

R & D REPORT

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A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPB: (SPRAGUE-DAWLEY)		HET T-1.1-3-(3)			
RATS AND CD ⁰ F (FISCHER 344-DERIVED) RATS		DATE ISSUED		March 18, 1980	
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K. J. Olson and K. S. Rao		☐ FINAL		and mainly: ☐ REVIEW	
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DESCRIPTIVE SUMMARY WITH CONCLUSIONS:					
Subchronic and chronic toxicity studies at the Toxicology Research Laboratory are currently conducted using CD⁰F (Fischer 344-derived) rats. In contrast, acute oral toxicity tests are currently conducted using Spb: (Sprague-Dawley) rats. In order to conform with repeated administration data, it has been suggested that acute oral toxicity tests should be conducted using CDF rats. This study was conducted to determine if strain differences in mortality, behavior, or pathology in response to single oral doses of a given compound exist. CDF rats (Charles River Breeding Laboratories, Portage, Michigan) and Sprague-Dawley rats (Spartan Research Animals, Inc., Haslett, Michigan), 7-8 weeks of age, received one of the following compounds: epichlorohydrin, 2,4,5-trichlorophenoxy acetic acid, allyl chloride, malathion, acrylic acid, or benzene. Five rats/sex/strain/dose level received doses of the chosen compound by single-dose oral gavage. Following dosage, body weights and behavioral signs of toxicity were monitored for 2 weeks. Survivors were submitted for gross pathological examination 2 weeks post-treatment. A 2-week single-dose oral LD50 for each sex and strain for each compound was calculated. Overall, a comparison of LD50 values revealed that CDF rats appeared to be at least as sensitive, if not slightly more sensitive, than Sprague-Dawley rats when dosed orally. Subtle differences in behavior also indicated that CDF rats may be slightly more sensitive to certain chemicals than Sprague-Dawley rats. Both strains were comparable with regard to body weight gain. With regard to gross pathology, Sprague-Dawley rats appeared to be slightly more sensitive than CDF rats when dosed with epichlorohydrin or benzene. In both instances Sprague-Dawley rats exhibited an increased incidence of gastric irritation when compared to CDF rats. For the remaining 4 compounds, both strains appeared to be equally sensitive, with regard to gross pathology data.					
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A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CD[®]F (FISCHER 344-DERIVED) RATS

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These data indicate that CDF and Sprague-Dawley rats are essentially comparable in overall response to single oral doses of a given chemical. It is therefore concluded that the use of CDF rats in acute oral toxicity studies is feasible and would not jeopardize the credibility of the existing Sprague-Dawley data base.

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SUMMARY

Subchronic and chronic toxicity studies at the Toxicology Research Laboratory are currently being conducted using CD[®]F (Fischer 344-derived) rats. In contrast, acute oral toxicity tests are currently conducted using Spb: (Sprague-Dawley) rats. In order to conform with repeated administration data, it has been suggested that acute oral toxicity tests should be conducted using CDF rats. This study was conducted to determine if strain differences in mortality, behavior, or pathology in response to single oral doses of a given compound exist.

CDF rats (Charles River Breeding Laboratories, Portage, Michigan) and Sprague-Dawley rats (Spartan Research Animals, Inc., Haslett, Michigan), 7-8 weeks of age, received one of the following compounds: epichlorohydrin, 2,4,5-trichlorophenoxy acetic acid, allyl chloride, malathion, acrylic acid, or benzene. Five rats/sex/strain/dose level received doses of the chosen compound by single-dose oral gavage. Following dosage, body weights and behavioral signs of toxicity were monitored for 2 weeks. Survivors were submitted for gross pathological examination 2 weeks post-treatment.

A 2-week single-dose oral LD50 for each sex and strain for each compound was calculated. Overall, a comparison of LD50 values revealed that CDF rats appeared to be at least as sensitive, if not slightly more sensitive, than Sprague-Dawley rats when dosed orally. Subtle differences in behavior also indicated that CDF rats may be slightly more sensitive

to certain chemicals than Sprague-Dawley rats. Both strains were comparable with regard to body weight gain. With regard to gross pathology, Sprague-Dawley rats appeared to be slightly more sensitive than CDF rats when dosed with epichlorohydrin or benzene. In both instances Sprague-Dawley rats exhibited an increased incidence of gastric irritation when compared to CDF rats. For the remaining 4 compounds, both strains appeared to be equally sensitive with regard to gross pathology data.

These data indicate that CDF and Sprague-Dawley rats are essentially comparable in overall response to single oral doses of a given chemical. It is therefore concluded that the use of CDF rats in acute oral toxicity studies is feasible and would not jeopardize the credibility of the existing Sprague-Dawley data base.

INTRODUCTION

Subchronic and chronic toxicity studies at the Toxicology Research Laboratory are currently conducted using CD[®]F (Fischer 344-Derived) rats (Charles River Breeding Laboratories, Inc., Portage, Michigan) because of their survivability, low mammary tumor incidence, and low incidence of severe chronic renal disease. In contrast, acute oral toxicity tests are currently conducted using Spb: (Sprague-Dawley) rats (Spartan Research Animals, Inc., Haslett, Michigan). In order to conform with repeated administration data, it has been suggested that acute oral toxicity tests should be conducted using CDF rats. The purpose of this study was to compare the single-dose oral LD50's and slopes of the dose-response curves for given compounds using both CDF and Sprague-Dawley rats.

EXPERIMENTAL

Test Articles

Six test articles were chosen on the basis of differing chemical structures, universality, availability, and differing acute oral LD50's for rats. The names of these test articles, structures, lot numbers or sources, analyses, and rat oral LD50's obtained from the literature are given in Table 1.

Test Animals

Acute oral toxicity tests were conducted on male and female Spb: (Sprague-Dawley) rats (Spartan Research Animals, Inc., Haslett, Michigan), 7-8 weeks of age, and male and female CD[®]F (Fischer 344-Derived) rats (Charles River Breeding Laboratories, Inc., Portage, Michigan), 7-8 weeks of age. All rats were maintained on a 12-hour light and dark cycle in animal care facilities fully accredited by the American Association for Accreditation of Laboratory Animal Care. The animal rooms are designed to maintain a temperature of 73°F and relative humidity of 45%, and to provide an air change approximately every 5 minutes. All rats were acclimated to the laboratory environment at least 1 week prior to testing, and all were uniquely identified by an individual metal ear tag. Rats were housed 2 or 3/cage, and were maintained on a diet of commercial laboratory chow (Ralston Purina Company, St. Louis, Missouri) and water ad libitum.

Design

Groups of rats, each consisting of 5 rats/sex/strain, initially received 4 dose levels of the selected test article by single-dose oral gavage. If

these initial dose levels failed to cause mortality, or, if a partial effect level was not achieved, more dose levels were added to calculate an LD50. Table 2 gives the test article, vehicle, and dose levels which each strain and sex received. The maximum volume with which Sprague-Dawley rats were dosed was 4.7 ml, while that for CDF rats was 2.8 ml.

All rats were fasted 16-18 hours prior to dosing. Each rat was weighed immediately prior to treatment, and weekly thereafter for a 2-week post-treatment observation period. The rats were observed each working day during this time for signs of toxicity. Survivors only were submitted for gross pathological examination (as described in the Pathology Group Standard Operating Procedures) 2 weeks post-treatment.

