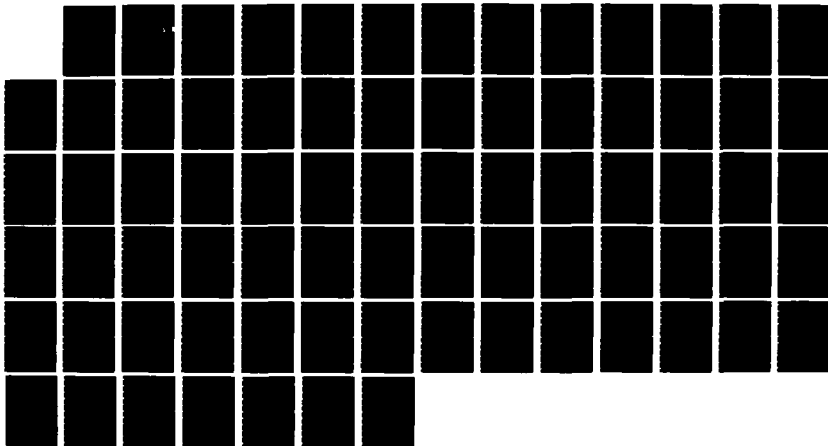


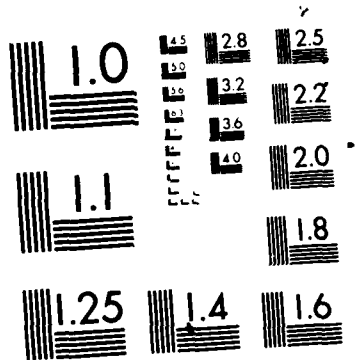
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DERMAL, EYE AND ORAL TOXICOLOGIC EVALUATIONS: PHASE II REPORT

ACUTE ORAL LD₅₀ DETERMINATIONS
OF BENZOTHAZOLE, DITHIANE, AND OXATHIANE

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SEPTEMBER 1986

SUPPORTED BY:

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
FORT DETRICK
FREDERICK, MD 21701-5012

CONTRACT NO. DAMD17-82-C-2301
WITH
BIOASSAY SYSTEMS CORPORATION
WOBURN, MA 01801

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The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.

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17. COSATI CODES		18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)	
FIELD	GROUP	Oral toxicity (LD ₅₀) in Rats Benzothiazole, Dithiane, and Oxathiane	
19. ABSTRACT (Continue on reverse if necessary and identify by block number) Benzothiazole, dithiane, and oxathiane were administered by oral gavage to groups of 5 male and 5 female Fischer 344 albino rats to establish their oral toxicity (median lethal dose). The oral median lethal dose (LD ₅₀) of Benzothiazole was determined to be 493 mg/kg for males, 466 mg/kg for females, and 479 mg/kg for the combined sexes. The oral LD ₅₀ of Dithiane was determined to be 3,680 mg/kg for males, 2,7 mg/kg for females, and 3,473 mg/kg for the combined sexes. The oral LD ₅₀ of Oxathiane was determined to be 3,328 mg/kg for males, 3,123 mg/kg for the combined sexes. The oral LD ₅₀ of Oxathiane for female was estimated to be approximately 3,000 mg/kg.			
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22a. NAME OF RESPONSIBLE INDIVIDUAL VIRGINIA MILLER		22b. TELEPHONE (Include Area Code) 301-663-7325	22c. OFFICE SYMBOL SGRD-RMS

EXECUTIVE SUMMARY

Benzothiazole, dithiane, and oxathiane were evaluated to determine their oral median lethal dose (LD₅₀) in Fischer 344 albino rats. Each test article was administered via oral gavage to groups of 5 male and 5 female albino rats. Animals were observed for 14 days post-dosing.

The oral median lethal dose (LD₅₀) of benzothiazole was determined to be 493 milligrams/kilogram of body weight (mg/kg) for male rats, 466 mg/kg for female rats, and 479 mg/kg for male and female rats (combined sexes).

The oral LD₅₀ of dithiane was determined to be 3,680 mg/kg for male rats, 2,768 mg/kg for female rats, and 3,473 for male and female rats.

The oral LD₅₀ of oxathiane was determined to be 3,328 mg/kg for male rats and 3,123 mg/kg for male and female rats. The oral LD₅₀ of oxathiane for female rats could not be calculated using the Litchfield-Wilcoxon method and the mortality pattern observed in this study. The oral LD₅₀ of oxathiane for female rats was estimated to be approximately 3,000 mg/kg.

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FOREWORD

All work relating to this study was done in conformity with the FDA Good Laboratory Practice Regulations.

PRINCIPAL INVESTIGATOR: *Dale A. Mayhew* 9/3/86
(Decatur, IL facility) Dale A. Mayhew, Ph.D. Date
Principal Investigator

PRINCIPAL INVESTIGATOR: *Indu A. Muni* 9/15/86
(Woburn, MA facility) Indu A. Muni, Ph.D. Date
Executive Vice President

These studies were inspected during their progress by Quality Assurance Specialists according to facility Standard Operating Procedures (SOP's). Management was informed at once of any serious problems found.

The data in the report were compared with the raw data and are in agreement. The report and study files were examined to assure that any problems found during Quality Assurance inspections or audits were corrected, and if necessary, their effect on the studies documented. Quality assurance inspection and audit dates are presented in Appendix A.

QUALITY ASSURANCE OFFICER (Decatur, IL facility) *Antoinette Skelley* 9/3/86
Antoinette Skelley Date
Manager, Quality Assurance and Regulatory Affairs

QUALITY ASSURANCE OFFICER (Woburn, MA facility) *Paul Lezberg* 9/23/86
Paul Lezberg, B.S. Date
Manager of Regulatory Compliance

All raw data relating to these studies will be stored at American Biogenics Corporation. Storage will conform to EPA and FDA regulations as per facility SOP's and may include volume reduction by conversion to certified microform.

Date of Report: 9/3/86

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INTRODUCTION

Acute oral median lethal dose (LD_{50}) determinations were performed on dithiane (1,4-dithiane), oxathiane (1,4-thioxane), and benzothiazole using albino rats. These studies were conducted at the request of the U.S. Army Medical Research and Development Command in order to form a basis for subsequent subchronic and chronic toxicology studies. The results of these evaluations would also permit the establishment of preliminary health effects criteria.

This report presents results of acute oral LD_{50} testing in albino rats of oxathiane conducted at the Woburn, MA facility of American Biogenics Corporation (ABC) from January 8 to 22, 1985, and oral LD_{50} testing of benzothiazole and dithiane conducted at the Decatur, IL facility of ABC from January 7 to February 20, 1986. ABC study numbers assigned to these studies were 11357-16 for oxathiane, 480-2455 for benzothiazole, and 410-2457 for dithiane.

MATERIALS & METHODS

Interlaboratory materiel and methodology differences specified in this section were those considered noteworthy with respect to any test article comparisons.

A. Test System/Husbandry

Young adult Fischer F-344 albino rats were utilized in these studies. Albino rats were obtained from Taconic Farms, Germantown, NY for oxathiane testing at Woburn, MA, and from Charles River Breeding Laboratories, Inc. (Kingston, NY) for benzothiazole and dithiane testing at Decatur, IL. The rat is the species routinely used in acute oral toxicity testing.

Animals were housed in cages that conformed to standards described in DHEW Publication (NIH) 78.23. Animals were group housed, five per cage, in polycarbonate, suspended, shoe box type cages at the Woburn, MA facility, and housed individually in stainless steel, wire-bottomed cages at the Decatur, IL facility.

The animals were held in quarantine for at least 7 days after receipt and observed during quarantine for mortality and abnormal health. Only animals considered to be in good health were used on study.

The animal housing rooms were cleaned and the housing cages were cleaned and sanitized as specified in facility SOP's. The animal housing rooms were well ventilated and air-conditioned. The temperature and relative humidity were monitored daily in the housing rooms. There were no deviations from SOP specified temperature and humidity ranges which were considered to have had an adverse effect on these studies. Flourescent lighting in the animal housing rooms was controlled to provide a 12 hour light/dark cycle.

The animals were fed ad libitum except for fasting overnight prior to dosing. Charles River R-M-H 3000 feed (Agway) was used at the Woburn, MA facility, and Purina Certified Rodent Chow 5002 was used at the Decatur, IL facility. Water was provided to the animals on an ad libitum basis.

B. Test Articles

The three test articles used in these studies, listed below, were obtained from Aldrich Chemical Company and were stored at ambient room temperature after receipt.

<u>Test Article</u>	<u>Lot/Batch Number(s)</u>	<u>CAS Number</u>	<u>ABC Code Number</u>
Benzothiazole, 99% (liquid)	1723LK	95-16-9	11/85-1134
Dithiane (1,4-dithiane), 97% (solid)	3030TH, KM0322CM	505-29-3	11/85-1136
Oxathiane (1,4-thioxane), 98% (liquid)	053117	15980-15-1	11357-16

Chemical analysis data for the test articles are presented in Appendix C.

Weight/volume dilutions of benzothiazole and dithiane in corn oil were prepared for administration to each dose level at a constant volume for each study. Oxathiane was administered as received.

C. Test Procedures

Groups of 5 male and/or 5 female albino rats of the healthy quarantine population were randomly assigned to the following treatment groups (dose levels).

<u>Test Article</u>	<u>Dose Levels (mg/kg)</u>	<u>Total Animals Used</u>
Oxathiane	2,601; 3,060; 3,600	30 (15M/15F)
Benzothiazole	398, 501, 631	30 (15M/15F)
Dithiane	Males - 2,818; 3,162; 3,548; 3,981 Females - 1,778; 2,818; 3,162; 3,981	40 (20M/20F)

Animals were fasted in the late afternoon on the day prior to dosing. The following day, initial body weights were recorded, dose volumes were calculated, and a measured volume of the test article or appropriate suspension was delivered to each animal by oral gavage. Oxathiane was administered as received in single doses. Benzothiazole suspensions in corn oil were administered in single doses at a constant volume of 10 milliliters/kilogram of body weight. Dithiane suspensions in corn oil were administered in two portions spaced approximately 2 to 3 hours apart at a total constant volume of 17 mg/kg of body weight. Diet was returned to the cage of each animal immediately after dosing (oxathiane and benzothiazole groups) or immediately after the second dose administration (dithiane).

Animals were observed frequently for mortality and toxic signs after dosing on day 0. Observations for mortality and toxic signs were done at least once daily thereafter (study days 1 to 14).

Body weights were recorded prior to dosing on day 0, at 3 or 4 day intervals thereafter (benzothiazole and dithiane studies), and prior to sacrifice on day 14 or at the time found dead. Body weights of the oxathiane study were recorded initially, on day 7, and at termination or death.

On day 14, all surviving animals were humanely sacrificed prior to necropsy. Animals found dead were necropsied as soon as possible after death was noted. The following of each animal were examined and all abnormal findings were recorded: all external surfaces and orifices, and the abdominal, thoracic, and pelvic cavities and their viscera.

The mean, standard deviation, and standard error were calculated for the body weight data and for the amount of test article administered. The milligrams of test article administered were calculated using dose volume values and the suspension concentration or test article density values.

The oral LD₅₀ value, the 95 percent confidence interval, the slope of the dose-response curve, and correction factors for 0 and 100 percent observed responses were calculated by computer program employing the methodology of Litchfield and Wilcoxon.* Dose-response curves were prepared by computer program.

*Litchfield, J.T., Jr. and Wilcoxon, F., "A Simplified Method of Evaluating Dose - Effect Experiments", Journal of Pharmacology and Experimental Therapeutics, Vol. 96, 1949, pages 99-113.

RESULTS

A summary of results for each oral LD₅₀ determination follows:

Benzothiazole

Oral LD₅₀ values for benzothiazole were determined to be 493.3 mg/kg for males, 465.6 mg/kg for females, and 478.6 mg/kg for the combined sexes. Incidences of mortalities follow:

<u>Benzothiazole Group (mg/kg)</u>	<u>Number Dead/Number Tested Combined</u>		
	<u>Males</u>	<u>Females</u>	<u>Sexes</u>
398	1/5	1/5	2/10
501	2/5	3/5	5/10
631	5/5	5/5	10/10

All mortalities occurred within 2 days after dosing.

Antemortem observations seen during the study included: lethargy, ataxia, prostration, lacrimation, squinting, body cool to touch, loose stool, few stools, no stool, crusty eye, crusty muzzle, and yellow/brown stained or damp fur in the perianal region.

Necropsy of animals found dead revealed: dark contents of stomachs and small intestines; multiple focal, black discoloration of glandular stomachs; diffuse, pale discoloration of livers; diffuse, pale or red discoloration of lungs; and a distended urinary bladder.

Necropsy of terminal sacrifice animals revealed: enlarged, dark red spleens; an ovarian cyst; a diaphragmatic hernia; and small testes.

