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Office of Toxic Substances
US Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Attn: Section 8(e) Coordinator (CAP Agreement)

RE: Report Submitted Pursuant to the TSCA Section 8(e) Compliance Audit Program

CAP ID No.: 8ECAP - 0004

Dear Sir/Madam:

On behalf of Rhône-Poulenc Inc. (RPI, CN 5266, Princeton, NJ 08543-5266) and its subsidiary Rhône-Poulenc Ag Company, the attached study report is being submitted to the Environmental Protection Agency (EPA) pursuant to the Toxic Substances Control Act (TSCA) Section 8(e) Compliance Audit Program and the Agreement for a TSCA Section 8(e) Compliance Audit Program (CAP Agreement) executed by RPI and EPA.

The enclosed study report provides information on chlormephos. The CAS number assigned to this compound is 24934-91-6. The CAS name is S-(chloromethyl) O,O-diethyl phosphorodithioate. This chemical was manufactured in Europe and imported for pesticide research and development. To our knowledge, a pesticide application on this chemical has never been submitted to EPA under the Federal Insecticide, Fungicide, and Rodenticide Act.

No claims of confidentiality are made for this submission. The title of the enclosed report is "Acute Oral LD50 with Chlormephos Technical in Rats". The following is a summary of the adverse effects observed in this study.

This study is being submitted under Section 8(e) because of the observed clinical signs. Doses used in the study included 15, 25, 35, 50 and 75 mg/kg body weight. The LD50 for males was 27 mg/kg with 95% confidence limits of 21.3 to 34.3 mg/kg, and for females, the LD50 was 18 mg/kg with 95% confidence limits of 14.0 to 23.2 mg/kg. Clinical signs included depression, trembling, lacrimation, salivation, and occasional ataxia. These signs were observed in animals surviving to study termination as well as those dying during the study.

One previous TSCA Section 8(e) notice was submitted on this chemical on August 31, 1978. We do not have an EPA Document Control Number for this submission in our records. In addition, approximately 15 submissions will be made on chlormephos under the CAP.

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In total, RPI is submitting three copies of the enclosed report and this cover letter: an original and two copies.

Further questions regarding this submission may be directed to the undersigned at 919-549-2222.

Sincerely,



Glenn S. Simon, PhD, DABT
Director of Toxicology

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

Study No. RCP0478

Report No. SEH 78:34

Toxicology-Pathology Laboratory
Rhodia Inc.
Ashland, Ohio 44805

July 24, 1978

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

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HESS & CLARK DIVISION
ASHLAND, OHIO 44805
Research Department



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Subject: Acute Oral LD₅₀, Chlormephos Technical

Book No. 5391 Page 99
5403 Pages 72-73, 66-71
5407 Pages 87-88
5408 Pages 36-82
5409 Page 17

Study No. RCP0478 Dates: 6-8-78 to 6-22-78

TITLE

Acute Oral LD₅₀ with Chlormephos Technical in Rats

PURPOSE

To determine the acute toxicity and lethality of Chlormephos Technical in rats according to the EPA proposed guidelines of April 1978; 162.81-1.

LOCATION

This study was conducted at the Rhodia, Inc., Toxicology-Pathology facility on the Hess & Clark Research Farm, Ashland, Ohio 44805.

SPONSOR

This study was sponsored by Rhodia Inc., Agricultural Division, Monmouth Junction, New Jersey.

SUMMARY

Preliminary results from a pilot study showed that the oral LD₅₀ of Chlormephos Technical in rats was approximately 35 mg/kg. Therefore, young adult male and unbred female rats were given single oral doses of Chlormephos Technical at dose levels of 15, 25, 35, 50 or 75 mg/kg body weight (b.w.) in an oral LD₅₀ study. The rats were observed for a total of 14 days and an LD₅₀ calculated from the mortality data. The LD₅₀ for the males was 27 mg/kg b.w. with 95% confidence limits of 21.3 to 34.3 mg/kg b.w. The calculated LD₅₀ for the females was 18 mg/kg b.w. with confidence limits of 14.0 to 23.2 mg/kg b.w.

All surviving males and females began gaining weight by day 4 post administration except for the one surviving female in the 25 mg/kg group. This female did not show any weight gain until day 10 post administration.