Statistics The acute oral median lethal dose, 95% confidence interval, and approximate slope of the dose-response curve for both strains for all test articles were calculated by the moving average method of Thompson and Weil (1952), as implemented by a computer program (Stephan, 1978). The approximate slope was calculated as $1/2 \log_{10} (LD84/LD16)$. Because this computer program also computes LD50's, 95% confidence intervals, and slopes by probit analysis (Finney, 1972), the values obtained from both methods of analysis are reported to assess the comparability of the 2 procedures.

RESULTS AND DISCUSSION

Animal Observations

Mortality of test rats, including LD50 and slope determinations, is given in Tables 3-8. With regard to mortality data, male and female

CDF rats appeared to be slightly more sensitive than Sprague-Dawley rats to benzene. Although the mortality of female rats of both strains receiving acrylic acid was comparable, male CDF rats appeared to be more sensitive than male Sprague-Dawley rats. Female CDF rats receiving 2,4,5-trichlorophenoxy acetic acid were actually less sensitive with regard to mortality than female Sprague-Dawley rats; both strains of male rats receiving 2,4,5-trichlorophenoxy acetic acid were comparable with regard to mortality. Males and females of both strains appeared to be equally sensitive to oral doses of epichlorohydrin, allyl chloride, and malathion.

Behavioral observations made during the 2-week post-treatment observation period are given in Tables 9-14. With regard to this parameter, no basic differences were observed between the strains when dosed with malathion. However, subtle behavioral differences between strains did occur for all other compounds tested. Female CDF rats dosed with 398 and 795 mg/kg epichlorohydrin had diarrhea, whereas female Sprague-Dawley rats did not; diarrhea was not observed in male rats of either species at any dose level. Following dosage with 2,4,5-trichlorophenoxy acetic acid, only CDF rats had piloerection. This observation may be equivocal, as CDF rats initially have rougher haircoats than Sprague-Dawley rats. Dosage with 795 mg/kg allyl chloride resulted in convulsions in 1/5 male CDF rats and 1/5 female CDF rats; no convulsions were observed in Sprague-Dawley rats. In general, CDF rats dosed with acrylic acid exhibited signs of toxicity at lower dose levels than did Sprague-Dawley rats. Of the rats receiving 2520 mg/kg benzene, only male Sprague-Dawley rats had dark exudate around the nose. In addition, only 1 female Sprague-Dawley rat of the 5000 mg/kg dose group had convulsions.

Mean ($\pm$ standard deviation) body weights of test rats are given in Tables 15-20. Male CDF rats dosed with 795 mg/kg and female Sprague-Dawley rats dosed with 398 mg/kg 2,4,5-trichlorophenoxy acetic acid exhibited a body weight loss during the 2-week post-treatment observation period. The body weights of these rats could not be compared to those of the opposite strain because they did not receive comparable doses. Individual male Sprague-Dawley rats of the 630, 1260 and 1580 mg/kg groups, female Sprague-Dawley rats of the 63, 126 and 158 mg/kg groups, male CDF rats of the 63, 126, 158 and 316 mg/kg groups, and female CDF rats of the 31.6, 63, 126, 158, 316 and 630 mg/kg groups exhibited a body weight loss 2 weeks after dosage with acrylic acid. Although a comparison of body weight loss is difficult due to the different doses received by each strain, the body weight losses of overlapping doses indicate that both strains were equally sensitive.

Pathology

Gross pathologic findings in both strains of rat for all test materials are presented in Tables 21-26. Comparison of both strains with regard to gross pathology was difficult because rats of each strain sometimes received different doses of the same compound. Of the rats which

could be compared, those receiving 2,4,5-trichlorophenoxy acetic acid, allyl chloride, malathion, and acrylic acid exhibited no major strain differences. The majority of Sprague-Dawley rats dosed with 100 mg/kg of epichlorohydrin exhibited thickening and roughening of the squamous epithelium of the stomach. Only 1 of 5 male CDF rats of the 100 mg/kg dose group exhibited gastric irritation; this was not seen in female CDF rats of the same group. Signs of gastric irritation were observed in both Sprague-Dawley and CDF rats dosed with 200 mg/kg epichlorohydrin. Thickening and roughening of the squamous epithelium of the stomach was also observed in female Sprague-Dawley rats dosed with 398 mg/kg of 2,4,5-trichlorophenoxy acetic acid. This observation may be equivocal, however, as gastric irritation was not observed in female Sprague-Dawley rats dosed with higher or lower doses. Thickening and roughening of the squamous epithelium of the stomach was observed in male Sprague-Dawley rats dosed with 630, 1260 or 2520 mg/kg benzene. These rats also exhibited focal thickening of the nonglandular stomach wall and erosion of the nonglandular epithelium of the stomach at the 2520 mg/kg dose level. Female Sprague-Dawley rats and male and female CDF rats did not exhibit gastric irritation at the 630 mg/kg level, and the incidence of this irritation at higher doses was greatly reduced over that of male Sprague-Dawley rats. No gastric irritation was observed in CDF rats fed 2520 mg/kg.

SUMMARY AND CONCLUSIONS

The purpose of this study was to compare the single-dose oral LD₅₀'s and slopes of the dose-response curves of CDF and Sprague-Dawley rats for each compound tested. Overall, a comparison of LD₅₀ values revealed that CDF rats appeared to be at least as sensitive, if not slightly more sensitive, than Sprague-Dawley rats when dosed orally. LD₅₀ values obtained by the moving average and probit methods of analysis correlated well. It is obvious, however, that the moving average method is more versatile than the probit method, as only 1 partial effect level is needed to estimate the LD₅₀.

The slope values obtained in this study were extremely variable, and it was concluded that more rats per dose would be needed to accurately determine a slope. Therefore, it was decided to eliminate slope values as a basis for comparing strains.

Subtle differences in behavior observed up to 2 weeks following dosage indicated that CDF rats may be slightly more sensitive than Sprague-Dawley rats. The behavioral responses of CDF rats appear to be slightly more obvious to the observer.

Body weight data indicated that both strains were essentially comparable.

With regard to gross pathology, Sprague-Dawley rats appeared to be slightly more sensitive than CDF rats when dosed with epichlorohydrin or benzene. In both instances Sprague-Dawley rats exhibited an increased incidence of gastric irritation when compared to CDF rats. For the remaining 4 compounds, both strains appeared to be equally sensitive.

These data indicate that CDF and Sprague-Dawley rats are essentially comparable in overall response to oral doses of a given chemical.

It is therefore concluded that the use of CDF rats in acute oral toxicity studies is feasible and would not jeopardize the credibility of the existing Sprague-Dawley data base.

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A Comparison of Single-Dose ORAL LD50's For SPB:
TITLE OF STUDY: (Sprague-Dawley) Rats and CD⁰F (Fischer 344-Derived) Rats

In compliance with Good Laboratory Practice Regulations, this study was inspected by the Quality Assurance Unit and the results of these inspections reported to Management and the Study Director on the dates listed below. The report accurately reflects the data generated in accordance with the regulations and standard operating procedures of the Laboratory. All data and the reports are located at the submitting laboratory.

