posture	0 (5 hr)-8
	Irregular respiration	2-5, 8
	Ocular discharge	2-7
	Reduced fecal volume, piloerection	2-8
	Facial staining	3-8
	Reduced food consumption	6-7
	Dead	9
3638	Hunched posture	0 (1 hr)-13
	Lethargic	0 (3 hr)-24 hr
	Facial staining	24 hr
	Reduced fecal volume	2, 4-9
	Reduced food consumption	6-7
	Irregular respiration	8-13
	Piloerection	8-14
	Active and healthy	15-21

TABLE - 9 (cont.)

INDIVIDUAL CAGE-SIDE OBSERVATIONS

DOSE LEVEL: 50 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>FEMALES</u>		
3639	Hunched posture, lethargic, irregular respiration	0 (1 hr)-24 hr
	Mouth discharge	0 (1-3 hr)
	Gasping, ano-genital staining, facial staining	24 hr
	Dead	2
3640	Lethargic	0 (1 hr), 2-6
	Hunched posture, irregular respiration	0 (1 hr)-6
	Ano-genital staining	24 hr
	Facial staining	24 hr-6
	Reduced fecal volume	2-6
	Piloerection	4-6
	Reduced food consumption	6
	Chromodacyorrhea	6
	Dead	7
3641	Active and healthy	0 (1 hr)
	Hunched posture, lethargic, irregular respiration	0 (3 hr)-24 hr
	Gasping, facial staining	24 hr
	Dead	2
3642	Hunched posture	0 (1 hr)-6
	Facial staining	0 (5 hr)-6
	Ano-genital staining	24 hr
	Lethargic, irregular respiration, piloerection, reduced fecal volume	2-6
	Reduced food consumption, chromodacyorrhea	6
	Dead	7
3643	Active and healthy	0 (1 hr)
	Hunched posture, lethargic	0 (3 hr)-24 hr
	Irregular respiration, ano-genital/ facial staining	24 hr
	Dead	2

TABLE - 10

INDIVIDUAL NECROPSY OBSERVATIONS

DOSE LEVEL: 50 mg/kg

<u>Animal Number</u>	<u>Tissue</u>	<u>Findings</u>
<u>MALES</u>		
3634	Lungs GI Tract Stomach	Mottled red Yellow/red Gaseous distention
3635	Lungs GI Tract, Stomach	Mottled red Black/red
3636	Lungs Stomach, Intestines	Mottled red Red
3637	Lungs GI Tract	Mottled red Red
3638	Lungs	Left lobe enlarged, pale, filled w/light green semi-solid material
<u>FEMALES</u>		
3639, 3640	Lungs Stomach, Intestines	Mottled red Red
3641	Lungs Intestines	Mottled red Red
3642	Lungs Intestines	Moderately red Moderately red, gaseous distention
3643	Lungs Intestines	Mottled red Red

TABLE - 11

BODYWEIGHT, DOSAGE AND MORTALITY

DOSE LEVEL: 200 mg/kg

Animal No.	Sex	Bodyweight (g)			Actual Dose ¹		Mortality	
		Initial	Day 7	Day 14	mg/kg	ml	Day	Weight
3304	M	241	-	-	200	0.06	5	158
3305	M	245	-	-	197	0.06	5	171
3306	M	243	-	-	199	0.06	6	162
3307	M	258	-	-	187	0.06	2	209
3308	M	236	-	-	205	0.06	7	156
3309	F	227	150	-	213	0.06	9	135
3310	F	209	-	-	193	0.05	4	182
3311	F	222	165	-	218	0.06	8	143
3312	F	223	-	-	217	0.06	3	185
3313	F	203	-	-	198	0.05	0	198

¹ Administered as received. Specific Gravity - 0.805 g/ml.