Dithiane

Oral LD₅₀ values for dithiane were determined to be 3,680 mg/kg for males, 2,768 mg/kg for females, and 3,473 mg/kg for the combined sexes. Incidences of mortalities follow:

<u>Dithiane Group (mg/kg)</u>	<u>Number Dead/Number Tested Combined</u>		
	<u>Males</u>	<u>Females</u>	<u>Sexes</u>
1,778	-	0/5	0/5
2,818	0/5	4/5	4/10
3,162	0/5	2/5	2/10
3,548	2/5	-	2/5
3,981	4/5	4/5	8/10

All mortalities occurred at 1 to 6 days after dosing.

Antemortem observations seen during the study included: crusty muzzle, hyperactivity, muscle tremors, red stained fur around eyes,



emaciation, crusty nose, crusty eyes, lethargy, few stools, no stools, ataxia, squinting, prostration, lacrimation, irregular breathing, damp fur and yellow/brown stained fur in the perianal region, and test article odor present in animal room (up to day 5 after dose administration).

Necropsy of animals found dead revealed: red or dark red discolorations of lungs; pale or red discoloration on parts or all of small intestine; gastrointestinal contents were dark, black, thick, red, fluid, and/or white; black discoloration of stomach; black or red discolorations, and/or smooth mucosa of glandular stomachs; pale or tan discolorations of liver; yellow fluid around mouth; yellow or green yellow discoloration of oral region; salivation around mouth; or black discolored fur around rectum.

Necropsy of one terminal sacrifice female of the 3,981 mg/kg dose group revealed a solitary, red cyst of the left ovary.

Oxathiane

Oral LD₅₀ values for oxathiane were determined to be 3,328 mg/kg for males and 3,123 mg/kg for combined sexes. No oral LD₅₀ value could be calculated for females using the Litchfield-Wilcoxon method (Slope = 0). The oral LD₅₀ for oxathiane was estimated to be approximately 3,000 mg/kg for female albino rats. Incidences of mortalities follow:

Oxathiane Group (mg/kg)	Number Dead/Number Tested		
	Males	Females	Combined Sexes
2,601	0/5	2/5	2/10
3,060	1/5	1/5	2/10
3,600	4/5	5/5	9/10

All mortalities occurred within 2 days after dosing.

Antemortem observations seen during the study included: coma, polypnea, lacrimation, dyspnea, lethargy, ataxia, cyanosis, squinted eyes, paralysis, epistaxis, wheezing, decreased body temperature, pilo-erection, hunched posture, and alopecia. These abnormalities were generally seen in all groups after dosing on day 0 and on day 1. Except for alopecia, no abnormal signs were seen after day 3.

Necropsy of animals found dead revealed: discolored (black, red, blue/purple, or dark yellow) and gel or liquid contents (black, amber, yellow, dark orange, dark red, or green/gray) of the intestines of nearly all animals. Gaseous stomachs and intestines, brown gel or liquid contents of stomachs, and distended and discolored urinary bladders were also seen for some found dead animals.

Necropsy of animals at terminal sacrifice revealed no abnormalities.

TABLE 1
 LITCHFIELD-WILCOXON LD₅₀ FOR MALES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: BENZOTHIAZOLE

Dose (mg/kg)	Observed Deaths Proportion	Deaths Percent	Expected Deaths Percent	Difference
398.0	1/5	20.0	15.8	4.2
501.0	2/5	40.0	52.9	-12.9
631.0	5/5	100.0 (90.5)	87.5	3.0

Total number of animals: 15

Note - The values in parentheses are those used by the Litchfield-Wilcoxon method to compute Chi Square contributions.

Calculated Chi Square: 0.442

Critical Chi Square (P=.05) for 1 degree of freedom: 3.956

The data are not significantly heterogeneous.

Calculated LD₅₀: 493.3 mg/kg

95% Confidence Limits: 378.5 - 642.9 mg/kg

The confidence limits are within 30.3% of the LD₅₀.

Slope: 10.77 (probits/log dose)

There are 5 animals included in groups with expected deaths between 16% (LD₁₆ = 398.4 mg/kg) and 84% (LD₈₄ = 610.9 mg/kg).

Given the slope calculated from the present data, a total of 11 animals would be needed in groups with expected deaths between 16% and 84% in order to get the confidence limits within 20% of the LD₅₀. However, adding more test groups may change the value of the slope.

TABLE 1 (Continued)

LITCHFIELD-WILCOXON LD₅₀ FOR FEMALES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: BENZOTHIAZOLE

Dose (mg/kg)	Observed Deaths Proportion	Deaths Percent	Expected Deaths Percent	Difference
398.0	1/5	20.0	17.5	2.5
501.0	3/5	60.0	66.9	-6.9
631.0	5/5	100.0 (97.1)	96.5	0.7

Total number of animals: 15

Note - The values in parentheses are those used by the Litchfield-Wilcoxon method to compute Chi Square contributions.

Calculated Chi Square: 0.134

Critical Chi Square (P=.05) for 1 degree of freedom: 3.956

The data are not significantly heterogeneous.

Calculated LD₅₀: 465.6 mg/kg

95% Confidence Limits: 401.9 - 539.4 mg/kg

The confidence limits are within 15.9% of the LD₅₀.

Slope: 13.71 (probits/log dose)

There are 10 animals included in groups with expected deaths between 16% (LD₁₆ = 393.6 mg/kg) and 84% (LD₈₄ = 550.7 mg/kg).

TABLE 1 (continued)
 LITCHFIELD-WILCOXON LD₅₀ FOR COMBINED SEXES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: BENZOTHAIAZOLE

Dose (mg/kg)	Observed Deaths Proportion	Observed Deaths Percent	Expected Deaths Percent	Difference
398.0	2/10	20.0	16.8	3.2
501.0	5/10	50.0	59.4	-9.4
631.0	10/10	100.0 (94.0)	92.5	1.5

Total number of animals: 30

Note - The values in parentheses are those used by the Litchfield-Wilcoxon method to compute Chi Square contributions.

Calculated Chi Square: 0.471

Critical Chi Square (P=.05) for 1 degree of freedom: 3.956

The data are not significantly heterogeneous.

Calculated LD₅₀: 478.6 mg/kg

95% Confidence Limits: 424.9 - 539.1 mg/kg

The confidence limits are within 12.6% of the LD₅₀.

Slope: 11.99 (probits/log dose)

There are 20 animals included in groups with expected deaths between 16% (LD₁₆ = 395.0 mg/kg) and 84% (LD₈₄ = 580.0 mg/kg).