Study Started: April 3, 1979

Report Issued Date: _____

Dates of Inspection: March 1979

Date of Report: March 1979

25 Oct 79

2 Nov 1979

28 Jan 80

5 Feb 80

20 Feb 80

21 Feb 80

W. E. Hoover

31 Mar 80
(Date)

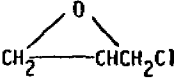
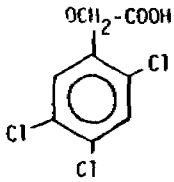
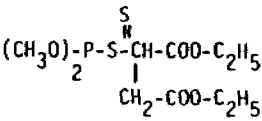
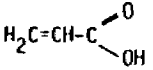
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Table 1

A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SIB: (SPRAGUE-DAWLEY) RATS AND CD¹F (FISCHER 344-DERIVED) RATS

TEST ARTICLES USED

TEST TEST ARTICLE	STRUCTURE	LOT NUMBER OR SOURCE	ANALYSIS	RAT ORAL LD50
Epichlorohydrin		TB 10047-1	99.8% Epichlorohydrin; 0.11% 2,3-dichloropropene; 0.03% cis-1,3-dichloropropene; 0.01% α-chloroallyl alcohol (Mensik, 1978).	90 mg/kg (Christensen <u>et al.</u> , 1973)
(2,4,5-trichlorophenoxy) acetic acid		AGR 133711	99.1% (2,4,5-Trichlorophenoxy) acetic acid; 0.67% 2,5-dichloro-4-methoxyphenoxyacetic acid; + 2,4,-dichloro-5-methoxyphenoxyacetic acid; 0.34% 4,5-dichloro-2-methoxyphenoxyacetic acid; 0.12% 2,5-dichlorophenoxy acetic acid; 0.14% unknown; 0.02% 2,4-dichlorophenoxyacetic acid; other impurities were below the detection limit of 0.02% (Kociba, <u>et al.</u> , 1978)	300-500 mg/kg (Rowe, 1945)
Allyl chloride	$H_2C = CHCH_2Cl$	TB 06308-3	98.6% Allyl chloride; 0.74% isopropyl chloride; 0.40% 1,5-hexadiene; 0.14% normal propyl chloride; 0.10% 2,2-dichloropropane (Mensik, 1978)	700 mg/kg (Christensen, <u>et al.</u> , 1973)
Malathion (diethyl mercaptosuccinate - O,O-dimethyl diethiophosphate)		American Cyanamid Company	96% O,O-dimethylphosphorodithioate of diethyl mercaptosuccinate; 4% inert ingredients (American Cyanamid Company)	1156 mg/kg (Christensen, <u>et al.</u> , 1973)
Acrylic acid		Vessel 547 (9/8/78)	99.7% Acrylic acid; 0.08% water; trace amounts of dimer, acetic acid, propionic acid; acrolein, ethyl acrylate, phenothiazine proto-anemonin, Furfural (Bailey, 1978)	2590 mg/kg (Christensen, <u>et al.</u> , 1973)
Benzene		J. T. Baker Chemical Co. #715990	Not available	3400 mg/kg (Christensen, <u>et al.</u> , 1973)

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Table 2
A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CDF (FISCHER 344-DERIVED) RATS
TEST ARTICLES, VEHICLES AND DOSAGES RECEIVED

TEST ARTICLE	VEHICLE	DOSE LEVELS (mg/kg)
Epichlorohydrin	Undiluted	Male Sprague-Dawley Rat : 25, 50, 100, 200, 398, 795
		Female Sprague-Dawley Rat: 25, 50, 100, 200, 398, 795
		Male CDF Rat : 25, 50, 100, 200, 210, 225, 252, 398, 795
		Female CDF Rat : 25, 50, 100, 200, 210, 225, 252, 398, 795
(2,4,5-Trichlorophenoxy) acetic acid	Acetone/corn oil ^a (1:9)	Male Sprague-Dawley Rat : 126, 252, 500, 1000, 1580
		Female Sprague-Dawley Rat: 126, 252, 350, 398, 450, 500, 1000
		Male CDF Rat : 126, 252, 500, 795, 1000, 2000
		Female CDF Rat : 126, 252, 500, 1000, 2000
Allyl Chloride	Undiluted	Male Sprague-Dawley Rat : 200, 390, 795, 1580
		Female Sprague-Dawley Rat: 200, 398, 795, 1580
		Male CDF Rat : 200, 398, 795, 1580
		Female CDF Rat : 63, 126, 200, 398, 795, 1580
Malathion	Undiluted	Male Sprague-Dawley Rat : 252, 500, 1000, 2000, 2100, 2250, 2520, 3980
		Female Sprague-Dawley Rat: 252, 500, 1000, 2000, 3980
		Male CDF Rat : 252, 500, 1000, 2000, 2520, 3980
		Female CDF Rat : 252, 500, 1000, 2000, 3980
Acrylic Acid	Undiluted	Male Sprague-Dawley Rat : 630, 1260, 1580, 2000, 2520, 5000
		Female Sprague-Dawley Rat: 63, 126, 158, 316, 630, 1260, 2520, 5000
		Male CDF Rat : 63, 126, 158, 316, 630, 1260, 2520, 5000
		Female CDF Rat : 31.6, 63, 126, 158, 316, 630, 1260, 2520, 5000
Benzene	Undiluted	Male Sprague-Dawley Rat : 630, 1260, 2520, 3160, 5000
		Female Sprague-Dawley Rat: 630, 1260, 2520, 5000, 10,000
		Male CDF Rat : 316, 630, 1260, 2520, 5000, 10,000
		Female CDF Rat : 316, 630, 1260, 2520, 5000

a) Corn oil - CX 1955 L543, Matheson Coleman and Bell Manufacturing Chemists

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Table 3
A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPE:
(SPRAGUE-DAWLEY) RATS AND CD[®]F (FISCHER 344-DERIVED) RATS

EPICHLOROHYDRIN: MORTALITY

Dose (mg/kg)	# Dead/# Treated			
	Male Sprague-Dawley	Female Sprague-Dawley	Male CDF	Female CDF
25	0/5	0/5	0/5	0/5
50	0/5	0/5	0/5	0/5
100	0/5	0/5	0/5	0/5
200	1/5	2/5	0/5	0/5
210	-	-	0/5	3/5
225	-	-	5/5	5/5
252	-	-	5/5	5/5
398	4/5	5/5	5/5	5/5
795	5/5	5/5	5/5	5/5

	Moving Average	Probit	Moving Average	Probit	Moving Average	Moving ^b Average
Single-dose Oral LD50 (mg/kg)	282	282	175	183	~218 ^a	210
95% Confidence Interval (mg/kg)	117-448	162-490	116-306	106-330	-	203-216
Slope	3.91	6.04	3.06	4.55	-	18.28

- a) No partial-effect level could be achieved for male CDF rats. Therefore, the LD50 is estimated by the average of 210 mg/kg (0% kill) and 225 mg/kg (100% kill).
- b) Probit could not be computed because less than 2 concentrations at which the percent dead was between 0 and 100 were achieved.

Table 4

A COMPARISON OF SINGLE-DOSE ORAL LD50's FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CD[®]F (FISCHER 344-DERIVED) RATS

2,4,5-TRICHLOROPHENOXY ACETIC ACID

Dead/# Treated

<u>Dose (mg/kg)</u>	<u>Male Sprague-Dawley</u>	<u>Female Sprague-Dawley</u>	<u>Male CDF</u>	<u>Female CDF</u>
126	0/5	0/5	0/5	0/5
252	0/5	0/5	0/5	0/5
350	-	0/5	-	-
398	-	1/5	-	-
450	-	0/5	-	-
500	1/5	5/5	0/5	0/5
795	-	-	4/5	-
1000	5/5	5/5	5/5	3/5
1580	5/5	-	-	-
2000	-	-	5/5	5/5

	Moving ^a Average	Moving ^a Average	Moving ^a Average	Moving ^a Average
Single-dose Oral LD50 (mg/kg)	588	474	692	950
95% Confidence Interval (mg/kg)	428-906	442-568	557-811	650-1339
Slope	4.82	12.46	7.06	4.23

a) Probit could not be computed because less than 2 concentrations at which the percent dead was between 0 and 100 were achieved.