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The survival rate for males was higher than for the females. The average days to death was less for the females than for the males at all dose levels except 75 mg/kg, where the females lived an average of 0.7 days and the males 0.2 days.

Clinical signs of toxicity included: a mild to severe depression, trembling, salivation, lacrimation, wet belly, occasional ataxia, prostration and death. As the dose levels increased, the toxic signs were more severe with a shorter onset time. All survivors were asymptomatic by day 7 post administration.

Necropsy observations on the rats which died during the study included, dark appearing liver and kidneys, hemorrhagic lungs, urinary bladders, sloughing and/or inflammation and erosion of the stomach mucosa. There were no significant necropsy findings on any of the survivors sacrificed at the termination of the study.



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EXPERIMENTAL

MATERIALS AND METHODS

ANIMALS

One hundred (100) Sprague Dawley derived outbred albino rats, 50 males and 50 females, from Flow Laboratories, Dublin, Virginia and weighing between 139 and 200 grams at the start of the study, were divided into 5 dose groups of 10 males and 10 females each for the LD₅₀ study.

HOUSING

Quarantine - the rats were held in a quarantine room for a one week acclimation period. The rats were randomly distributed from the shipping crates into gang cages. The rats were housed 3 to 4 per sex per cage in suspended 1.3 cm wire mesh cages, 43 x 18 x 25 cm. The rats received feed and water ad libitum. The feeders, water bottles, cages and racks were changed once per week.

The quarantine and test rooms were temperature ($72^{\circ} \text{F} \pm 1^{\circ}$), humidity (50%) and light (12 hours on, 12 hours off) controlled.

During the quarantine-acclimation period the rats were examined by a veterinarian with respect to their state of health and suitability as test animals. Conventional disease control was practiced during the quarantine-acclimation and study periods.

Study Room - at the end of the quarantine period, the cage racks containing the test animals were moved to the test room. The rats were randomly distributed from the quarantine racks into individual suspended stainless steel 1.3 cm wire mesh cages, 18 x 18 x 23 cm. The rats were weighed. If the mean body weights of any dose group varied significantly from any other group, the rats were redistributed so that the mean body weights of all dose groups did not vary significantly. The rats received food and water ad libitum. The feeders, water bottles, cages and racks were changed once per week.



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DIET

The rats were maintained on a diet of Wayne Lab-Blox, manufactured by Allied Mills, Fort Wayne, Indiana and containing 24% crude protein, 4% crude fat and 4.5% crude fiber. Tap water was provided by 8 oz. water bottles with sipper tubes.

IDENTIFICATION

The rats on the LD50 study were identified by ear notches. An identifying tag was placed on each rat cage indicating the number of the rat in the cage and the treatment level.

<u>Rat No.</u>	<u>Treatment Level</u>
101-110 M	15 mg/kg
151-160 F	
201-210 M	25 mg/kg
251-260 F	
301-310 M	35 mg/kg
351-360 F	
401-410 M	50 mg/kg
451-460 F	
501-510 M	75 mg/kg
551-560 F	

TEST SUBSTANCE

The test substance was Chlormephos Technical P.O.X. 150, Batch No. DA 109, a clear liquid organophosphate insecticide supplied by Rhodia Inc., Agricultural Division, Monmouth Junction, New Jersey, shipped from Rhodia Inc., Agricultural Division, St. Joseph, Missouri, and received April 26, 1978, with GLC analysis of 94.4%. A density of 1 gm/ml was assumed. Each ml of test substance would contain 944 mg of Chlormephos Technical.

TEST PROCEDURE

The test substance was suspended in corn oil to give dose levels of 15, 25, 35, 50 and 75 mg/kg body weight. Each concentration was mixed continuously on a magnetic stirrer during the



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dosing. Each rat received a dose volume of 10 ml/kg body weight of the concentration for that dose group. The rats were orally gavaged one time with a curved 18 g x 2 w/2½ mm ball dosing needle. The rats were fasted from food 18 hours prior to dosing.