FIGURE 1: DOSE-RESPONSE CURVE FOR MALES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: BENZOTHIAZOLE

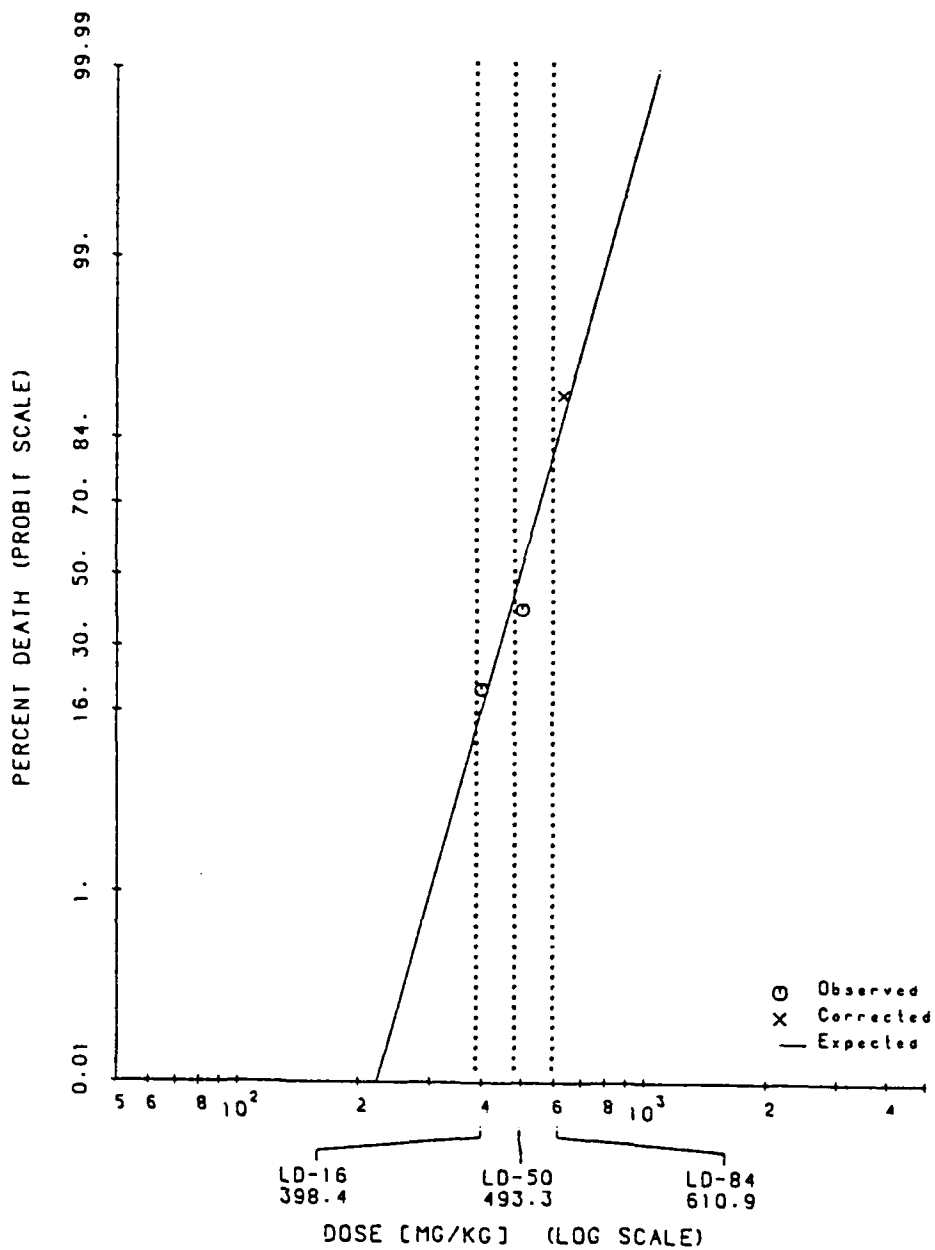


FIGURE 2: DOSE-RESPONSE CURVE FOR FEMALES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: BENZOTHAIAZOLE

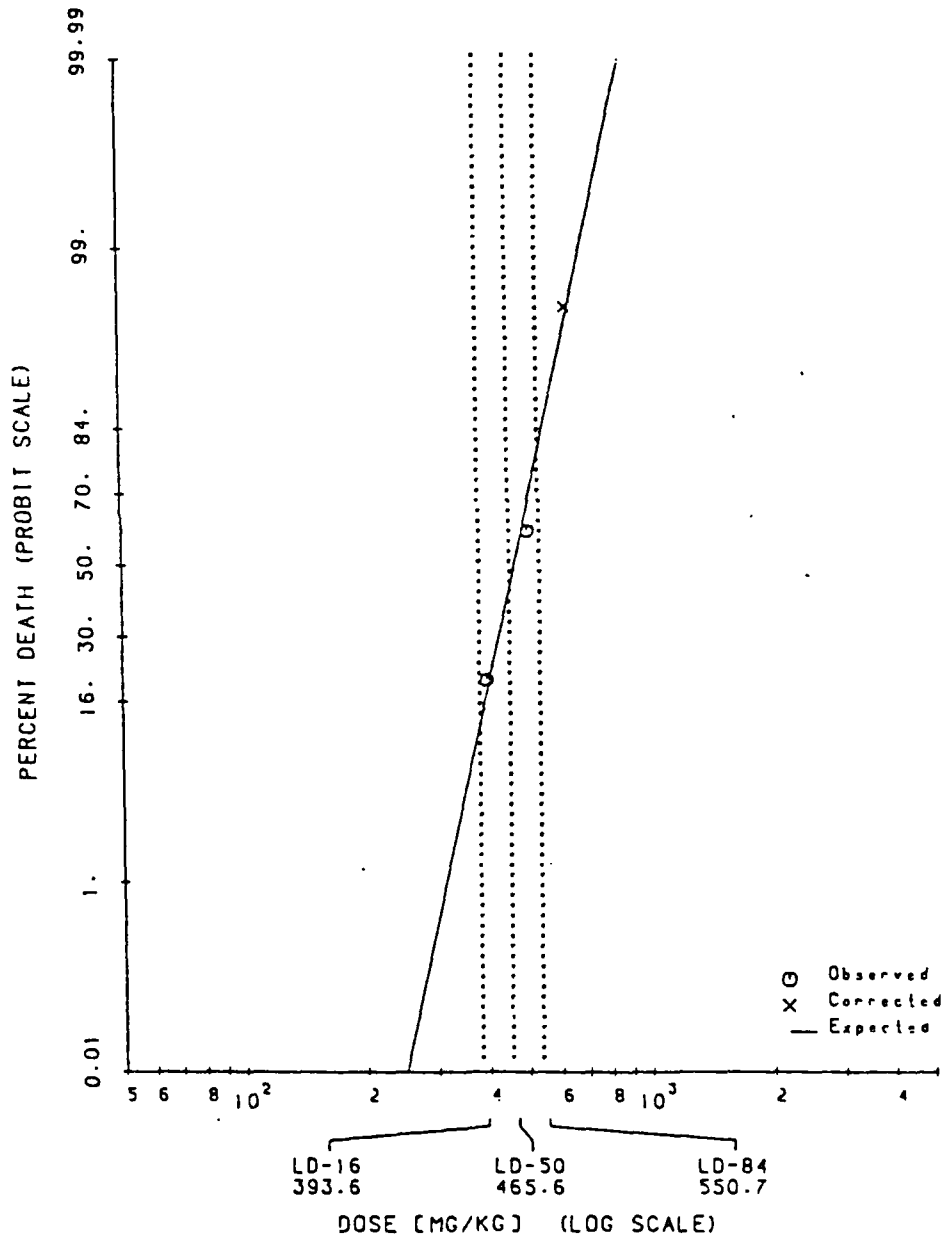


FIGURE 3: DOSE-RESPONSE CURVE FOR COMBINED SEXES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: BENZOTHIAZOLE

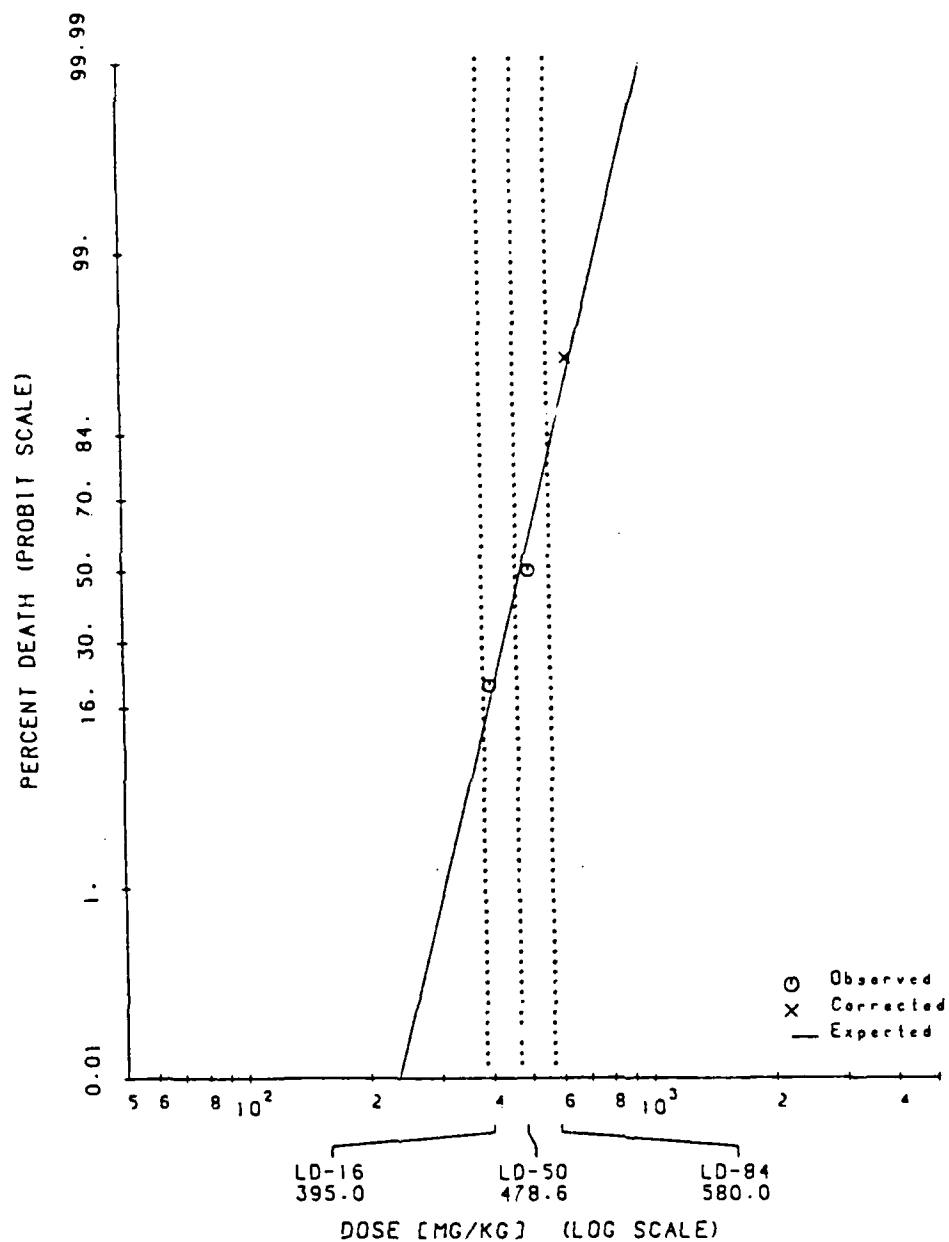


TABLE 2: INDIVIDUAL BODY WEIGHT
AND TEST ARTICLE ADMINISTRATION DATA

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: BENZOTHAIAZOLE

Dose Group: 398 mg/kg

Animal Number	Sex	Body Weights (grams) Day of Study						Amount of Test Article Administered	
		0	2	3	7	10	14	(mg)	(ml)
AH4196	M	222	-	234	252	258	268	88	2.2
AH4197	M	207	-	205	223	232	244	84	2.1
AH4198	M	206	(199)	-	-	-	-	84	2.1
AH4199	M	213	-	224	244	254	255	84	2.1
AH4200	M	<u>206</u>	-	<u>208</u>	<u>225</u>	<u>232</u>	<u>247</u>	<u>84</u>	<u>2.1</u>
Mean		211		218	236	244	254	85	2.1
S.D.		7		14	14	14	11	2	0.0
S.E.		3		7	7	7	5	1	0.0
AH4239	F	171	-	178	187	188	195	68	1.7
AH4240	F	166	-	178	186	185	188	68	1.7
AH4241	F	167	-	179	186	183	191	68	1.7
AH4242	F	150	-	149	165	169	180	60	1.5
AH4243	F	<u>154</u>	(148)	-	-	-	-	<u>60</u>	<u>1.5</u>
Mean		162		171	181	181	189	65	1.6
S.D.		9		15	11	8	6	4	0.1
S.E.		4		7	5	4	3	2	0.0

* Day 0 denotes fasted body weight the day of dose administration; day 14 denotes final body weight prior to sacrifice. Values in parentheses denote found dead body weights and are not included in the statistical analyses.

- = Not applicable.

TABLE 2 (Continued): INDIVIDUAL BODY WEIGHT
AND TEST ARTICLE ADMINISTRATION DATA

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: BENZOTHAIAZOLE

Dose Group: 501 mg/kg

Animal Number	Sex	Body Weights (grams)							Amount of Test Article Administered	
		0	1	Day of Study*		10	14	(mg)	(ml)	
AH4186	M	215	-	(200)	-	-	-	-	110	2.2
AH4187	M	211	-	(200)	-	-	-	-	105	2.1
AH4188	M	217	-	-	229	242	252	260	110	2.2
AH4189	M	202	-	-	193	200	213	234	100	2.0
AH4190	M	<u>200</u>	-	-	<u>208</u>	<u>221</u>	<u>228</u>	<u>237</u>	<u>100</u>	<u>2.0</u>
Mean		209			210	221	231	244	105	2.1
S.D.		8			18	21	20	14	5	0.1
S.E.		3			10	12	11	8	2	0.0
AH4229	F	155	(155)	-	-	-	-	-	80	1.6
AH4230	F	152	-	-	156	165	167	173	75	1.5
AH4231	F	151	(147)	-	-	-	-	-	75	1.5
AH4232	F	164	-	-	163	174	179	189	80	1.6
AH4233	F	<u>160</u>	(154)	-	-	-	-	-	<u>80</u>	<u>1.6</u>
Mean		156			160	170	173	181	78	1.6
S.D.		6			5	6	8	11	3	0.1
S.E.		2			4	5	6	8	1	0.0

* Day 0 denotes fasted body weight the day of dose administration; day 14 denotes final body weight prior to sacrifice. Values in parentheses denote found dead body weights and are not included in the statistical analyses.

- = Not applicable.

TABLE 2 (Continued): INDIVIDUAL BODY WEIGHT
AND TEST ARTICLE ADMINISTRATION DATA

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: BENZOTHIAZOLE

Dose Group: 631 mg/kg

Animal Number	Sex	Body Weights (grams) Day of Study*			Amount of Test Article Administered	
		0	1	2	(mg)	(ml)
AH4201	M	222	-	(222)	139	2.2
AH4202	M	210	(212)	-	133	2.1
AH4203	M	224	-	(222)	139	2.2
AH4204	M	230	(225)	-	145	2.3
AH4205	M	<u>231</u>	-	(220)	<u>145</u>	<u>2.3</u>
Mean		223			140	2.2
S.D.		8			5	0.1
S.E.		4			2	0.0
AH4244	F	161	(159)	-	101	1.6
AH4245	F	154	-	(155)	95	1.5
AH4246	F	156	-	(153)	101	1.6
AH4247	F	152	(148)	-	95	1.5
AH4248	F	<u>161</u>	-	(161)	<u>101</u>	<u>1.6</u>
Mean		157			99	1.6
S.D.		4			3	0.1
S.E.		2			1	0.0

*Day 0 denotes fasted body weight the day of dose administration; day 14 denotes final body weight prior to sacrifice. Values in parentheses denote found dead body weights and are not included in the statistical analyses.

- = Not applicable.

TABLE 3
 INDIVIDUAL ANTE-MORTEM OBSERVATIONS
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: RENZOTHIAZOLE

Finding	Animal No. (Sex)	Day(s) Finding Observed									
		AH4196 (M)	AH4197 (M)	AH4198 (M)	AH4199 (M)	AH4200 (M)	AH4239 (F)	AH4240 (F)	AH4241 (F)	AH4242 (F)	AH4243 (F)
Lethargy									2		0
Ataxia	0	0,1	0	0	0	0	0	0	0,2		0
Prostration			1						1		1
Lacrimation			1			0		0	0-2		0,1
Squinting		0		0	0	0	0	0	0		0
No stool										2	
Crusty eye							1			3	
Crusty muzzle					1						
Damp fur-perianal region								1			
Death											2
No abnormalities		1-14	2-14	2	1-14	2-14	2-14	2-14	2-14	1-14	4-14

TABLE 3 (Continued)

INDIVIDUAL ANTE-MORTEM OBSERVATIONS

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: BENZOTHIADIAZOLE

Dose Group: 501 mg/kg

Finding	Animal No. (Sex)	Day(s) Finding Observed										
		AH4186 (M)	AH4187 (M)	AH4188 (M)	AH4189 (M)	AH4190 (M)	AH4229 (F)	AH4230 (F)	AH4231 (F)	AH4232 (F)	AH4233 (F)	
Lethargy	0				1,2		0	1			2	0
Ataxia	0			0	0,1	0	0	0,1	0	0	0,2	0
Prostration	1	1					0			0	1	0
Lacrimation	0,1	1	1		0	0	0	0,1	0	0	0-2	0
Squinting	0		0	0	0	0	0	0,1	0	0	0,2	0
Body cool to touch	1	1							0		1	0
Few stools					1						2,3	
Loose stool	1	1					0					0
Crusty eye				2				1				
Crusty muzzle				2								
Yellow/brown stained fur-perianal region	1	1					0					0
Damp fur-perianal region								1			1	
Death	2	2					1		1			1
No abnormalities			1-14	3-14	1-14	1-14		2-14			4-14	

TABLE 3 (Continued)
 INDIVIDUAL ANTEMORTEM OBSERVATIONS
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: BENZOTHAIAZOLE

Finding	Animal No. (Sex)	Day(s) Finding Observed																				
		AH4201 (M)	AH4202 (M)	AH4203 (M)	AH4204 (M)	AH4205 (M)	AH4244 (F)	AH4245 (E)	AH4246 (F)	AH4247 (F)	AH4248 (F)											
Lethargy	1				0	0																
Ataxia	0,1		0	0	0	0								0	0							0
Prostration		1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	1
Lacrimation	0	0,1	0	1	0	1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1
Squinting	0,1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Body cool to touch																						0
Loose stool	0																					0
Crusty muzzle																						1
Yellow/brown stained fur-perianal region	0,1																					0
Damp fur-perianal region																						1
Death	2	1	1	2	1	2	1	2	1	2	1	2	2	2	1	2	2	2	1	1	2	2

TABLE 4
 INDIVIDUAL NECROPSY FINDINGS
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: BENZOTHIAZOLE

Dose Group: 398 mg/kg

Animal Number	Sex	Abnormalities Noted at Necropsy (Organ - Abnormality)
AH4196	M	Spleen - enlarged; discoloration, dark red
AH4197	M	Spleen - enlarged; discoloration, dark red
AH4198*	M	Stomach - dark contents Glandular stomach - discoloration, multiple focal, black, on mucosa Small intestine - dark contents Liver - discoloration, diffuse, pale
AH4199	M	Spleen - enlarged; discoloration, dark red
AH4200	M	Spleen - enlarged; discoloration, dark red
AH4239	F	Spleen - enlarged; discoloration, dark red
AH4240	F	Spleen - enlarged; discoloration, dark red
AH4241	F	Spleen - enlarged; discoloration, dark red
AH4242	F	Spleen - enlarged; discoloration, dark red Ovary - cyst, solitary, clear, left
AH4243*	F	Glandular stomach - discoloration, multiple focal, black, on mucosa Liver - discoloration, diffuse, pale

* Animal found dead prior to final sacrifice.