Table 5

A COMPARISON OF SINGLE-DOSE ORAL LD50's FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CD[®]F (FISCHER 344-DERIVED) RATS

ALLYL CHLORIDE: MORTALITY

Dead/# Treated

<u>Dose (mg/kg)</u>	<u>Male Sprague-Dawley</u>	<u>Female Sprague-Dawley</u>	<u>Male CDF</u>	<u>Female CDF</u>
63	-	-	-	0/5
126	-	-	-	3/10
200	0/5	0/5	0/5	1/5
398	3/5	3/5	2/5	2/5
795	5/5	4/5	5/5	5/5
1580	5/5	5/5	5/5	5/5

	Moving ^a Average	Moving Average	Probit	Moving ^a Average	Moving Average	Probit
Single-dose Oral LD50 (mg/kg)	379	455	435	419	275	293
95% Confidence Interval (mg/kg)	259-533	260-685	241-751	298-612	180-526	177-719
Slope	4.64	3.44	4.56	4.25	2.18	2.54

a) Probit could not be computed because less than 2 concentrations at which the percent dead was between 0 and 100 were achieved.

Table 6

A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CD[®]F (FISCHER 344-DERIVED) RATS

MALATHION: MORTALITY

Dead/# Treated

<u>Dose (mg/kg)</u>	<u>Male Sprague-Dawley</u>	<u>Female Sprague-Dawley</u>	<u>Male CDF</u>	<u>Female CDF</u>
252	0/5	0/5	0/5	0/5
500	0/5	0/5	0/5	0/5
1000	0/5	0/5	0/5	0/5
2000	0/5	2/5	1/5	3/5
2100	3/5	-	-	-
2250	5/5	-	-	-
2520	5/5	-	10/10	-
3980	5/5	5/5	4/4	5/5

	Moving ^a Average	Moving ^a Average	Moving ^a Average	Moving ^a Average
Single-dose Oral LD50 (mg/kg)	2101	2102	1875	1898
95% Confidence Interval (mg/kg)	2035-2164	1493-3068	1578-2191	1300-2671
Slope	18.28	4.63	7.49	4.24

- a) Probit could not be computed because less than 2 concentrations at which the percent dead was between 0 and 100 were achieved.

Table 7

A COMPARISON OF SINGLE-DOSE ORAL LD50's FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CDF (FISCHER 344-DERIVED) RATS

ACRYLIC ACID: MORTALITY

Dose (mg/kg)	# Dead/# Treated			
	Male Sprague-Dawley	Female Sprague-Dawley	Male CDF	Female CDF
31.6	-	-	-	0/5
63	-	0/5	0/5	3/9 ^a
126	-	3/10	2/5	0/5
158	-	1/9 ^a	4/5	2/5
316	-	2/5	3/4 ^a	1/4 ^a
630	0/5	1/5	5/5	2/5
1260	1/5	3/5	5/5	6/9 ^a
1580	4/5	-	-	-
2000	5/5	-	-	-
2520	5/5	5/5	5/5	5/5
5000	5/5	5/5	5/5	5/5

	Moving Average	Probit	Moving Average	Probit	Moving Average	Probit	Moving Average	Probit
Single-dose Oral LD50 (mg/kg)	1337	1409	718	617	151	146	526	468
95% Confidence Interval (mg/kg)	936-1680	1030-1750	408-1567	323-2120	94-227	84-255	308-979	211-1497
Slope	7.82	17.79	1.50	1.52	3.18	3.91	1.23	1.21

- a) Because the test material was deposited into the lungs of 1 rat of this test group, this rat was not considered in LD50 calculations.

Table 8
A COMPARISON OF SINGLE-DOSE ORAL LD50's FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CDF (FISCHER 344-DERIVED) RATS

BENZENE: MORTALITY

Dose (mg/kg)	# Dead/# Treated			
	Male Sprague-Dawley	Female Sprague-Dawley	Male CDF	Female CDF
316	-	-	0/5	0/5
630	0/5	0/5	3/10	2/10
1260	1/5	1/5	1/5	1/5
2520	0/5	3/5	4/5	3/5
3160	4/5	-	-	-
5000	5/5	2/5	4/5	5/5
10,000	-	5/5	5/5	-

	Moving Average	Probit	Moving Average	Probit	Moving Average	Probit	Moving Average	Probit
Single-dose Oral LD50 (mg/kg)	3093	2654	2951	3123	1618	1527	1606	1659
95% Confidence Interval (mg/kg)	2495-3621	1582-4074	1790-5458	1606-6830	369-2856	855-2982	1047-2902	1012-1100
Slope	6.86	4.71	2.19	2.54	2.01	2.26	2.65	2.81

Table 9

A COMPARISON OF SINGLE-DOSE ORAL LD50's FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CD®F (FISCHER 344-DERIVED) RATS

EPICHLOROHYDRIN: BEHAVIORAL SIGNS OF TOXICITY

Dose (mg/kg)	Signs of Toxicity ^a	# Affected/# Treated			
		Male Sprague-Dawley	Female Sprague-Dawley	Male CDF	Female CDF
200	Slight lethargy	5/5	5/5	5/5	0/5
210	Slight lethargy Piloerection	-	-	5/5 5/5	5/5 5/5
225	Lethargy Piloerection	-	-	5/5 5/5	5/5 5/5
252	Extreme Lethargy Piloerection Shallow breathing Darkened extremities	-	-	5/5 5/5 5/5 5/5	5/5 0/5 5/5 0/5
398	Lethargy Hyperactivity Watery eyes Diarrhea	5/5 1/5 0/5 0/5	5/5 0/5 0/5 0/5	5/5 0/5 0/5 0/5	5/5 0/5 5/5 5/5
795	Lethargy Severe diarrhea	5/5 0/5	5/5 0/5	5/5 0/5	5/5 5/5

a) No signs of toxicity were observed in rats of the 25, 50, or 100 mg/kg dose groups.

Table 10

A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CD[®]F (FISCHER 344-DERIVED) RATS
2,4,5-TRICHLOROPHENOXY ACETIC ACID: BEHAVIORAL SIGNS OF TOXICITY

Dose (mg/kg)	Signs of Toxicity ^a	# Affected/# Treated			
		Male Sprague-Dawley	Female Sprague-Dawley	Male CDF	Female CDF
252	Slight lethargy	5/5	0/5	5/5	0/5
350	None	-	5/5	-	-
398	Slight lethargy	-	3/5	-	-
450	None	-	5/5	-	-
500	Lethargy Piloerection	5/5 0/5	5/5 0/5	5/5 5/5	5/5 5/5
795	Lethargy Piloerection	-	-	5/5 5/5	-
1000	Lethargy Piloerection Diarrhea	5/5 0/5 0/5	5/5 0/5 0/5	5/5 5/5 0/5	5/5 5/5 3/5
1580	Lethargy	5/5	-	-	-
2000	Lethargy Piloerection Diarrhea	-	-	5/5 5/5 0/5	5/5 0/5 3/5

a) No signs of toxicity were observed in rats of the 126 mg/kg dose group.