TABLE - 12

INDIVIDUAL CAGE-SIDE OBSERVATIONS

DOSE LEVEL: 200 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>MALES</u>		
3304	Hunched posture, piloerection	0 (0.5 hr)-5
	Lethargic	0 (1 hr)-5
	Irregular respiration	0 (3 hr)-5
	Nasal discharge	0 (20.5 hr)-5
	Mouth/ocular discharge	3-5
	Ano-genital staining	5
	Dead	5 (11:10 AM)
3305	Irregular respiration	0 (0.5 hr)-5
	Hunched posture	0 (1 hr)-5
	Lethargic	0 (1 hr), 24 hr-5
	Nasal/mouth discharge	0 (20.5 hr)-5
	Piloerection	3-5
	Ano-genital staining	5
	Dead	5 (11:10 AM)
3306	Hunched posture, irregular respiration	0 (0.5 hr)-5
	Lethargic	0 (3 hr), 24 hr-5
	Piloerection	0 (20.5), 3-5
	Nasal/mouth discharge	0 (20.5 hr)-5
	Gasping	5
	Dead	6
3307	Hunched posture, lethargic	0 (0.5 hr)-2
	Irregular respiration	0 (1 hr)-2
	Mouth/nasal discharge	0 (20.5 hr)-2
	Dead	2 (3:35 PM)
3308	Hunched posture, lethargic	0 (0.5 hr)-6
	Irregular respiration	0 (0.5 hr)-2, 5-6
	Tremors	0 (0.5)-1 hr
	Ano-genital staining	0 (20.5 hr)-4
	Mouth discharge	0 (20.5 hr)-24 hr
	Nasal discharge	0 (20.5 hr)-5
	Dead	7

TABLE - 12 (cont.)

INDIVIDUAL CAGE-SIDE OBSERVATIONS

DOSE LEVEL: 200 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>FEMALES</u>		
3309	Active and healthy	0 (0.5 hr)
	Hunched posture	0 (1 hr)-8
	Nasal discharge	0 (20.5 hr)-9
	Ocular discharge, irregular respiration, lethargic,	
	piloerection, mouth discharge	3-9
	Ano-genital staining	5-9
	Gasping	5-7
	Prone	9
	Dead	9 (2:45 PM)
3310	Active and healthy	0 (0.5 hr)
	Hunched posture	0 (1 hr)-3
	Tremors	0 (3 hr)
	Irregular respiration, lethargic, mouth discharge	0 (3 hr)-3
	Nasal discharge	0 (20.5 hr)-3
	Piloerection, ocular discharge	3
	Dead	4
3311	Tremors	0 (0.5 hr)
	Hunched posture	0 (0.5 hr)-7
	Facial staining	0 (20.5 hr)-3
	Nasal discharge	4-7
	Unthrifty	5-7
	Piloerection	6-7
	Dead	8
3312	Hunched posture, irregular respiration, lethargic	0 (0.5 hr)-2
	Gasping	0 (20.5 hr)-24 hr
	Mouth/nasal discharge	0 (20.5 hr)-2
	Ocular discharge	2
	Dead	3
3313	Hunched posture, irregular respiration	0 (0.5-1 hr)
	Lethargic, tremors	0 (1 hr)
	Dead	0 (3 hr)

TABLE - 13

INDIVIDUAL NECROPSY OBSERVATIONS

DOSE LEVEL: 200 mg/kg

<u>Animal Number</u>	<u>Tissue</u>	<u>Findings</u>
<u>MALES</u>		
3304, 3305	Lungs GI Tract	Mottled red Discolored
3306	Lungs GI Tract/Stomach	Mottled red Red
3307	Stomach/GI Tract Lungs	Discolored Mottled red
3308	Lungs GI Tract	Mottled red Red
<u>FEMALES</u>		
3309	Lungs GI Tract	Mottled red Red, moderate gaseous distention
3310	Lungs GI Tract	Mottled red Discolored
3311	Lungs GI Tract Stomach	Mottled red Discolored Connected to abdominal wall
3312	Stomach/GI Tract Lungs	Discolored Mottled red
3313	Stomach Lungs	Extremely red Mottled red