TABLE 4 (Continued)

INDIVIDUAL NECROPSY FINDINGS

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: BENZOTHAIAZOLE

Dose Group: 501 mg/kg

Animal Number	Sex	Abnormalities Noted at Necropsy (Organ - Abnormality)
AH4186*	M	Glandular stomach - discoloration, multiple focal, black, >5, approximately 0.2 cm Small intestine - dark content
AH4187*	M	Glandular stomach - discoloration, multiple focal, black, >5, approximately 0.1 cm Small intestine - dark content Urinary bladder - distended
AH4188	M	Spleen - enlarged; discoloration, diffuse, dark red Liver - diaphragmatic hernia
AH4189	M	Spleen - enlarged; discoloration, diffuse, dark red
AH4190	M	Spleen - enlarged; discoloration, diffuse, dark red Testis - small, diffuse, bilateral
AH4229*	F	Glandular stomach - discoloration, multiple focal, black, on mucosa
AH4230	F	Spleen - enlarged; discoloration, diffuse, dark red
AH4231*	F	Glandular stomach - discoloration, multiple focal, black, on mucosa
AH4232	F	Spleen - enlarged; discoloration, diffuse, dark red
AH4233*	F	Glandular stomach - discoloration, multiple focal, black, on mucosa Liver - discoloration, diffuse, pale

* Animal found dead prior to final sacrifice.

TABLE 4 (Continued)
 INDIVIDUAL NECROPSY FINDINGS
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: BENZOTHIAZOLE

Dose Group: 631 mg/kg

Animal Number	Sex	Abnormalities Noted at Necropsy (Organ - Abnormality)
AH4201	M	Lung - discoloration, diffuse, red
AH4202	M	None
AH4203	M	None
AH4204	M	Glandular stomach - discoloration, multiple focal, black, on mucosa
AH4205	M	Glandular stomach - discoloration, multiple focal, black, on mucosa Lung - discoloration, diffuse, red
AH4244	F	Stomach - small amount of dark contents Lung - discoloration, diffuse, dark red
AH4245	F	Glandular stomach - discoloration, multiple focal, black, on mucosa Small intestine - dark contents Liver - discoloration, diffuse, pale Lung - discoloration, diffuse, pale
AH4246	F	Glandular stomach - discoloration, multiple focal, black, on mucosa Liver - discoloration, diffuse, pale
AH4247	F	Glandular stomach - discoloration, multiple focal, black, on mucosa Liver - discoloration, diffuse, pale
AH4248	F	Glandular stomach - discoloration, multiple focal, black, on mucosa Liver - discoloration, diffuse, pale

NOTE: All animals found dead prior to final sacrifice.

TABLE 5
LITCHFIELD-WILCOXON LD₅₀ FOR MALES
ACUTE ORAL LD₅₀ DETERMINATION IN RATS
TEST ARTICLE: DITHIANE

Dose (mg/kg)	Observed Deaths Proportion	Deaths Percent	Expected Deaths Percent	Difference
2818.0	0/5	0.0 (0.3)	0.2	0.1
3162.0	0/5	0.0 (2.9)	4.9	-2.0
3548.0	2/5	40.0	34.5	5.5
3981.0	4/5	80.0	80.5	-0.5

Total number of animals: 20

Note - The values in parentheses are those used by the Litchfield-Wilcoxon method to compute Chi Square contributions.

Calculated Chi Square: 0.113

Critical Chi Square (P=.05) for 2 degrees of freedom: 6.080

The data are not significantly heterogeneous.

Calculated LD₅₀: 3680.1 mg/kg

95% Confidence Limits: 3396.5 - 3987.4 mg/kg.

The confidence limits are within 8.4% of the LD₅₀.

Slope: 25.15 (probits/log dose)

There are 10 animals included in groups with expected deaths between 16% (LD₁₆ = 3358.2 mg/kg) and 84% (LD₈₄ = 4033.0 mg/kg).

TABLE 5 (Continued)

LITCHFIELD-WILCOXON LD₅₀ FOR FEMALES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: DITHIANE

Dose (mg/kg)	Observed Deaths Proportion	Deaths Percent	Expected Deaths Percent	Difference
1778.0	0/5	0.0 (10.5)	14.0	-3.6
2818.0	4/5	80.0	51.7	28.3
3162.0	2/5	40.0	62.7	-22.7
3981.0	4/5	80.0	81.2	-1.2

Total number of animals: 20

Note - The values in parentheses are those used by the Litchfield-Wilcoxon method to compute Chi Square contributions.

Calculated Chi Square: 2.760

Critical Chi Square (P=.05) for 2 degrees of freedom: 6.080

The data are not significantly heterogeneous.

Calculated LD₅₀: 2768.1 mg/kg

95% Confidence Limits: 2063.9 - 3712.7 mg/kg

The confidence limits are within 34.1% of the LD₅₀.

Slope: 5.61 (probits/log dose)

There are 15 animals included in groups with expected deaths between 16% (LD₁₆ = 1836.2 mg/kg) and 84% (LD₈₄ = 4173.0 mg/kg).

Given the slope calculated from the present data, a total of 39 animals would be needed in groups with expected deaths between 16% and 84% in order to get the confidence limits within 20% of the LD₅₀. However, adding more test groups may change the value of the slope.

TABLE 5 (Continued)
 LITCHFIELD-WILCOXON LD₅₀ FOR COMBINED SEXES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: DITHIANE

Dose (mg/kg)	Observed Deaths Proportion	Deaths Percent	Expected Deaths Percent	Difference
1778.0	0/5	0.0 (0.4)	0.5	-0.1
2818.0	4/10	40.0	21.0	19.0
3162.0	2/10	20.0	35.9	-15.9
3548.0	2/5	40.0	53.3	-13.3
3981.0	8/10	80.0	70.1	9.9

Total number of animals: 40

Note - The values in parentheses are those used by the Litchfield-Wilcoxon method to compute Chi Square contributions.

Calculated Chi Square: 3.564

Critical Chi Square (P=.05) for 3 degrees of freedom: 7.812

The data are not significantly heterogeneous.

Calculated LD₅₀: 3472.7 mg/kg

95% Confidence Limits: 3076.4 - 3920.0 mg/kg

The confidence limits are within 12.9% of the LD₅₀.

Slope: 8.90 (probits/log dose)

There are 35 animals included in groups with expected deaths between 16% (LD₁₆ = 2680.9 mg/kg) and 84% (LD₈₄ = 4498.2 mg/kg).