Table 11
A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CD[®]F (FISCHER 344-DERIVED) RATS

ALLYL CHLORIDE: BEHAVIORAL SIGNS OF TOXICITY

<u>Dose (mg/kg)</u>	<u>Signs of Toxicity</u>	# Affected/# Treated			
		<u>Male Sprague-Dawley</u>	<u>Female Sprague-Dawley</u>	<u>Male CDF</u>	<u>Female CDF</u>
63	Slight lethargy	-	-	-	5/5
126	Slight lethargy	-	-	-	10/10
200	Lethargy	5/5	5/5	5/5	5/5
	Piloerection	0/5	0/5	5/5	5/5
398	Lethargy	5/5	5/5	5/5	5/5
	Diarrhea	3/5	3/5	2/5	2/5
	Piloerection	0/5	5/5	5/5	5/5
795	Extreme lethargy	5/5	5/5	5/5	5/5
	Diarrhea	5/5	4/5	5/5	5/5
	Piloerection	0/5	0/5	0/5	0/5
	Convulsions	0/5	0/5	1/5	1/5
1580	Extreme lethargy	5/5	5/5	5/5	5/5
	Severe diarrhea	5/5	5/5	5/5	5/5

Table 12

A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CD[®]F (FISCHER 344-DERIVED) RATS
MALATHION: BEHAVIORAL SIGNS OF TOXICITY
Affected/# Treated

<u>Dose (mg/kg)</u>	<u>Signs of Toxicity</u>	<u>Male Sprague-Dawley</u>	<u>Female Sprague-Dawley</u>	<u>Male CDF</u>	<u>Female CDF</u>
500	None	5/5	5/5	2/5	5/5
	Slight lethargy	0/5	0/5	3/5	0/5
1000	None	5/5	0/5	0/5	0/5
	Total body tremors	0/5	5/5	0/5	5/5
	Bluish face	0/5	5/5	0/5	0/5
	Slight lethargy	0/5	0/5	5/5	5/5
2000	Total body tremors	5/5	5/5	5/5	5/5
	Piloerection	5/5	0/5	5/5	0/5
	Heightened tail color	5/5	0/5	0/5	0/5
	Slight lethargy	5/5	0/5	5/5	5/5
	Bluish face	0/5	5/5	0/5	0/5
2100	Total body tremors	5/5	-	-	-
	Lethargy	5/5	-	-	-
	Piloerection	1/5	-	-	-
	Convulsions	5/5	-	-	-
2250	Total body tremors	3/3 ^b	-	-	-
	Dark exudate around eyes	1/1 ^b	-	-	-
2520	Total body tremors	5/5	-	0/5	-
	Slight lethargy	0/5	-	5/5	-
3980	Lethargy	2/2 ^b	0/5	3/5	0/5
	Gasping	2/2 ^b	0/5	0/5	0/5
	None	0/2 ^b	5/5	4/5	5/5
	Total body tremors	0/5	0/5	1/5	0/5

- a) No signs of toxicity were observed in rats of the 252 mg/kg dose group.
- b) The number affected given is per number of survivors.

Table 13

A COMPARISON OF SINGLE-DOSE OPAL LIR-O's FOR LTB:
 (SPRAGUE-DAWLEY) RATS AND CDF (FISCHER 344-DERIVED) RATS
 ACRYLIC ACID: BEHAVIORAL SIGNS OF TOXICITY

Dose (mg/kg)	Signs of Toxicity	# Affected/# Treated			
		Male Sprague-Dawley	Female Sprague-Dawley	Male CDF	Female CDF
31.6	None	-	-	-	5/5
63	Lethargy	-	0/5	5/5	5/5
	Piloerection		0/5	5/5	5/5
	Dark exudate around nose and mouth		0/5	0/5	5/5
126	Slight lethargy	-	3/10	5/5	0/5
	Piloerection		0/10	5/5	0/5
	None		0/10	0/5	5/5
158	None	-	9/9 ^b	0/5	0/5
	Lethargy		0/9	5/5	5/5
	Piloerection		0/9	3/3 ^a	0/5
316	Lethargy	-	5/5	4/4 ^b	4/4 ^b
	Piloerection		0/5	4/4	4/4
630	Lethargy	5/5	5/5	5/5	5/5
	Piloerection	5/5	0/5	5/5	5/5
	Dark exudate around nose and mouth	0/5	0/5	5/5	0/5
1260	Lethargy	5/5	5/5	5/5	9/9 ^b
	Piloerection	5/5	5/5	5/5	9/9
	Dark exudate around nose and mouth	0/5	0/5	5/5	4/9
1580	Lethargy	5/5	-	-	-
2000	Lethargy	5/5	-	-	-
2520	Lethargy	5/5	5/5	5/5	5/5
5000	Lethargy	5/5	5/5	5/5	5/5

a) The number affected given is per number of survivors.

b) Because the test material was deposited into the lungs of 1 rat of this test group, this rat was not considered in the observation.

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Table 14

A COMPARISON OF SINGLE-DOSE ORAL LD50's FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CD⁶F (FISCHER 344-DERIVED) RATS

BENZENE: BEHAVIORAL SIGNS OF TOXICITY

Affected/# Treated

<u>Dose (mg/kg)</u>	<u>Signs of Toxicity</u>	<u>Male Sprague-Dawley</u>	<u>Female Sprague-Dawley</u>	<u>Male CDF</u>	<u>Female CDF</u>
316	None	-	-	5/5	0/5
	Slight lethargy			0/5	5/5
630	Lethargy	5/5	5/5	10/10	10/10
1260	Total body tremors	5/5	5/5	5/5	5/5
	Lethargy	5/5	5/5	5/5	5/5
	Hyperventilation	5/5	5/5	0/5	0/5
	Dark exudate around the nose	5/5	0/5	0/5	0/5
	Severe diarrhea	0/5	1/5	0/5	0/5
2520	Total body tremors	5/5	5/5	5/5	5/5
	Lethargy	5/5	5/5	5/5	5/5
	Hyperventilation	5/5	5/5	5/5	5/5
	Dark exudate around nose	5/5	0/5	0/5	0/5
3160	Total body tremors	1/1 ^a	-	-	-
	Lethargy	1/1			
	Piloerection	1/1			
	Hyperventilation	1/1			
5000	Total body tremors	5/5	5/5	5/5	5/5
	Lethargy	5/5	5/5	5/5	5/5
	Hyperventilation	0/5	5/5	5/5	5/5
	Convulsions	0/5	1/5	0/5	0/5
10,000	Lethargy	-	0/5	2/2 ^a	-
	Labored breathing		0/5	2/2	

a) The number affected given is per number of survivors.

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TABLE 15
A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CDF (FISCHER 344-DERIVED) RATS

EPICHLOROHYDRIN: MEAN ($\pm$ STANDARD DEVIATION) INITIAL (FASTED) AND FINAL BODY WEIGHTS

Dose (mg/kg)	Male Sprague-Dawley				Female Sprague-Dawley				Male CDF				Female CDF			
	n	Initial	n	Final	n	Initial	n	Final	n	Initial	n	Final	n	Initial	n	Final
		Weight (g)		Weight (g)		Weight (g)		Weight (g)		Weight (g)		Weight (g)		Weight (g)		Weight (g)
25	5	269±11	5	381±16	5	192±3	5	248±7	5	109±5	5	200±4	5	91±2	5	139±4
50	5	265±11	5	366±17	5	197±11	5	251±16	5	111±3	5	199±13	5	92±5	5	139±8
100	5	262±18	5	370±21	5	194±9	4	246±20	5	109±4	5	194±10	5	89±3	5	135±6
200	5	274±13	4	374±20	5	193±7	3	239±3	5	108±5	5	193±5	5	88±5	5	135±5
210	-	--	-	--	-	--	-	--	5	167±9	5	217±16	5	111±8	2	139±4
225	-	--	-	--	-	--	-	--	5	161±6	a	--	5	131±5	a	--
252	-	--	-	--	-	--	-	--	5	185±3	a	--	5	118±7	a	--
398	5	320±22	a	--	5	208±4	a	--	5	104±4	a	--	5	81±7	a	--
795	5	325±13	a	--	5	199±13	a	--	5	103±8	a	--	5	79±5	a	--

a) No survivors

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TABLE 16
A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CDF (FISCHER 344-DERIVED) RATS