OBSERVATIONS

The animals were weighed prior to dosing to determine the volume of dosing solution required. Survivors were weighed on days 1, 4, 7, 10 and 14 of the 14 day observation period. The weighing was performed on a Mettler electronic balance interfaced to a programmable calculator, HP 9815A. The day of dosing was designated as day 0. The rats were observed frequently during the first 8 hours post treatment and then twice daily (a.m. and p.m.) for 14 days. All relevant clinical signs including the nature, onset, severity and duration of each toxic or pharmacological sign, and time of death were recorded. All survivors from the study were sacrificed on day 15. No clinical observations were recorded for day 15.

GROSS NECROPSY

A gross necropsy was performed on all the rats. The examination included: heart, lung, spleen, liver, kidney, stomach, small and large intestine and urinary bladder. All lesions were recorded.

RECORDS MAINTAINED

A study record book was maintained and included the following records:

1. Pilot Study
2. Body weights - days 0, 1, 4, 7, 10 and 14
3. Day 0 observations
4. Daily observations
5. Necropsy observations
6. Data analysis

STORAGE OF DATA

All raw data generated during this study and the final report were stored in the archives at Rhodia Inc., Toxicology-Pathology facility in Ashland, Ohio.



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RESULTS AND DISCUSSION

Mortalities per test day are recorded in Table 1. The individual day 0 body weights, dose volumes and days to death are recorded in Table 2. The individual and average body weights for days 0, 1, 4, 7, 10 and 14 are recorded in Table 3. Table 4 is a record of the individual clinical and necropsy observations.

Male body weights were comparable for all the dose groups at day 1 post administration except for the 75 mg/kg dose group, where there were no survivors. All surviving males in all dose groups were gaining weight by day 4 post administration. Survivors in the 25, 35 and 50 mg/kg dose groups gained less weight throughout the observation period than the 15 mg/kg group males. The 8 surviving females in the 15 mg/kg dose group showed a weight gain by day 4 post administration. Only one female survived in the 25 mg/kg dose group and this female did not show any weight gain until day 10 post administration.

The survival rate was higher for the males than the females. There were no female survivors in the 35, 50 or 75 mg/kg dose groups. Only 1 of 10 females survived in the 25 mg/kg group and 8 of 10 females survived in the 15 mg/kg dose group. There were no male survivors in the 75 mg/kg dose group. Three of 10 males survived in the 50 mg/kg group, 2 of 10 in the 35 mg/kg group, 6 of 10 in the 25 mg/kg group and 8 of 10 males survived in the 15 mg/kg group.

The average days to death was less for the females than the males for all dose groups except the 75 mg/kg dose group where the females lived an average of 0.7 days versus 0.2 days for the males.

Clinical signs of toxicity were observed in all dose groups. These toxic signs included a mild to severe depression, trembling, salivation, lacrimation, wet belly, occasional ataxia, prostration and death. As the dose levels increased, the toxic signs became more severe and had a shorter onset time. All surviving males and females in the 15 mg/kg dose group were asymptomatic by day 4 post administration. All survivors in the higher dose groups of 25, 35, and 50 mg/kg were asymptomatic by day 7 post administration.

Necropsy observations on rats which died during the study included: dark appearing livers and kidneys, hemorrhagic lungs and urinary bladders, sloughing and/or inflammation and erosion of the stomach mucosa.



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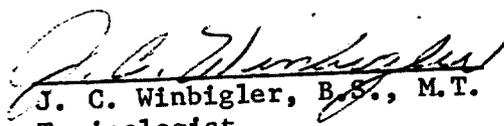


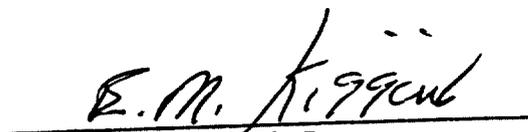
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No significant gross alterations or lesions were noted in any of the survivors sacrificed at the termination of the study. When doses of 15, 25, 35, 50 or 75 mg/kg body weight are plotted against the percent mortality, an LD₅₀ was calculated for the males at 27 mg/kg b.w. with 95% confidence limits of 21.3 to 34.3 mg/kg b.w. and for the females the LD₅₀ was apparent at 18 mg/kg b.w. with 95% confidence limits of 14.0 to 23.2 mg/kg b.w. The calculated acute oral LD₅₀ for males and females is graphically illustrated in Figures 1 and 2, respectively.