TABLE - 14

BODYWEIGHT, DOSAGE AND MORTALITY

DOSE LEVEL: 500 mg/kg

Animal No.	Sex	Bodyweight (g)			Actual Dose ¹		Mortality	
		Initial	Day 7	Day 14	mg/kg	ml	Day	Weight
3244	M	222	-	-	508	0.14	0	196
3245	M	228	-	-	494	0.14	5	158
3246	M	206	-	-	508	0.13	3	168
3247	M	202	-	-	518	0.13	5	132
3248	M	212	-	-	494	0.13	4	189
3249	F	201	-	-	481	0.12	0	197
3250	F	197	-	-	490	0.12	0	192
3251	F	201	134	-	481	0.12	8	121
3252	F	200	-	-	483	0.12	5	148
3253	F	205	-	-	510	0.13	0	200

¹ Administered as received. Specific Gravity - 0.805 g/ml.

TABLE - 15

INDIVIDUAL CAGE-SIDE OBSERVATIONS

DOSE LEVEL: 500 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>MALES</u>		
3244	Hunched posture, irregular respiration, mouth discharge, piloerection	0 (40 min-3 hr)
	Tremors	0 (1-3 hr)
	Lethargic	0 (3 hr)
	Dead	0 (22 hr)
3245	Tremors	0 (40 min)
	Hunched posture, irregular respiration	0 (40 min)-5
	Lethargic	0 (40 min-3 hr), 3-5
	Piloerection	0 (3 hr)-5
	Chromodacryorrhea	0 (22 hr)-5
	Decreased food consumption, moist rales	2
	Decreased fecal volume, facial staining	2-4
	Moist rales	2
Dead	5 PM	
3246	Tremors	0 (40 min-3 hr)
	Hunched posture, irregular respiration	0 (40 min)-3
	Lethargic, piloerection	0 (3 hr)-3
	Reduced food consumption, mouth discharge	2
	Chromodacryorrhea, reduced fecal volume	2-3
	Dead	3 (2:45 PM)
3247	Hunched posture, irregular respiration	0 (40 min)-4
	Lethargic	0 (3 hr)-4
	Dyspnea	0 (22 hr)-2
	Reduced food consumption	2
	Facial staining, reduced fecal volume	2-4
	Ocular discharge, piloerection	3-4
	Dead	5
3248	Hunched posture	0 (40 min)-3
	Irregular respiration, lethargic, piloerection	0 (1 hr)-3
	Tremors	0 (1-3 hr)
	Reduced food consumption	2
	Moist rales, reduced fecal volume	2-3
	Mouth/ocular discharge	3
	Dead	4

TABLE - 15 (cont.)

INDIVIDUAL CAGE-SIDE OBSERVATIONS

DOSE LEVEL: 500 mg/kg

<u>Animal Number</u>	<u>Finding</u>	<u>Day of Occurrence</u>
<u>FEMALES</u>		
3249, 3253	Dead	0 (40 min)
3250	Hunched posture, irregular respiration, gasping	0 (40 min)
	Dead	0 (1 hr)
3251	Tremors	0 (40 min-3 hr)
	Hunched posture	0 (40 min)-7
	Irregular respiration, lethargic	0 (1 hr)-7
	Piloerection	0 (1 hr)-1
	Facial staining	0 (22 hr)-2
	Reduced food consumption	2
	Chromodacryorrhea	2-7
	Reduced fecal volume	2-4
	Mouth, ocular discharge	3-7
	Dead	8
3252	Hunched posture, irregular respiration	0 (40 min)-4
	Tremors	0 (3 hr)
	Facial staining	0 (22 hr)-2
	Piloerection	0 (1-22 hr), 3-4
	Lethargic	0 (22 hr)-4
	Mouth/ocular discharge, ano-genital staining, reduced fecal volume	3-4
	Dead	5