2,4,5-TRICHLOROPHENOXY ACETIC ACID: MEAN (+ STANDARD DEVIATION) INITIAL (FASTED) AND FINAL BODY WEIGHTS

Dose (mg/kg)	Male Sprague-Dawley				Female Sprague-Dawley				Male CDF				Female CDF			
	n	Initial Weight (g)	n	Final Weight (g)	n	Initial Weight (g)	n	Final Weight (g)	n	Initial Weight (g)	n	Final Weight (g)	n	Initial Weight (g)	n	Final Weight (g)
126	5	322 $\pm$ 15	5	424 $\pm$ 26	5	201 $\pm$ 9	5	253 $\pm$ 7	5	141 $\pm$ 9	5	226 $\pm$ 10	5	90 $\pm$ 4	5	137 $\pm$ 7
252	5	313 $\pm$ 26	5	405 $\pm$ 37	5	195 $\pm$ 2	5	240 $\pm$ 3	5	141 $\pm$ 12	5	219 $\pm$ 16	5	92 $\pm$ 5	5	140 $\pm$ 3
350	-	--	-	--	5	200 $\pm$ 13	5	233 $\pm$ 14	-	--	-	--	-	--	-	--
398	-	--	-	--	5	208 $\pm$ 9	4	163 $\pm$ 8	-	--	-	--	-	--	-	--
450	-	--	-	--	5	203 $\pm$ 15	5	235 $\pm$ 16	-	--	-	--	-	--	-	--
500	5	311 $\pm$ 15	4	380 $\pm$ 18	5	196 $\pm$ 5	a	--	5	144 $\pm$ 9	5	221 $\pm$ 9	5	95 $\pm$ 4	5	144 $\pm$ 5
795	-	--	-	--	-	--	-	--	5	156 $\pm$ 8	1	124	-	--	-	--
1000	5	306 $\pm$ 12	a	--	5	190 $\pm$ 4	a	--	5	144 $\pm$ 4	a	--	5	94 $\pm$ 3	2	139 $\pm$ 2
1580	5	289 $\pm$ 7	a	--	-	--	-	--	-	--	-	--	-	--	-	--
2000	-	--	-	--	-	--	-	--	5	129 $\pm$ 9	a	--	5	90 $\pm$ 4	a	--

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TABLE 17
A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR STB:
(SPRAGUE-DAWLEY) RATS AND CDF (FISCHER 344-DERIVED) RATS
ALLYL CHLORIDE: MEAN (+ STANDARD DEVIATION) INITIAL (FASTED) AND FINAL BODY WEIGHTS

Dose (mg/kg)	n	Male		n	Female		n	Male		n	Female		n	Female		
		Sprague-Dawley			Sprague-Dawley			CDF			CDF					
		Initial Weight (g)	Final Weight (g)		Initial Weight (g)	Final Weight (g)		Initial Weight (g)	Final Weight (g)		Initial Weight (g)	Final Weight (g)				
63	-	--	-	--	-	--	-	--	-	--	-	--	5	82±5	5	133±2
126	-	--	-	--	-	--	-	--	-	--	-	--	5	83±5	3	133±8
200	5	308±13	5	403±22	5	193±6	5	236±8	5	139±7	5	214±7	5	92±1	4	143±7
398	5	296±12	2	284±10	5	191±3	2	238±6	5	135±7	3	136±9	5	91±4	3	143±3
795	5	308±8	a	--	5	189±4	1	250	5	136.2±6	a	--	5	94±2	a	--
1580	5	318±13	a	--	5	196±12	a	--	5	135±6	a	--	5	88±4	a	--

a) No survivors

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TABLE 18
A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR STB:
(SPRAGUE-DAWLEY) RATS AND CDF (FISCHER 344-DERIVED) RATS

MALATHION: MEAN (+ STANDARD DEVIATION) INITIAL (FASTED) AND FINAL BODY WEIGHTS

Dose (mg/kg)	Male Sprague-Dawley				Female Sprague-Dawley				Male CDF				Female CDF			
	n	Initial Weight (g)	n	Final Weight (g)	n	Initial Weight (g)	n	Final Weight (g)	n	Initial Weight (g)	n	Final Weight (g)	n	Initial Weight (g)	n	Final Weight (g)
252	5	231+22	5	349+	5	171+5	5	224+12	5	144+3	5	222+6	5	100+3	5	140+3
500	5	229+3	5	343+7	5	180+7	5	242+10	5	148+4	5	219+5	5	100+3	5	138+4
1000	5	220+6	5	337+16	5	176+6	5	224+8	5	149+10	5	227+13	5	98+4	5	138+2
2000	5	235+8	5	350+15	5	179+11	3	232+21	5	150+1	4	226+7	5	100+6	2	121+5
2100	5	244+5	2	348+6	-	--	-	--	-	--	-	--	-	--	-	--
2250	5	357+9	a	--	-	--	-	--	-	--	-	--	-	--	-	--
2520	5	296+21	a	--	-	--	-	--	10	185+30	a	--	-	--	-	--
3980	5	274+11	a	--	5	200+7	a	--	5	185+7	a	--	5	92+5	a	--

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TABLE 19
A COMPARISON OF SINGLE-DOSE ORAL LD50's FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CDF (FISCHER 344-DERIVED) RATS
ACRYLIC ACID: MEAN (+ STANDARD DEVIATION) INITIAL (FASTED) AND FINAL BODY WEIGHTS

Dose (mg/kg)	Male				Female				Male				Female			
	Sprague-Dawley				Sprague-Dawley				CDF				CDF			
	Initial		Final		Initial		Final		Initial		Final		Initial		Final	
	n	Weight (g)	n	Weight (g)	n	Weight (g)	n	Weight (g)	n	Weight (g)	n	Weight (g)	n	Weight (g)	n	Weight (g)
31.6	-	--	-	--	-	--	-	--	-	--	-	--	5	120+6	5	142+29
63	-	--	-	--	5	219+7	5	230+35	5	178+6	5	193+46	10	122+11	6	105+21
126	-	--	-	--	5	221+9	4	227+32	5	189+4	3	209+61	5	114+9	5	104+30
158	-	--	-	--	5	217+8	4	225+26	5	101+8	1	70	5	114+2	3	119+47
316	-	--	-	--	5	195+4	2	236+18	5	104+3	1	98	5	120+2	3	109+20
630	5	279+13	5	279+74	5	191+6	4	211+31	5	115+5	a	--	5	92+2	3	107+24
1260	5	275+10	4	215+74	5	194+6	2	224+20	5	114+3	a	--	10	114+21	3	112+16
1580	5	328+20	1	213	-	--	-	--	-	--	-	--	-	--	-	--
2000	5	311+9	a	--	-	--	-	--	-	--	-	--	-	--	-	--
2520	5	258+18	a	--	5	197+11	a	--	5	114+6	a	--	5	94+4	a	--
5000	5	274+11	a	--	5	188+7	a	--	5	101+5	a	--	5	93+3	a	--

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TABLE 20

A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CDF (FISCHER 344-DERIVED) RATS