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ACUTE ORAL LD50 WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 2

Individual Day 0 Body Weights, Dose Volume and Days to Death

Animal No.	Males			Females			
	Body Wt (gm)	Dose Volume (ml)	Days to Death	Animal No.	Body Wt (gm)	Dose Volume (ml)	Days to Death
<u>Dose Group: 15 mg/kg</u>							
101	150	1.5	D, 0	151	158	1.6	14
102	171	1.7	14	152	162	1.6	FD, 4
103	200	2.0	14	153	168	1.7	14
104	166	1.7	14	154	160	1.6	14
105	174	1.7	14	155	168	1.7	14
106	148	1.5	14	156	168	1.7	14
107	173	1.7	14	157	164	1.6	FD, 1
108	145	1.5	14	158	152	1.5	14
109	164	1.6	14	159	177	1.8	14
110	144	1.4	7	160	164	1.6	14
Average	164	1.6	11.9	Average	164	1.6	11.7
<u>Dose Group: 25 mg/kg</u>							
201	170	1.7	FD, 1	251	166	1.7	FD, 1
202	180	1.8	14	252	154	1.5	D, 1
203	146	1.5	14	253	175	1.8	FD, 1
204	180	1.8	D, 1	254	156	1.6	14
205	185	1.9	14	255	169	1.7	FD, 2
206	175	1.8	D, 0	256	142	1.4	D, 0
207	171	1.7	14	257	180	1.8	FD, 1
208	186	1.9	14	258	178	1.8	FD, 2
209	180	1.8	FD, 2	259	167	1.7	FD, 1
210	176	1.8	14	260	148	1.5	D, 0
Average	175	1.8	8.8	Average	164	1.7	2.3

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 2 (Cont'd)

Individual Day 0 Body Weights, Dose Volume and Days to Death

Animal No.	Males			Females			
	Body Wt (gm)	Dose Volume (ml)	Days to Death	Animal No.	Body Wt (gm)	Dose Volume (ml)	Days to Death
<u>Dose Group: 35 mg/kg</u>							
301	185	1.9	14	351	161	1.6	FD, 1
302	153	1.5	FD, 2	352	166	1.7	FD, 2
303	187	1.9	D, 0	353	178	1.8	D, 0
304	196	2.0	D, 0	354	143	1.4	FD, 1
305	183	1.8	D, 0	355	161	1.6	FD, 2
306	180	1.8	D, 0	356	160	1.6	D, 2
307	170	1.7	FD, 3	357	169	1.7	D, 1
308	171	1.7	FD, 1	358	161	1.6	FD, 1
309	171	1.7	FD, 1	359	155	1.6	D, 0
310	177	1.8	14	360	178	1.8	D, 1
Average	177	1.8	3.5	Average	163	1.6	1.1
<u>Dose Group: 50 mg/kg</u>							
401	183	1.8	14	451	144	1.4	FD, 1
402	177	1.8	14	452	150	1.5	FD, 2
403	139	1.4	D, 2	453	156	1.6	FD, 1
404	156	1.6	D, 0	454	165	1.7	D, 1
405	170	1.7	14	455	165	1.7	FD, 1
406	166	1.7	D, 4	456	174	1.7	FD, 1
407	183	1.8	D, 0	457	167	1.7	FD, 2
408	187	1.9	FD, 1	458	175	1.8	FD, 2
409	175	1.8	D, 0	459	180	1.8	D, 2
410	175	1.8	FD, 2	460	176	1.8	FD, 1
Average	171	1.7	5.1	Average	165	1.7	1.4

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 2 (Cont'd)

Individual Day 0 Body Weights, Dose Volume and Days to Death

Animal No.	Males			Animals No.	Females		
	Body Wt (gm)	Dose Volume (ml)	Days to Death		Body Wt (gm)	Dose Volume (ml)	Days to Death
<u>Dose Group: 75 mg/kg</u>							
501	198	2.0	FD, 1	551	159	1.6	D, 0
502	164	1.6	D, 0	552	165	1.7	FD, 1
503	175	1.8	D, 0	553	154	1.5	D, 0
504	161	1.6	D, 0	554	166	1.7	D, 0
505	187	1.9	D, 0	555	153	1.5	D, 0
506	180	1.8	D, 0	556	157	1.6	FD, 1
507	144	1.4	D, 0	557	168	1.7	FD, 1
508	179	1.8	FD, 1	558	149	1.5	FD, 1
509	172	1.7	D, 0	559	176	1.8	FD, 1
510	178	1.8	D, 0	560	174	1.7	FD, 2
Average	174	1.7	0.2	Average	162	1.6	0.7