TABLE - 16

INDIVIDUAL NECROPSY OBSERVATIONS

DOSE LEVEL: 500 mg/kg

<u>Animal Number</u>	<u>Tissue</u>	<u>Findings</u>
<u>MALES</u>		
3244	Lungs GI Tract Liver	Moderately red Extremely brown, distended w/dark fluid Mottled moderately brown
3245	Lungs Stomach/GI Tract	Mottled red Extremely distended, red/black/green
3246, 3248	Lungs GI Tract	Mottled red Yellow/red/black, gaseous distention
3247	Lungs GI Tract Stomach	Mottled red Discolored Green/black/red
<u>FEMALES</u>		
3249	Lungs Stomach Wall	Mottled red, slight edema Black/green/red
3250	Lungs Stomach Wall	Mottled red Black/green/red
3251	Lungs Stomach/GI Tract	Mottled red Discolored
3252	Lungs GI Tract Stomach	Mottled red Discolored Green/black/red
3253	Lungs Stomach Wall	Red, moderate edema Black/green/red

APPENDIX A

Animal feed analysis independently performed on September 20, 1993 for presence of chlorinated insecticides:

Aldrin	DDE
Dieldrin	DDD
Heptachlor	DDT
Heptachlor Epoxide	Endosulfan I & II
Chlordane	Endrin
Methoxychlor	Endrin aldehyde
alpha, beta, delta & gamma BHC	Toxaphene
	Endosulfan Sulfate

and for the presence of organophosphate insecticides:

Malathion	Ethyl Parathion
Methyl Parathion	Ethion
Diazinon	Parathion

LABORATORY: INDUSTRIAL LABORATORIES
1450 East 62nd Street
Denver, CO 80216

STUDY NUMBERS: IL93107446, IL93107447 and IL93107448

Water analysis performed on August 19, 1993 for NJDEPE Safe Drinking Water Act parameters and percent fluoride content.

LABORATORY: NEW JERSEY LABORATORIES
DEPE #12660
A.A. Labs Division
222 Easton Avenue
New Brunswick, NJ 08901

STUDY NUMBER: 12660

Results of feed and water tests: Acceptable; none detected or within regulatory standards.

QUALITY ASSURANCE INSPECTIONS

Intervals for QA inspections are randomly selected prior to study initiation by the Quality Assurance Unit, if not previously selected by the sponsor or Study Director. Records of the results of these procedures are kept on file; the summary below provides verification of statements made in the final report section which addresses Quality Assurance audits.

For Study No. 3027, inspections were made of:

RAW DATA 8-2, 8-3-94

DRAFT REPORT 8-2, 8-3

FINAL REPORT 8-10-94

LABORATORY RECORDS: ENVIRONMENTAL MAINTENANCE OF ROOM(S)
ANIMAL RECEIPT OTHER _____

PREPARATION OF: TEST MATERIAL TEST DIET CONTROL DIET(S)

TEST INITIATION (dosing) 5-31-94

INITIAL BODY WEIGHTS 5-13-94

BODY WEIGHTS POST-INITIATION DAY 7 DAY 7 DAY
5-13-94 7-15-94

TERMINAL BODY WEIGHTS 6-21-94 DAY 5 DAY DAY
5-16-94

IN-LIFE OBSERVATIONS DAY 5 DAY DAY
5-16-94

EVALUATION OF CONDITIONS PRODUCED FROM DOSING

NECROPSY 6-21-94

OTHER: Decedent bodyweight collection + necropsy 6/3/94;

Findings reported to: Study Director 5/17, 6/1, 6/16, 6/22, 8/3/94, 7/15/94, 6/13/94

Management 6/10/94, 6/23, 7/20/94

Comments: Total of 5 test groups.


Kathryn Hackett-Fields 8-10-94
Quality Assurance Auditor