BENZENE: MEAN (+ STANDARD DEVIATION) INITIAL (FASTED) AND FINAL BODY WEIGHTS

Dose (mg/kg)	Male Sprague-Dawley				Female Sprague-Dawley				Male CDF				Female CDF			
	n	Initial Weight (g)	n	Final Weight (g)	n	Initial Weight (g)	n	Final Weight (g)	n	Initial Weight (g)	n	Final Weight (g)	n	Initial Weight (g)	n	Final Weight (g)
316	-	--	-	--	-	--	-	--	5	134+3	5	225+2	5	118+3	5	156+3
630	5	314+9	5	405+22	5	195+8	5	244+14	10	118+16	7	210+23	10	100+19	8	143+17
1250	5	327+9	4	434+10	5	201+5	5	256+9	5	100+3	4	179+10	5	81+5	4	125+3
2520	5	312+8	5	418+15	5	196+4	2	248+7	5	101+3	1	157	5	82+7	2	136+1
3160	5	276+15	1	341	-	--	-	--	-	--	-	--	-	--	-	--
5000	5	311+11	a	--	5	197+7	3	256+6	5	103+4	1	172	5	81+7	a	--
10,000	-	--	-	--	5	194+7	a	--	5	125+7	a	--	-	--	-	--

a) No survivors

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Table 21

A COMPARISON OF SINGLE-DOSE ORAL LD50's FOR 3PH:
(SPRAGUE-DAWLEY) RATS AND CDF (FISCHER 344-DERIVED) RATS

EPICHLOROHYDRIN: GROSS PATHOLOGIC FINDINGS

		Dose mg/kg																		
		25				50				100				200				210		398
Gross Observations ^a		Male S.D.	Female S.D.	Male CDF	Female CDF	Male S.D.	Female S.D.	Male CDF	Female CDF	Male S.D.	Female S.D.	Male CDF	Female CDF	Male S.D.	Female S.D.	Male CDF	Female CDF	Male CDF	Female CDF	Male S.D.
<u>General</u>																				
No visible lesions		4/5	5/5	3/5	5/5	3/5	5/5	5/5	5/5	0/5	1/4	4/5	3/5	0/4	1/3	2/5	1/5	0/5	2/2	1/1
Focal corneal cloudiness		1/5	0/5	2/5	0/5	1/5	0/5	0/5	0/5	1/5	0/4	0/5	2/5	1/4	0/3	2/5	2/5	3/5	0/2	0/1
Accumulation of exudate around eyes		0/5	0/5	0/5	0/5	2/5	0/5	0/5	0/5	1/5	0/4	0/5	0/5	1/4	0/3	0/5	0/5	0/5	0/2	0/1
<u>Gastrointestinal System</u>																				
<u>Stomach</u>																				
Thickening and roughing of squamous epithelium		0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	5/5	3/4	1/5	0/5	4/4	2/3	2/5	4/5	4/5	0/2	0/1
Focal thickening of nonglandular stomach wall		0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/4	0/5	0/5	0/4	1/3	0/5	0/5	0/5	0/2	0/1
Erosion of nonglandular epithelium		0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/4	0/5	0/5	0/4	1/3	0/5	0/5	0/5	0/2	0/1
Healed perforated ulcer		0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/4	0/5	0/5	1/4	0/3	0/5	0/5	0/5	0/2	0/1
Fibrous adhesions between stomach and abdominal musculature		0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/4	0/5	0/5	1/4	0/3	0/5	0/5	0/5	0/2	0/1
<u>Liver</u>																				
Diaphragmatic hernia		0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/4	0/5	0/5	0/4	0/3	0/5	0/5	1/5	0/2	0/1

a) Data presented as number affected/number examined.

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Table 22

A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPB:
(SIRAGUE-DAWLEY) RATS AND CUF (FISCHER 344-DERIVED) RATS

2,4,5-TRICHLOROPHOXY ACETIC ACID: GROSS PATHOLOGIC FINDINGS

Dose (mg/kg)															
Gross Observations ^a	126				252				350	398	450	500			795
	Male S.D.	Female S.D.	Male CDF	Female CDF	Male S.D.	Female S.D.	Male CDF	Female CDF	Female S.D.	Female S.D.	Female S.D.	Male S.D.	Male CDF	Female CDF	Male CDF
<u>General</u>															
No visible lesion	3/5	4/5	4/5	5/5	2/5	4/5	4/5	4/5	4/5	0/4	3/5	2/4	3/5	5/5	0/1
Focal corneal cloudiness	2/5	1/5	1/5	0/5	0/5	0/5	0/5	1/5	1/5	0/4	1/5	0/4	2/5	0/5	1/1
Accumulation of exudate around eyes	1/5	0/5	0/5	0/5	2/5	1/5	1/5	0/5	0/5	0/4	0/5	2/4	0/5	0/5	0/1
<u>Respiratory System</u>															
<u>Lungs</u>															
Multiple pinpoint gray Foci scattered throughout all lobes	0/5	0/5	0/5	0/5	1/5	0/5	0/5	0/5	0/5	0/4	1/5	0/4	0/5	0/5	0/1
<u>Renal System</u>															
	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	0/5	4/4	0/5	0/4	0/5	0/5	1/1

examined.

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Table 23

A COMPARISON OF SINGLE-DOSE ORAL LD50's FOR NH₂
(SPRAGUE-DAWLEY) RATS AND CD₀₁F (FISCHER 344-DERIVED) RATS

ALLYL CHLORIDE: GROSS PATHOLOGIC FINDINGS

Dose (mg/kg)

	63	126	200				398			
Gross Observations ^a	Female CDF	Female CDF	Male S.D.	Female S.D.	Male CDF	Female CDF	Male S.D.	Female S.D.	Male CDF	Female CDF
<u>General</u>										
No visible lesion	2/5	1/7	0/5	0/5	1/5	3/4	0/2	0/3	0/3	1/3
Focal corneal cloudiness	3/5	0/7	0/5	0/5	1/5	0/4	0/2	1/3	1/3	0/3
Accumulation of exudate around eyes	0/5	0/7	0/5	0/5	0/5	0/4	1/2	0/3	1/3	0/3
<u>Respiratory System</u>										
<u>Lungs</u>										
Multiple pinpoint gray Foci scattered throughout all lobes	0/5	0/7	0/5	1/5	0/5	0/4	0/2	0/3	0/3	0/3
<u>Gastrointestinal System</u>										
<u>Stomach</u>										
Thickening and roughening of nonglandular squamous epithelium	0/5	5/7	5/5	5/5	4/5	1/4	1/2	2/3	3/3	2/3
Focal thickening of nonglandular stomach wall	0/5	0/7	1/5	3/5	0/5	0/4	0/2	0/3	0/3	0/3
Erosion of nonglandular epithelium	0/5	0/7	0/5	0/5	0/5	0/4	1/2	2/3	2/3	0/3
Firm, nodular-like foci throughout epithelial surface	0/5	0/7	0/5	0/5	0/5	0/4	0/2	0/3	1/3	0/3
Perforated Ulcer	0/5	0/7	0/5	0/5	0/5	0/4	0/2	1/3	0/3	0/3
Fibrous adhesions between stomach and liver, spleen, or diaphragm	0/5	0/7	0/5	0/5	0/5	0/4	1/2	2/3	1/3	0/3

a) Data presented as number affected/number examined.