FIGURE 4: DOSE-RESPONSE CURVE FOR MALES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: DITHIANE

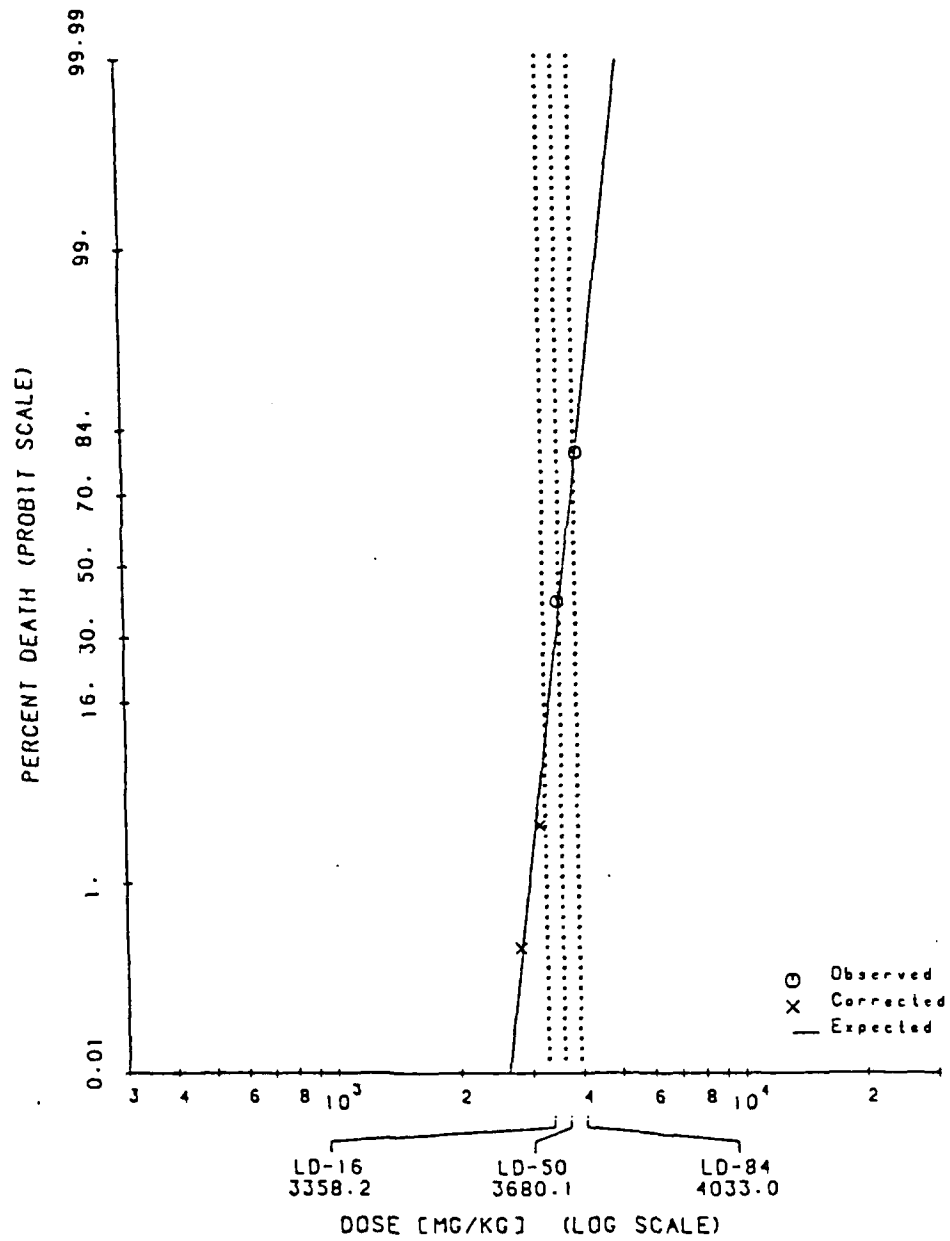


FIGURE 5: DOSE-RESPONSE CURVE FOR FEMALES

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: DITHIANE

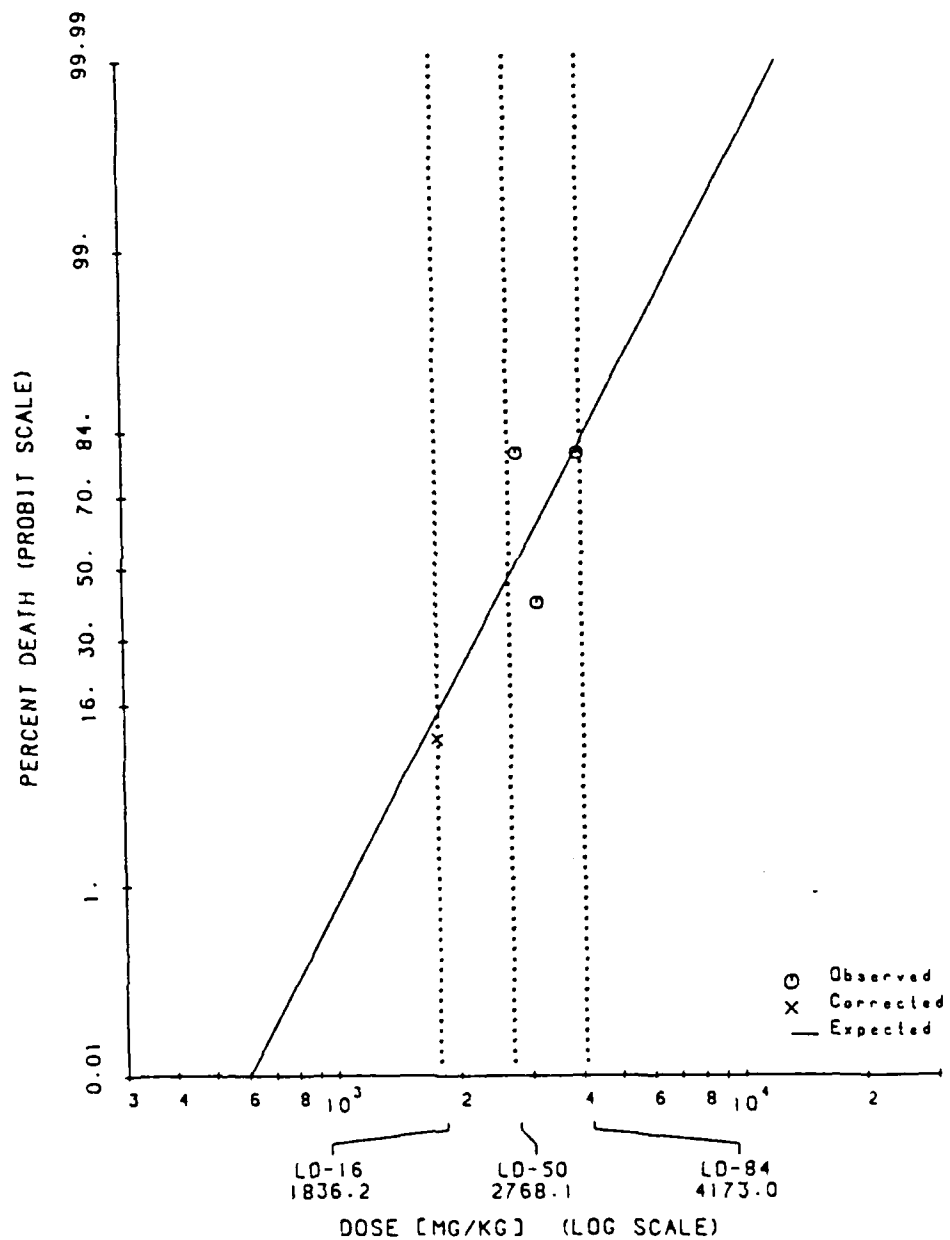


FIGURE 6: DOSE-RESPONSE CURVE FOR COMBINED SEXES

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: DITHIANE

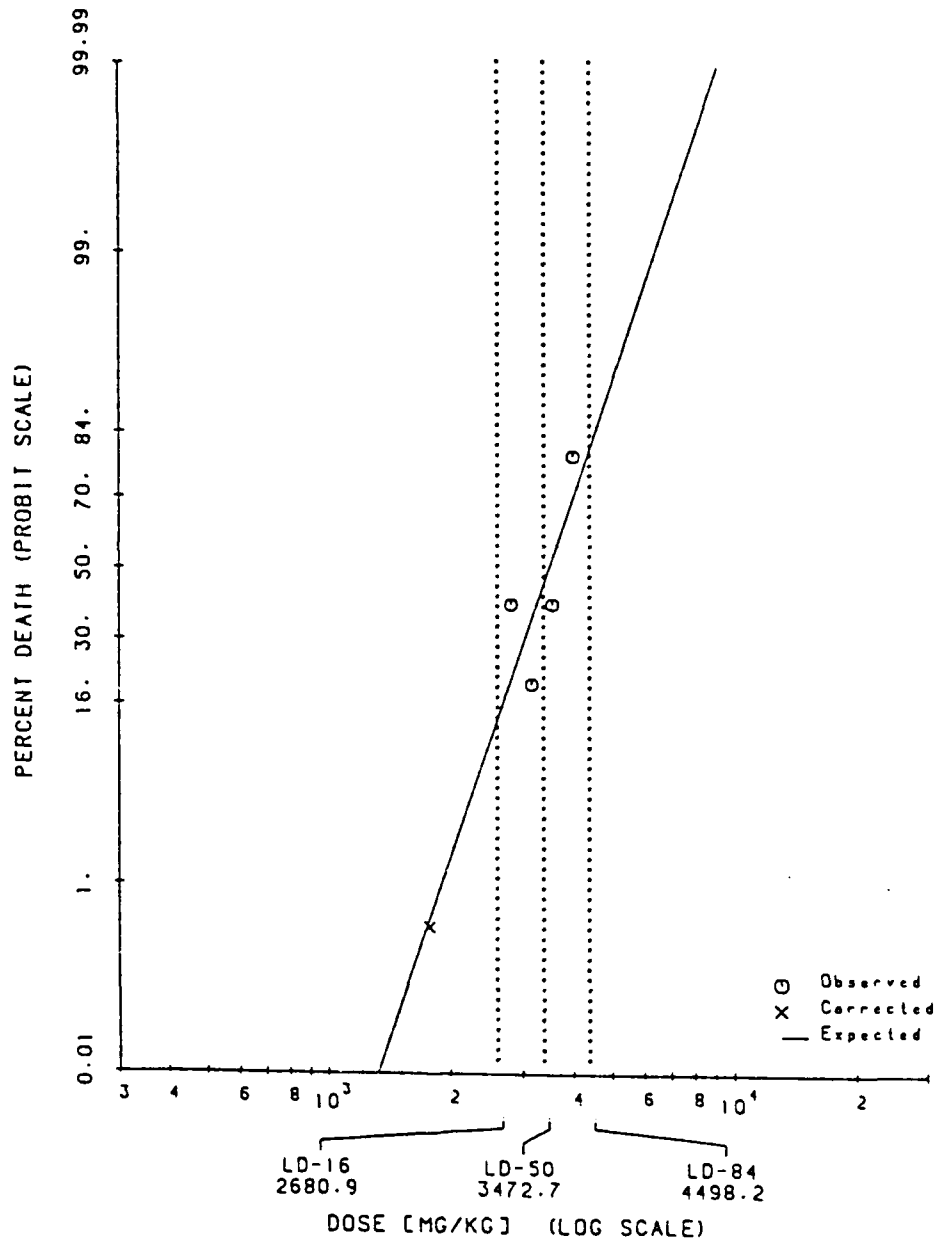


TABLE 6
 INDIVIDUAL BODY WEIGHT
 AND TEST ARTICLE ADMINISTRATION DATA
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: DITHIANE

Dose Group: 1778 mg/kg

Animal Number	Sex	Body Weights (grams)					Amount of Test Article Administered	
		0	4	7	10	14	(mg)	(ml)
AH4259	F	159	171	178	177	178	282	2.7
AH4260	F	160	172	182	181	186	282	2.7
AH4261	F	166	175	185	186	188	293	2.8
AH4262	F	159	175	183	183	184	282	2.7
AH4263	F	<u>153</u>	<u>141</u>	<u>157</u>	<u>163</u>	<u>173</u>	<u>272</u>	<u>2.6</u>
Mean		159	167	177	178	182	282	2.7
S.D.		5	15	11	9	6	7	0.1
S.E.		2	6	5	4	3	3	0.0

* Day 0 denotes fasted body weight the day of dose administration; day 14 denotes final body weight prior to final sacrifice.

TABLE 6 (Continued)

INDIVIDUAL BODY WEIGHT
AND TEST ARTICLE ADMINISTRATION DATA
ACUTE ORAL LD₅₀ DETERMINATION IN RATS
TEST ARTICLE: DITHIANE

Dose Group: 2818 mg/kg

Animal Number	Sex	Body Weights (grams) Day of Study*						Amount of Test Article Administered	
		0	1	3	7	10	14	(mg)	(ml)
AH4191	M	208	-	217	233	238	253	580	3.5
AH4192	M	212	-	223	227	234	247	597	3.6
AH4193	M	207	-	212	235	244	262	580	3.5
AH4194	M	207	-	200	226	238	256	580	3.5
AH4195	M	208	-	202	227	234	248	580	3.5
Mean		208		211	230	238	253	583	3.5
S.D.		2		10	4	4	6	8	0.0
S.E.		1		4	2	2	3	3	0.0
AH4234	F	165	-	160	178	186	192	464	2.8
AH4235	F	161	(154)	-	-	-	-	448	2.7
AH4236	F	159	-	(139)	-	-	-	448	2.7
AH4237	F	167	(161)	-	-	-	-	464	2.8
AH4238	F	159	(154)	-	-	-	-	448	2.7
Mean		162						454	2.7
S.D.		4						9	0.1
S.E.		2						4	0.0

* Day 0 denotes fasted body weight the day of dose administration; day 14 denotes final body weight prior to final sacrifice. Values in parentheses denote found dead body weights and are not included in the statistical analyses.
- = Not applicable.

TABLE 6 (Continued)

INDIVIDUAL BODY WEIGHT
AND TEST ARTICLE ADMINISTRATION DATAACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: DITHIANE

Dose Group: 3162 mg/kg

Animal Number	Sex	Body Weights (grams)							Amount of Test Article Administered	
		0	1	Day of Study*			10	14	(mg)	(ml)
AH4208	M	216	-	204	-	222	239	250	688	3.7
AH4209	M	220	-	214	-	233	246	257	688	3.7
AH4210	M	234	-	227	-	247	265	279	744	4.0
AH4211	M	227	-	225	-	248	264	276	725	3.9
AH4212	M	<u>232</u>	-	<u>224</u>	-	<u>237</u>	<u>251</u>	<u>267</u>	<u>725</u>	<u>3.9</u>
Mean		226		219		237	253	266	714	3.8
S.D.		8		10		11	11	12	25	0.1
S.E.		3		4		5	5	6	11	0.1
AH4251	F	155	-	149	-	158	173	179	484	2.6
AH4252	F	177	-	172	-	184	193	199	558	3.0
AH4253	F	170	(169)	-	-	-	-	-	539	2.9
AH4253	F	155	-	148	-	164	170	176	484	2.6
AH4255	F	<u>161</u>	-	<u>137</u>	(119)	-	-	-	<u>502</u>	<u>2.7</u>
Mean		164		152		169	179	185	513	2.8
S.D.		10		15		14	13	13	34	0.2
S.E.		4		7		8	7	7	15	0.1

* Day 0 denotes fasted body weight the day of dose administration; day 14 denotes final body weight prior to final sacrifice. Values in parentheses denote found dead body weights and are not included in the statistical analyses.

- = Not applicable.

TABLE 6 (Continued)
 INDIVIDUAL BODY WEIGHT
 AND TEST ARTICLE ADMINISTRATION DATA
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: DITHIANE

Dose Group: 3548 mg/kg

Animal Number	Sex	Body Weights (grams)						Amount of Test Article Administered	
		0	1	Day of Study*				(mg)	(ml)
				3	7	10	14		
AH4213	M	211	(208)	-	-	-	-	751	3.6
AH4219	M	245	-	231	254	269	273	877	4.2
AH4220	M	239	(235)	-	-	-	-	856	4.1
AH4221	M	225	-	220	238	252	252	793	3.8
AH4222	M	<u>229</u>	-	<u>215</u>	<u>233</u>	<u>247</u>	<u>251</u>	<u>814</u>	<u>3.9</u>
Mean		230		222	242	256	259	818	3.9
S.D.		13		8	11	12	12	50	0.2
S.E.		6		5	6	7	7	22	0.1

* Day 0 denotes fasted body weight the day of dose administration; day 14 denotes final body weight prior to final sacrifice. Values in parentheses denote found dead body weights and are not included in the statistical analyses.

- = Not applicable.

TABLE 6 (Continued)

INDIVIDUAL BODY WEIGHT
AND TEST ARTICLE ADMINISTRATION DATA
ACUTE ORAL LD₅₀ DETERMINATION IN RATS
TEST ARTICLE: DITHIANE

Dose Group: 3981 mg/kg

Animal Number	Sex	Body Weights (grams) Day of Study*							Amount of Test Article Administered		
		0	1	2	3	4	7	10	14	(mg)	(ml)
AH4207	M	222	-	(203)	-	-	-	-	-	890	3.8
AH4214	M	243	-	-	-	241	267	266	280	960	4.1
AH4216	M	222	-	(204)	-	-	-	-	-	890	3.8
AH4217	M	230	-	-	(198)	-	-	-	-	913	3.9
AH4218	M	233	-	(213)	-	-	-	-	-	937	4.0
Mean		230								918	3.9
S.D.		9								30	0.1
S.E.		4								14	0.1
AH4249	F	174	(172)	-	-	-	-	-	-	703	3.0
AH4250	F	165	-	-	(156)	-	-	-	-	656	2.8
AH4256	F	165	-	-	(152)	-	-	-	-	656	2.8
AH4257	F	166	(163)	-	-	-	-	-	-	656	2.8
AH4258	F	165	-	-	-	162	181	182	190	656	2.8
Mean		167								665	2.8
S.D.		4								21	0.1
S.E.		2								9	0.0

* Day 0 denotes fasted body weight the day of dose administration; day 14 denotes final body weight prior to final sacrifice. Values in parentheses denote found dead body weights and are not included in the statistical analyses.