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Table 24
A COMPARISON OF SINGLE-DOSE ORAL LD50's FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CD¹F (FISCHER 344-DERIVED) RATS

MALATHION: GROSS PATHOLOGIC FINDINGS

Dose (mg/kg)

Gross Observations ^a	252				500				1000				2000				2100
	Male S.D.	Female S.D.	Male CDF	Female CDF	Male S.D.	Female S.D.	Male CDF	Female CDF	Male S.D.	Female S.D.	Male CDF	Female CDF	Male S.D.	Female S.D.	Male CDF	Female CDF	Male S.D.
<u>General</u>																	
No visible lesion	5/5	5/5	3/5	5/5	5/5	5/5	1/5	5/5	5/5	4/5	4/5	4/5	5/5	2/3	3/4	2/2	2/2
Focal corneal cloudiness	0/5	0/5	2/5	0/5	0/5	0/5	4/5	0/5	0/5	1/5	1/5	1/5	0/5	1/3	1/4	0/2	0/2

a) Data presented as number affected/number examined.

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Table 25

A COMPARISON OF SINGLE-DOSE ORAL LD₅₀'s FOR ST-4:
(SPRAGUE-DAWLEY) RATS AND CDF (FITCHER 344-REFINED) RATS

ACRYLIC ACID: GROSS PATHOLOGIC FINDINGS

Dose (mg/kg)

	0.316	63				126				158				316				630				1260				1580
Gross Observations ^a	male CDF	Female S.D.	Male CDF	Female CDF	Female S.D.	Male CDF	Female CDF	Female S.D.	Male CDF	Female CDF	Female S.D.	Male CDF	Female CDF	Female S.D.	Male CDF	Female CDF	Female S.D.	Male CDF	Female CDF	Female S.D.	Male CDF	Female CDF	Female S.D.	Male CDF	Female CDF	Female S.D.
<u>General</u>																										
No visible lesion	1/5	3/5	2/5	1/5	5/7	1/3	1/5	6/8	0/1	2/3	3/3	0/1	0/3	1/5	0/4	0/3	0/4	0/2	0/3	0/1						
Focal corneal cloudiness	3/5	2/5	2/5	1/5	1/7	1/3	1/5	0/8	0/1	0/3	0/3	0/1	0/3	1/5	1/4	0/3	0/4	0/2	0/3	0/1						
Secretory material around mouth and nose	0/5	0/5	0/5	1/6	0/7	0/3	0/5	0/8	0/1	0/3	0/3	0/1	0/3	0/5	0/4	0/3	0/4	0/2	0/3	0/1						
Depletion of body fat and muscular atrophy	1/5	0/5	1/5	5/6	0/7	1/3	3/5	1/8	0/1	0/3	0/3	0/1	0/3	0/5	0/4	1/3	1/4	0/2	0/3	1/1						
Loss of body condition	0/5	0/5	0/5	0/6	0/7	0/3	0/5	0/8	1/1	1/3	0/3	1/1	3/3	0/5	0/4	0/3	0/4	0/2	0/3	0/1						
<u>Respiratory System</u>																										
<u>Lungs</u>																										
Multiple pinpoint foci scattered throughout all lobes	0/5	0/5	0/5	0/6	1/7	0/3	0/5	1/8	0/1	0/3	0/3	0/1	0/3	0/5	0/4	0/3	0/4	0/2	0/3	0/1						
Pulmonary atelectasis	0/5	0/5	0/5	0/6	0/7	0/3	0/5	0/8	0/1	0/3	0/3	0/1	0/3	1/5	0/4	0/3	0/4	0/2	0/3	0/1						
<u>Gastrointestinal System</u>																										
<u>Stomach</u>																										
Thickening and roughening of squamous epithelium	0/5	0/5	0/5	1/6	1/7	1/3	1/5	0/8	0/1	0/3	0/3	1/1	2/3	4/5	4/4	3/3	4/4	2/2	3/3	1/1						
Focal thickening of nonglandular stomach wall	0/5	0/5	0/5	1/6	0/7	0/3	0/5	0/8	0/1	0/3	0/3	0/1	0/3	0/5	0/4	1/3	0/4	0/2	0/3	1/1						
Hemolyzed blood in glandular portion	0/5	0/5	0/5	0/6	0/7	0/3	0/5	0/8	1/1	1/3	0/3	0/1	0/3	0/5	0/4	0/3	0/4	0/2	0/3	0/1						
Thickened area at junction of glandular and nonglandular mucosa	0/5	0/5	0/5	0/6	0/7	0/3	0/5	0/8	0/1	0/3	0/3	0/1	0/3	0/5	1/4	0/7	0/4	0/2	0/7	0/1						
Distention of stomach by mucus	0/5	0/5	0/5	0/6	0/7	0/3	0/5	0/8	0/1	0/3	0/3	0/1	0/3	0/5	0/4	0/3	1/4	0/2	0/3	0/1						
Gaseous distention of stomach and/or intestinal tract	0/5	0/5	0/5	0/6	0/7	0/3	0/5	0/8	0/1	0/3	0/3	0/1	0/3	0/5	0/4	0/3	1/4	0/2	0/3	0/1						
Fibrous adhesions between stomach and liver	0/5	0/5	0/5	0/6	0/7	0/3	0/5	0/8	0/1	0/3	0/3	0/1	0/3	0/5	0/4	0/3	1/4	0/2	0/3	0/1						
<u>Intestinal tract</u>																										
Presence of mucoid, yellow bile-like fluid in intestinal tract	0/5	0/5	0/5	0/6	0/7	0/3	0/5	0/8	0/1	0/3	0/3	1/1	1/3	0/5	0/4	0/3	2/4	0/1	0/3	0/1						
Hemorrhagic appearance of cecum	0/5	0/5	0/5	0/6	0/7	0/3	0/5	0/8	0/1	0/3	0/3	0/1	0/3	0/5	0/4	0/3	1/4	0/1	0/3	0/1						
<u>Spleen</u>																										
Decreased size	0/5	0/5	0/5	0/6	0/7	0/3	0/5	0/8	0/1	0/3	0/3	0/1	0/3	0/5	0/4	0/3	0/4	0/2	0/3	0/1						

^a Data presented as number affected/number examined.

Table 26

A COMPARISON OF SINGLE-DOSE ORAL LD50'S FOR SPB:
(SPRAGUE-DAWLEY) RATS AND CDF (FISCHER 344-DERIVED) RATS

BENZENE: GROSS PATHOLOGIC FINDINGS

Gross Observations ^a	0.316		0.63				1.26				2.52				3.16	5.0	
	Male CDF	Female CDF	Male S.D.	Female S.D.	Male CDF	Female CDF	Male S.D.	Female S.D.	Male CDF	Female CDF	Male S.D.	Female S.D.	Male CDF	Female CDF	Male S.D.	Female S.D.	Male CDF
<u>General</u>																	
No visible lesion	4/5	4/5	1/5	5/5	5/7	4/8	1/4	3/4	1/4	3/4	1/5	1/2	0/1	2/2	1/1	2/3	1/1
Focal corneal cloudiness	1/5	1/5	1/5	0/5	2/7	4/8	1/4	0/4	2/4	1/4	0/5	0/2	1/1	0/2	0/1	0/3	0/1
<u>Gastrointestinal System</u>																	
<u>Stomach</u>																	
Thickening and roughening of nonglandular squamous epithelium	0/5	0/5	3/5	0/5	0/7	0/8	3/4	1/4	1/4	0/4	4/5	1/2	0/1	0/2	0/1	1/3	0/1
Focal thickening of nonglandular stomach wall	0/5	0/5	0/5	0/5	0/7	0/8	0/4	0/4	0/4	0/4	1/5	0/2	0/1	0/2	0/1	0/3	0/1
Erosion of nonglandular epithelium	0/5	0/5	0/5	0/5	0/7	0/8	0/4	0/4	0/4	0/4	1/5	0/2	0/1	0/2	0/1	0/3	0/1

a) Data presented as number affected/number examined.

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