- = Not applicable.

TABLE 7
 INDIVIDUAL ANTEMORTEM OBSERVATIONS
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: DITHIANE

Dose Group: 1778 mg/kg

Finding	Animal No.: Sex:	Day(s) Finding Observed				
		AH4259 (F)	AH4260 (F)	AH4261 (F)	AH4262 (F)	AH4263 (F)
Ataxia		0,1	0,1	1	1	0-4
Lacrimation				1	1	1
Damp fur-perianal region				2		2,3
Yellow/brown stained fur-perianal region						4-9
Crusty nose					1	
Crusty eye		1	1,2	2-4	1,2	2-5
Lethargy						2,3
No abnormalities		2-14	3-14	0,5-14	0,3-14	10-14

TABLE 7 (Continued)

INDIVIDUAL ANTEMORTEM OBSERVATIONS

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: DITHIANE

Dose Group: 2818 mg/kg

Finding	Animal No.: Sex:	Day(s) Finding Observed														
		AH4191 (M)	AH4192 (M)	AH4193 (M)	AH4194 (M)	AH4195 (M)	AH4234 (F)	AH4235 (F)	AH4236 (F)	AH4237 (F)	AH4238 (F)					
Lacrimation		1	1	1	1	1	0-2	0	0-2	0	0	0	0	0	0	0
Crusty nose			2,3	2,3	2,3	2,3	3		2							
Prostration				1			1		1,2							
Muscle tremors							2									
Yellow/brown stained fur-perianal region								2,3	2							
Squinting									2							
Ataxia	0		0,1	0,2	0,2	1,2	0,2	0	0	0	0	0	0	0	0	0
Lethargy													0	0		
Crusty eye				2,3	2,3	2,3	2-5									
Damp fur-perianal region				0												
Death		1-14	2-14	4-14	4-14	0,4-14	6-14		1	3	1	1	1	1	1	1
No abnormalities																

TABLE 7 (Continued)

INDIVIDUAL ANTEMORTEM OBSERVATIONS

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: DITHIANE

Dose Group: 3162 mg/kg

Finding	Animal No.: Sex:	Day(s) Finding Observed											
		AH4208 (M)	AH4209 (M)	AH4210 (M)	AH4211 (M)	AH4212 (M)	AH4251 (F)	AH4252 (F)	AH4253 (F)	AH4254 (F)	AH4255 (F)		
Crusty muzzle	0	2											4-6
Red stained fur around eyes	2	2				1			1,2				4-6
Emaciated													1,2
No stools													3-6
Crusty eyes	3,4	3,4	2-4	2-4	2-6	3,4	2-5						3-6
Crusty nose			3	2,3	2,3		2,3						1-3
Yellow/brown stained fur-perianal region													3-6
Hyperactivity													
Prostration			1										1
Muscle tremors													2,3,6
Lethargy	1	1			1	2	1						2,5,6
Ataxia	0-2	0,1	0,2	0,1	0,1	0,2	1,2	0					0,2-6
Few stools													3
Lacrimation			1	1	1	1,2	1						1,2
Death													6
No abnormalities			5-14	5-14	5-14	7-14	5-14	0,6-14					7-14

TABLE 7 (Continued)
 INDIVIDUAL ANTEMORTEM OBSERVATIONS
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: DITHIANE

Dose Group: 3548 mg/kg

Finding	Animal No.: Sex:	Day(s) Finding Observed				
		AH4213 (M)	AH4219 (M)	AH4220 (M)	AH4221 (M)	AH4222 (M)
Ataxia		0	0-2	0	0,1	0-2
Lethargy		0		0	1	1
Lacrimation		0	1,2	0	1	0-2
Crusty eyes			2,3		2,3	3-5
Crusty nose					2	
Few stools			2		2	3
No stools						2
Damp fur-perianal region						3-5
Death		1		1		
No abnormalities			4-14		4-14	6-14

TABLE 7 (Continued)

INDIVIDUAL ANTEORTHEM OBSERVATIONS

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: DITHIANE

Dose Group: 3981 mg/kg

Finding	AH4207		AH4214		AH4216		AH4217		AH4218		AH4249		AH4250		AH4256		AH4257		AH4258	
	(M)	(F)	(M)	(F)	(M)	(F)	(M)	(F)	(M)	(F)	(M)	(F)	(M)	(F)	(M)	(F)	(M)	(F)	(M)	(F)
Ataxia	0,1		0,1		0		0,1		0		0		0-2		0-2		0		0,1	
Lacrimation	1		1		1		0-2		1		0		0-2		1,2		0		0,1	
Yellow/brown stained fur-perianal region																			4-9	
Lethargy	1				1				0		0		1,2		1,2		0		0,1	
Crusty nose			2																3,4	
Irregular breathing							2													
Crusty eyes			2-4																2-5	
Prostration					1		2		1											
Damp fur-perianal region											0		1,2		1,2				1-3	
Death	2				2		3		2		1		3		3		1			
No abnormalities			5-14																10-14	



TABLE 8
INDIVIDUAL NECROPSY FINDINGS
ACUTE ORAL LD₅₀ DETERMINATION IN RATS
TEST ARTICLE: DITHIANE

Dose Group: 1778 mg/kg

Animal Number	Sex	Abnormalities Noted at Necropsy (Organ - Abnormality)
AH4259	F	None
AH4260	F	None
AH4261	F	None
AH4262	F	None
AH4263	F	None

TABLE 8 (Continued)
 INDIVIDUAL NECROPSY FINDINGS
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: DITHIANE

Dose Group: 2818 mg/kg

Animal Number	Sex	Abnormalities Noted at Necropsy (Organ - Abnormality)
AH4191	M	None
AH4192	M	None
AH4193	M	None
AH4194	M	None
AH4195	M	None
AH4234	F	None
AH4235*	F	Liver - discoloration, diffuse, pale
AH4236*	F	Stomach - dark contents Small intestine - dark contents Liver - discoloration, diffuse, pale Glandular stomach - discoloration, multiple focal, black, on mucosa
AH4237*	F	Jejunum - discoloration, diffuse, pale Liver - discoloration, diffuse, pale
AH4238*	F	Lung - discoloration, diffuse, red Jejunum - discoloration, diffuse, pale

* Animal found dead prior to final sacrifice.

TABLE 8 (Continued)
 INDIVIDUAL NECROPSY FINDINGS
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: DITHIANE

Dose Group: 3162 mg/kg

Animal Number	Sex	Abnormalities Noted at Necropsy (Organ - Abnormality)
AH4208	M	None
AH4209	M	None
AH4210	M	None
AH4211	M	None
AH4212	M	None
AH4251	F	None
AH4252	F	None
AH4253*	F	Lung - discoloration, diffuse, red Small intestine - discoloration, diffuse, red, multiple areas
AH4254	F	None
AH4255*	F	External surfaces - fur around rectum discolored black Glandular stomach - mucosa smooth/dyscoloration, red, multiple Cecum - contained thick black material Ileum - red fluid contents Colon - red fluid contents Duodenum - red fluid contents

* Animal found dead prior to final sacrifice.

TABLE 8 (Continued)

INDIVIDUAL NECROPSY FINDINGS

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: DITHIANE

Dose Group: 3548 mg/kg

Animal Number	Sex	Abnormalities Noted at Necropsy (Organ - Abnormality)
AH4213*	M	Stomach - contained white fluid material
AH4219	M	None
AH4220*	M	Oral region - discoloration, diffuse, green yellow Stomach - contained white fluid material Small intestines - white content
AH4221	M	None
AH4222	M	None

* Animal found dead prior to final sacrifice.

TABLE 8 (Continued)
 INDIVIDUAL NECROPSY FINDINGS
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: DITHIANE

Dose Group: 3981 mg/kg

Animal Number	Sex	Abnormalities Noted at Necropsy (Organ - Abnormality)
AH4207*	M	External surfaces - salivation around mouth Stomach - contained dark material; discolorations, multiple, black Intestinal tract - contained dark material
AH4214	M	None
AH4216*	M	External surfaces - discoloration on fur around mouth, yellow Lung - discolored, dark red, diffuse Stomach - contained dark material Glandular stomach - discolorations, multiple, black
AH4217*	M	External surfaces - yellow fluid around mouth Lung - discolored red, diffuse Stomach - contents dark Glandular stomach - discoloration, black, multiple Intestines - contained dark fluid
AH4218*	M	External surfaces - fur discolored yellow around mouth Stomach - contained dark material Glandular stomach - discoloration, multiple, black

* Animal found dead prior to final sacrifice.

TABLE 8 (Continued)

INDIVIDUAL NECROPSY FINDINGS

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: DITHIANE

Dose Group: 3981 mg/kg (cont.)

Animal Number	Sex	Abnormalities Noted at Necropsy (Organ - Abnormality)
AH4249*	F	Lung - discoloration, diffuse, red Small intestine - discoloration, diffuse, red Stomach - dark content
AH4250*	F	External surfaces - yellow fluid around mouth Lung - discolored, dark red, diffuse Stomach - contents dark Glandular stomach - discolorations, multiple red Intestines - dark fluid contents
AH4256*	F	External surfaces - yellow fluid around mouth Lung - discolored, red, diffuse Liver - discolorations, multiple, tan Intestines - red fluid content
AH4257*	F	Lung - discoloration, diffuse, red Small intestine - discoloration, diffuse, red
AH4258	F	Ovary - cyst, solitary, red, left

* Animal found dead prior to final sacrifice.

TABLE 9
 LITCHFIELD-WILCOXON LD₅₀ FOR MALES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: OXATHIANE

Dose (mg/kg)	Observed Deaths Proportion	Observed Deaths Percent	Expected Deaths Percent	Difference
2601.0	0/5	0.0 (0.2)	0.2	-0.0
3060.0	1/5	20.0	16.9	3.1
3600.0	4/5	80.0	81.6	-1.6

Total number of animals: 15

Note - The values in parentheses are those used by the Litchfield-Wilcoxon method to compute Chi Square contributions.

Calculated Chi Square: 0.043

Critical Chi Square (P=.05) for 1 degree of freedom: 3.956

The data are not significantly heterogeneous.

Calculated LD₅₀: 3327.6 mg/kg

95% Confidence Limits: 3082.2 - 3592.4 mg/kg

The confidence limits are within 8.0% of the LD₅₀.

Slope: 26.33 (probits/log dose)

There are 10 animals included in groups with expected deaths between 16% (LD₁₆ = 3049.0 mg/kg) and 84% (LD₈₄ = 3631.6 mg/kg).

TABLE 9 (Continued)

LITCHFIELD-WILCOXON LD₅₀ FOR FEMALES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: OXATHIANE

Dose (mg/kg)	Observed Deaths Proportion	Observed Deaths Percent	Expected Deaths Percent	Difference
2601.0	2/5	40.0	40.0	
3060.0	1/5	20.0	20.0	
3600.0	5/5	100.0	NOT VALID FOR THIS CALCULATION	

Total number of animals: 15

Slope: -8.34 (probits/log dose)

The LD₅₀ cannot be calculated when the slope is zero.

TABLE 9 (continued)
 LITCHFIELD-WILCOXON LD₅₀ FOR COMBINED SEXES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: OXATHIANE

Dose (mg/kg)	Observed Deaths Proportion	Deaths Percent	Expected Deaths Percent	Difference
2601.0	2/10	20.0	11.6	8.4
3060.0	2/10	20.0	44.7	-24.7
3600.0	9/10	90.0	82.3	7.7

Total number of animals: 30

Calculated Chi Square: 3.558

Critical Chi Square (P=.05) for 1 degree of freedom: 3.956

The data are not significantly heterogeneous.

Calculated LD₅₀: 3123.3 mg/kg

95% Confidence Limits: 2840.7 - 3433.9 mg/kg

The confidence limits are within 9.9% of the LD₅₀.

Slope: 15.04 (probits/log dose)

There are 20 animals included in groups with expected deaths between 16% (LD₁₆ = 2679.9 mg/kg) and 84% (LD₈₄ = 3640.0 mg/kg).

FIGURE 7: DOSE-RESPONSE CURVE FOR MALES
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: OXATHIANE

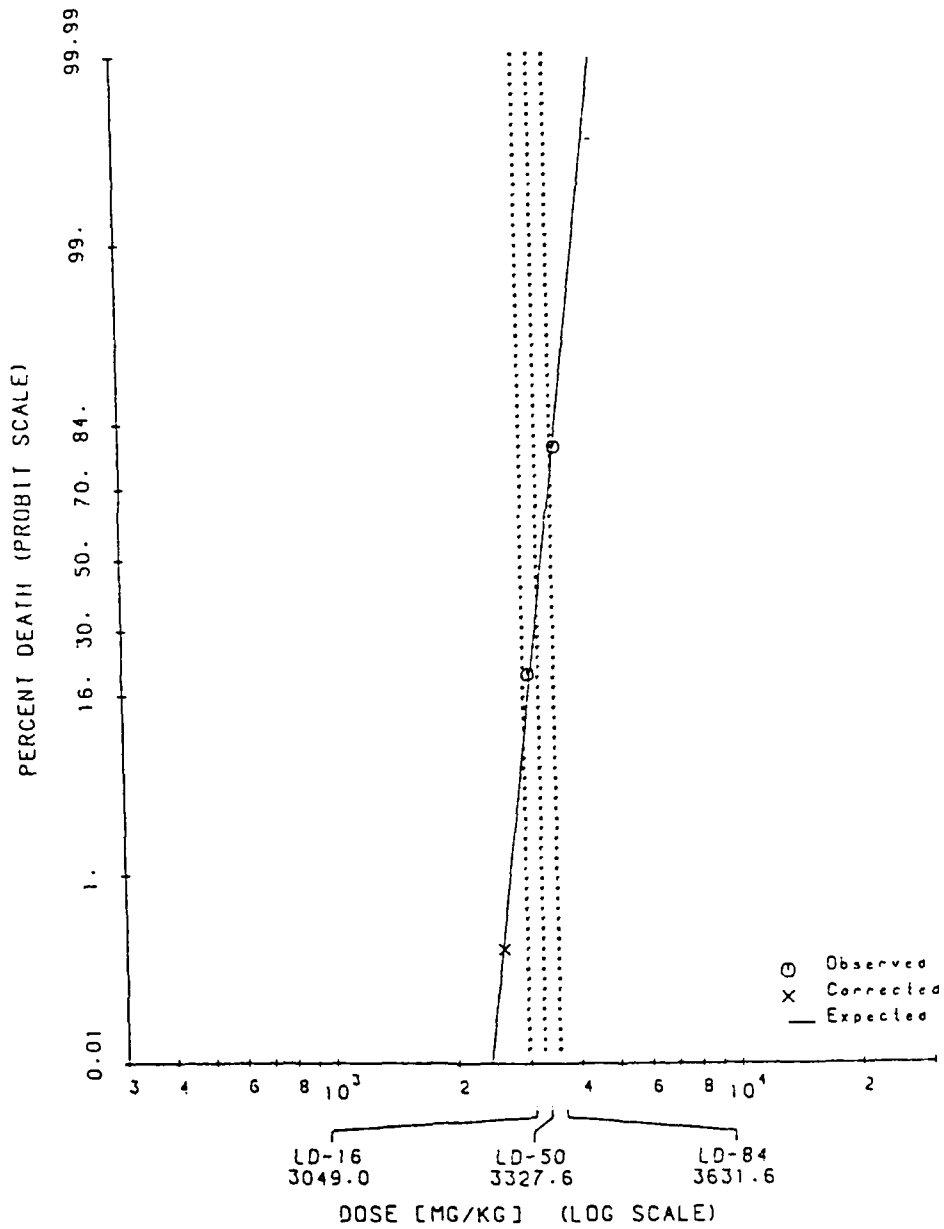


FIGURE 8: DOSE-RESPONSE CURVE FOR COMBINED SEXES

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: OXATHIANE

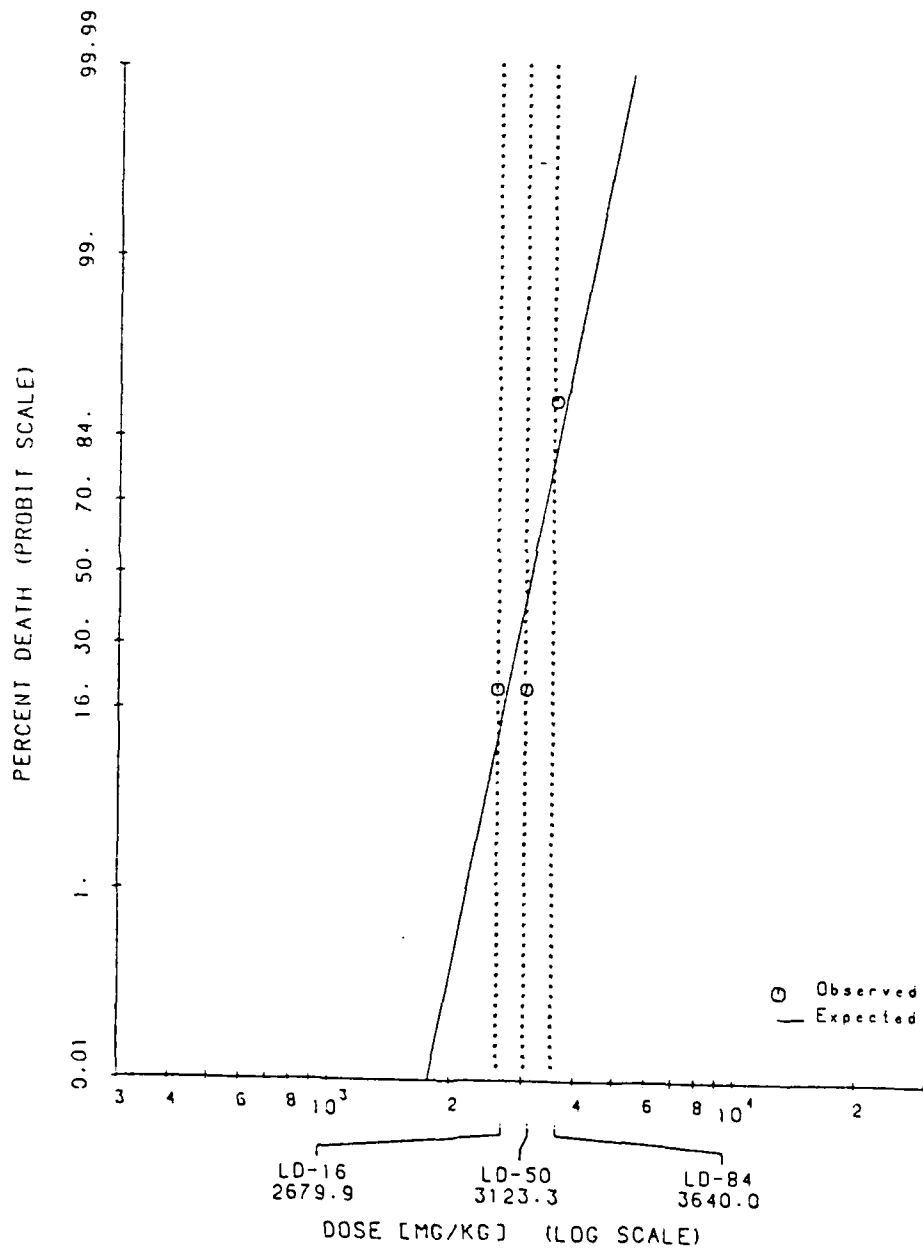


TABLE 10
 INDIVIDUAL BODY WEIGHT
 AND TEST ARTICLE ADMINISTRATION DATA
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: OXATHIANE

Dose Group: 2601 mg/kg

Animal Number	Sex	Body Weights (grams)				Amount of Test Article Administered	
		0	Day of Study*		14	(mg)	(ml)
13913	M	234	-	247	260	611	0.55
13956	M	231	-	242	255	599	0.54
13911	M	225	-	232	245	588	0.53
13937	M	217	-	233	246	566	0.51
13920	M	<u>216</u>	-	<u>226</u>	<u>242</u>	<u>566</u>	<u>0.51</u>
Mean		225		236	250	586	0.53
S.D.		8		8	8	20	0.02
S.E.		4		4	3	9	0.01
13996	F	177	(171)	-	-	455	0.41
13988	F	162	-	160	173	422	0.38
14013	F	159	-	161	171	411	0.37
13963	F	155	-	156	168	400	0.36
13965	F	<u>144</u>	(140)	-	-	<u>377</u>	<u>0.34</u>
Mean		159		159	171	413	0.37
S.D.		12		3	3	29	0.03
S.E.		5		2	1	13	0.01

* Day 0 denotes fasted body weight the day of dose administration; day 14 denotes final body weight prior to final sacrifice. Values in parentheses denote found dead body weights and are not included in the statistical analyses.

- = Not applicable.

TABLE 10 (continued)

INDIVIDUAL BODY WEIGHT
AND TEST ARTICLE ADMINISTRATION DATA
ACUTE ORAL LD₅₀ DETERMINATION IN RATS
TEST ARTICLE: OXATHIANE

Dose Group: 3060 mg/kg

Animal Number	Sex	Body Weights (grams)					Amount of Test Article Administered	
		0	0	Day of Study*		14	(mg)	(ml)
13922	M	241	-	-	246	274	733	0.66
13935	M	233	-	-	242	267	710	0.64
13944	M	225	-	-	230	255	688	0.62
13931	M	223	-	(203)	-	-	677	0.61
13941	M	217	-	-	225	252	666	0.60
Mean		228			236	262	695	0.63
S.D.		9			10	10	27	0.02
S.E.		4			5	5	12	0.01
13993	F	173	-	-	174	182	533	0.48
13975	F	170	-	-	169	186	522	0.47
14010	F	158	-	-	162	173	488	0.44
14003	F	153	(148)	-	-	-	466	0.42
13979	F	142	-	-	147	161	433	0.39
Mean		159			163	176	488	0.44
S.D.		13			12	11	41	0.04
S.E.		6			6	6	18	0.02

* Day 0 denotes fasted body weight the day of dose administration; day 14 denotes final body weight prior to final sacrifice. Values in parentheses denote found dead body weights and are not included in the statistical analyses.

- = Not applicable.

TABLE 10 (continued)

INDIVIDUAL BODY WEIGHT
AND TEST ARTICLE ADMINISTRATION DATA
ACUTE ORAL LD₅₀ DETERMINATION IN RATS
TEST ARTICLE: OXATHIANE

Dose Group: 3600 mg/kg

Animal Number	Sex	Body Weights (grams)					Amount of Test Article Administered	
		0	0	Day of Study*		14	(mg)	(ml)
13905	M	233	(225)	-	-	-	844	0.76
13910	M	232	-	(221)	-	-	833	0.75
13916	M	225	(225)	-	-	-	810	0.73
13919	M	218	-	-	212	243	788	0.71
13957	M	<u>203</u>	-	(197)	-	-	<u>733</u>	<u>0.66</u>
Mean		222			212	243	802	0.72
S.D.		12					44	0.04
S.E.		6					20	0.02
13968	F	171	(166)	-	-	-	611	0.55
14014	F	164	-	(161)	-	-	588	0.53
13962	F	160	-	(153)	-	-	577	0.52
13974	F	151	-	(143)	-	-	544	0.49
14002	F	<u>146</u>	-	(140)	-	-	<u>522</u>	<u>0.47</u>
Mean		158					568	0.51
S.D.		10					35	0.03
S.E.		4					16	0.01

* Day 0 denotes fasted body weight the day of dose administration; day 14 denotes final body weight prior to final sacrifice. Values in parentheses denote found dead body weights and are not included in the statistical analyses.

- = Not applicable.

TABLE 11
 INDIVIDUAL ANTEROFTEREM OBSERVATIONS
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: OXATHIANE

Dose Group: 2601 mg/kg

Finding	Day(s) Finding Observed											
	13913 (M)	13956 (M)	13911 (M)	13937 (M)	13920 (M)	13996 (F)	13988 (F)	14013 (F)	13963 (F)	13965 (F)		
Coma	0	0	0	0	0	0	0	0	0,1	0		
Polypnea - Mild	0	0	0	0	0	0	0	0	0	0		
- Moderate	0	0	0	0	0	0	0	0	0	0		
Lacrimation - Mild	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a		
- Moderate	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a		
- Severe	0 ^a	0 ^a	0 ^a	0 ^{a,b}	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a		
Ataxia - Mild	1	0,1	1	1	0,1	0	1	1	1	0		
- Moderate	0	0	1	0	1	0	0,1	0,1	1	0		
- Severe	0	0	0	0	0	0	0,1	0,1	0	0		
Lethargy - Mild	1	0,1	2,3	0,1	0,1	0,1	0,1	1,2	1	0		
- Moderate	0	0	1	0	0,1	0	0,1	0,1	0	0		
- Severe	0	0	0	0	0	0	0	0	0	0		
Epistaxis - mild	0	0	0	0	0	0 ^b	0	0	0	0		
Munched posture	1,2	1,2	1,2,3	0,1,2	1,2	0,1,2	0,1,2	1,2	1,2	1,2		
Squinted eyes	1	1	1	1	1	0	1	1	1	0		
Feels cold	0	0	0	0	0	0	0	0	0	0		
Dyspnea	0	0	0	0	0	0	0	0	0	0		
Wheezing	0	0	0	0	0	0	0	0	0	0		
Tremors	0	0	0	0	0	0	0	0	0	0		
Pilo-erection	0	0	1	1	1	1	1	1	1	1		
Alopecia - Mild, around eyes	10,11,12	10,11,12	0,9	8,9	8,9	3-14	3-14	3-14	8,9	1		
Death	0	0	0	0	0	1	0	0	0	0		
No abnormalities	3-9,13, 14	3-9,13, 14	4-7, 10-14	3-14	3-7, 10-14	3-14	3-14	3-14	3-7, 10-14	1		

a = clear b = red

TABLE 11 (continued)

INDIVIDUAL ANTEMORTEM OBSERVATIONS

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: OXATHIANE

Dose Group: 3060 mg/kg

Finding	Animal No. (Sex)	Day(s) Finding Observed										
		13922 (M)	13935 (M)	13944 (M)	13931 (M)	13941 (M)	13993 (F)	13975 (F)	14010 (F)	14003 (F)	13979 (F)	
Coma		0	0	0	0	0	0	1	0	0	0	
Polypnea - Mild		1	0	0	0,1	0	0	1	0	0	0,1	
- Moderate		0	0	0,1	0	0	0	0	0	0	0	
Lacrimation - Mild		0 ^a ,1 ^a	1 ^a	0 ^a ,1 ^a	0 ^a ,1 ^a	0 ^a	0 ^a ,1 ^a	0 ^a	0 ^a	0 ^a	0 ^a ,1 ^a	
- Moderate		0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	1 ^a ,3 ^a	0 ^a	0 ^a	0 ^a	0 ^a ,1 ^a	
- Severe		0 ^a	0 ^a	0 ^a	0 ^a	1 ^a	0 ^a	1 ^a	0 ^a	0 ^a	0 ^a ,1 ^a	
Ataxia - Mild		1	1	1	1	1	0	0	0	0	0,1	
- Moderate		1	1	1	1	1	0,1	0	0	0	0,1	
- Severe		1	0	0,1	1	0	0,1	0,1	0,1	0	0,1	
Cyanotic					0							
Feels cold					0							
Lethargy - Mild		1	1	1	1	1	0	0,3	0	0	0	
- Moderate		1	1	1	1	1	0,1	0	0	0	0,1	
- Severe		1	1	1	1	1	0,1	0,1	1	0,1	0,1	
Dyspnea - moderate								0	0	0		
Squinted eyes		1	1	1	1	1	1	0,1	0,1	0,1	0,1	
Wheezing - mild		1			1							
Hunched posture		2	1,2	2	1,2	1,2	2	2	2	1,2	1,2	
Pilo-erection		1		1	1	1,2					1	
Alopecia - Mild, around eyes		8-12	8-12				8-12	8-12	8-12	8-12	8-12	
Death					2					0		
No abnormalities		3-7,13, 14	3-7,13, 14	3-14	3-14	3-14	3-7,13, 14	4-7,13, 14	3-7,13, 14	3-7,13, 14	3-7,13, 14	

a = clear

b = red

TABLE 11 (continued)

INDIVIDUAL ANTE-MORTEM OBSERVATIONS

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: OXATHIANE

Dose Group: 3600 mg/kg

Finding	Animal No. (Sex)	Day(s) Finding Observed									
		13905 (M)	13910 (M)	13916 (M)	13919 (M)	13957 (M)	13968 (F)	13962 (F)	14014 (F)	13974 (F)	14002 (F)
Coma		0	0	0	0	0	0	0	0	0	0
Polypnea - Mild		0	0	0	0	0	0	0	0	0	0
- Moderate		0	0	0	0,1	0	0	0	0	0	0
Lacrimation - Mild		0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a	0 ^a
- Moderate					1 ^a						
- Severe											
Dyspnea - moderate		0						0			0
Ataxia - Mild											0
- Moderate		0			1					0	
- Severe											
Cyanotic				0			0				
Feels cold				0			0			0	
Squinted eyes										0	
Lethargy - Severe					1					0	
Paralysis - hind legs										0	
Pilo-erection					1						
Hunched posture					2						
Death		0	1	0		1	0	1	1	1	1
No abnormalities											3-14

a = clear

TABLE 12
 INDIVIDUAL NECROPSY FINDINGS
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: OXATHIANE

Dose Group: 2601 mg/kg

Animal Number	Sex	Abnormalities Noted at Necropsy (Organ - Abnormality)
13913	M	NVL
13456	M	NVL
13911	M	NVL
13937	M	NVL
13920	M	NVL
13996	F	Duodenum - contained amber gel Jejunum - blackened, contained black gel Ileum - contained yellow gel
13988	F	NVL
14013	F	NVL
13963	F	NVL
13965	F	Intestinal tract - contained amber gel

NVL = No Visible Lesions

TABLE 12 (Continued)
 INDIVIDUAL NECROPSY FINDINGS
 ACUTE ORAL LD₅₀ DETERMINATION IN RATS
 TEST ARTICLE: OXATHIANE

Dose Group: 3060 mg/kg

Animal Number	Sex	Abnormalities Noted at Necropsy (Organ - Abnormality)
13922	M	NVL
13935	M	NVL
13944	M	NVL
13931	M	Stomach - gaseous, contained brown gel Intestinal tract - gaseous, reddened, contained amber gel Bladder - distended, maroon in color, full of urine
13941	M	NVL
13993	F	NVL
13975	F	NVL
14010	F	NVL
14003	F	Duodenum - reddened, contained dark orange gel
13979	F	NVL

NVL = No Visible Lesions

TABLE 12 (Continued)

INDIVIDUAL NECROPSY FINDINGS

ACUTE ORAL LD₅₀ DETERMINATION IN RATS

TEST ARTICLE: OXATHIANE

Dose Group: 3600 mg/kg

Animal Number	Sex	Abnormalities Noted at Necropsy (Organ - Abnormality)
13905	M	Duodenum - reddened, contained dark red gel Ileum and Jejunum - dark bluish/purple color, contained black gel Bladder - dark blue, contained dark brownish/ red liquid
13910	M	Intestinal tract - blackened, gaseous, contained black gel
13916	M	Duodenum - reddened, contained yellow liquid Ileum and Jejunum - dark yellow in color, contained yellow liquid, gaseous (Ileum)
13919	M	NVL
13957	M	Duodenum and Jejunum - black in color, gaseous, contained black gel Ileum - contained yellow gel
13968	F	Intestine - dark bluish/purple color, contained black gel
14014	F	Duodenum - black in color, black gel contents Jejunum - gaseous, black in color, black contents Ileum - contained greenish-gray gel
13962	F	Duodenum - reddened, contained amber gel Ileum and Jejunum - contained yellow gel
13974	F	Stomach - gaseous, contained brown liquid Duodenum and Jejunum - black in color, contained black gel Ileum - contained yellow gel
14002	F	Duodenum - reddened, contained dark red gel Jejunum - contained greenish/gray gel Ileum - contained yellow gel

NVL - No Visible Lesions

APPENDIX A
QUALITY ASSURANCE INSPECTIONS

QUALITY ASSURANCE INSPECTIONS

QA Phase	<u>OXATHIANE</u>		
	QA Inspections	Technical Supervisor/ Study Director	Findings Reported Management
Protocol Review	10/13/82	10/13/82	11/23/82
Test Article Administration	01/08/85	01/08/85	01/11/85
Data Observations	01/15/85	01/15/85	01/21/85
Draft Report Review	04/03/85	04/08/85	04/15/85
Final Report Review	08/27/86	08/27/86	09/23/86

QA Phase	<u>BENZOTHIAZOLE AND DITHIANE</u>	
	QA Inspections	Findings Reported Management/Study Director
Status Report Audit (Benzothiazole)	02/13/86	02/13/86
Status Report Audit (Dithiane) Audit	03/19&25/86	03/25/86
Data and Draft Report Audit	05/8-9/86	05/09/86
Final Report Audit	08/14/86	08/14/86

APPENDIX B
LIST OF PERSONNEL

PERSONNEL

American Biogenics Corporation personnel listed below participated in the conduct and/or report preparation of these studies:

OXATHIANE: Woburn, MA facility (1/8/85 - 1/22/85)

Joyce R. Mappes, B.S.	Technician
Cathleen P. Flynn, Assoc. Degree	Technician
Carla Farragher, A.A.S.	Technician
Jane B. Goodband	Operations Supervisor
Indu A. Muni, Ph.D.	Principal Investigator and Executive Vice President
Paul Lezberg, B.S.	Manager of Regulatory Compliance
Nancy Gervino, B.S.	Quality Assurance Specialist

BENZOTHIAZOLE AND DITHIANE (repeat studies): Decatur, IL
facility (1/7/86 - 2/20/86)

Gary L. Doyle, B.S.	Acute Department, Technician
Jonathan C. Kreuger, B.A.	Acute Department, Technician
Kathy Mellon, M.S.	Acute Department, Technician
Sandra H. Smith	Acute Department, Project Supervisor
Dale A. Mayhew, Ph.D.	Director, Toxicology and Principle Investigator
Stephen V. Becker, D.V.M.	Experimental Pathology Laboratories, Veterinary and Pathology Services
Antoinette Skelley	Manager, Quality Assurance and Regulatory Affairs, Archives

APPENDIX C

CHEMICAL ANALYSIS RESULTS:
BENZOTHIAZOLE, DITHIANE, AND OXATHIANE

SGRD-UBG-L

24 July 84

MEMORANDUM FOR DR. REDDY

SUBJECT: Results from the Chemical Analysis of Three Compounds Slated for Toxicity Testing

Benzothiazole, 1,4-thioxane and 1,4-dithiane were given by Dr. Reddy for analysis on 15 June 84. The following is a summary of the results from those analysis:

	% of Total	Formula	Compound	Other Possibilities
<u>Benzothiazole</u>				
	98.88	C ₇ H ₅ NS	Benzothiazole	
	0.61	C ₈ H ₇ NS	2-Methylbenzothiazole	(isomers)
	0.26	C ₆ H ₅ N ₃	Aniline	3 or 4-Cyanopyrazole
	0.12	C ₁₀ H ₁₀ S ₂	Diphenyldisulfide	
	0.11	C ₇ H ₉ N	Toluidine (isomers)	Benzylamine, N-Methylaniline
	0.03	C ₈ H ₇ NS	Methylbenzothiazole	(isomers)
<u>1,4-Thioxane</u>				
	98.93	C ₄ H ₈ OS	1,4-Thioxane	
	1.06	C ₄ H ₈ S ₂	1,4-Dithiane	
<u>1,4-Dithiane</u>				
	99.92	C ₄ H ₈ S ₂	1,4-Dithiane	
	0.08	C ₄ H ₈ S ₃	Methyltrithiane	

Alan B Rosencrance
 ALAN B. ROSENCRANCE
 Research Chemist

CF:
 Dr. Kulkarni
 Dr. Rosenblatt



Chemists Helping Chemists in Research and Industry

aldrich chemical company, inc.

ANALYTICAL DATA

Date June 18, 1984.

Our: 10133-8 Benzothiazole, 99%

Batch No.: 1723LK

Analytical Results:

Appearance : Dark gold liquids

m.p.

b.p.

n_D 1.6423[α]_D

Spectral Data:

I.R. Conforms to structure and standard as illustrated on page 1278-D of Edition-III, of "The Aldrich Library of Infrared Spectra".

U.V.

N.M.R.

Assay:

V.P.C. 99+%

Titration

Other:

DS/kb

A. Napiorkowski
Anna Napiorkowski, Manager
Quality Control/Quality Assurance



Chemists Helping Chemists in Research and Industry

Aldrich chemical company, inc.

ANALYTICAL DATA

Date June 18, 1984

Our: D21770-0 Para-dithiane, 97%

Batch No.: 3030TH

Analytical Results:

Appearance Off white crystals

m.p. 111-113 deg. C b.p.

 n_D^{20} $[\alpha]_D$

Spectral Data:

I.R. Conforms to structure and standard as illustrated on page 160 B of Edition III, of "The Aldrich Library of Infrared Spectra".

U.V.

N.M.R.

Assay:

V.P.C.

Titration 99.9%, S-Content

Other:

KB/kb

A. Napiorkowski
Anna Napiorkowski, Manager
Quality Control/Quality Assurance



Chemists Helping Chemists in Research and Industry

aldrich chemical company, inc.

ANALYTICAL DATA

Date June 18, 1984

Our: 13197-0 1,4-Thioxane, 98%

Batch No.: 053177

Analytical Results:

Appearance Colorless liquid

m.p.

b.p.

 n_D^{20} 1.5070 $[\alpha]_D^{20}$

Spectral Data:

I.R. Conforms to structure and standard as illustrated on page 160 E of Edition III, of "The Aldrich Library of Infrared Spectra".

U.V.

N.M.R.

Assay:

V.P.C. 99+%,

Titration

Other:

DS/kb

A. Napiorkowski
Anna Napiorkowski, Manager
Quality Control/Quality Assurance

APPENDIX D
DISTRIBUTION LIST

DISTRIBUTION LIST

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