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 3

Individual and Average Body Weights (gm)

Animal No.	Males					Females							
	Test Day					Test Day							
	0	1	4	7	10	14	0	1	4	7	10	14	
			Dose Group: 15 mg/kg										
101	150	D ^a	-	-	-	-	158	143	179	194	204	232	
102	171	156	190	222	235	266	162	143	D	-	-	-	
103	200	216	248	275	296	327	168	151	158	182	194	220	
104	166	154	191	227	259	301	160	148	158	181	186	204	
105	174	169	197	222	236	273	168	164	184	203	213	227	
106	148	153	181	214	236	282	168	154	180	199	202	216	
107	173	172	205	225	247	287	164	D	-	-	-	-	
108	145	132	145	175	207	255	152	136	151	162	168	186	
109	164	149	186	216	230	274	177	166	191	197	207	226	
110	144	132	130	D	-	-	164	158	164	189	199	228	
Average	164	159	186	222	243	283	164	151	171	188	197	217	
			Dose Group: 25 mg/kg										
201	170	D	-	-	-	-	166	D	-	-	-	-	
202	180	164	147	185	219	255	154	D	-	-	-	-	
203	146	128	120	147	170	208	175	D	-	-	-	-	
204	180	160	D	-	-	-	156	144	133	153	167	195	
205	185	167	211	247	261	295	169	D	-	-	-	-	
206	175	D	-	-	-	-	142	159	D	-	-	-	
207	171	155	-	206	228	255	180	D	-	-	-	-	
208	186	171	186	218	236	275	178	162	D	-	-	-	
209	180	163	D	-	-	-	167	D	-	-	-	-	
210	176	161	152	191	211	255	148	D	-	-	-	-	
Average	175	159	167	199	221	257	164	155	133	153	167	195	

^a D = Dead

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 3 (Cont'd)

Individual and Average Body Weights (gm)

Animal No.	Males							Females							
	Test Day							Test Day							
	0	1	4	7	10	14	Animal No.	0	1	4	7	10	14		
	Dose Group: 35 mg/kg								Dose Group: 50 mg/kg						
301	185	172	162	194	217	254	351	161	D	-	-	-	-		
302	153	139 ^a	D	-	-	-	352	166	155	D	-	-	-		
303	187	D	-	-	-	-	353	178	D	-	-	-	-		
304	196	D	-	-	-	-	354	143	D	-	-	-	-		
305	183	D	-	-	-	-	355	161	147	D	-	-	-		
306	180	D	-	-	-	-	356	160	146	D	-	-	-		
307	170	154	D	-	-	-	357	169	D	-	-	-	-		
308	171	D	-	-	-	-	358	161	D	-	-	-	-		
309	171	D	-	-	-	-	359	155	D	-	-	-	-		
310	177	157	192	215	241	280	360	178	D	-	-	-	-		
Average	177	156	177	205	229	267	Average	163	149	-	-	-	-		
401	183	165	156	189	214	262	451	144	D	-	-	-	-		
402	177	159	152	181	203	246	452	150	140	D	-	-	-		
403	139	127	D	-	-	-	453	156	D	-	-	-	-		
404	156	D	-	-	-	-	454	165	D	-	-	-	-		
405	170	153	190	222	251	291	455	165	D	-	-	-	-		
406	166	150	131	D	-	-	456	174	D	-	-	-	-		
407	183	D	-	-	-	-	457	167	152	D	-	-	-		
408	187	D	-	-	-	-	458	175	163	D	-	-	-		
409	175	D	-	-	-	-	459	180	160	D	-	-	-		
410	175	155	D	-	-	-	460	176	D	-	-	-	-		
Average	171	152	157	197	223	266	Average	165	154	-	-	-	-		

^aD = Dead

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 3 (Cont'd)

Individual and Average Body Weights (gm)

Animal No.	Males						Females							
	Test Day			Animal No.	Test Day			Animal No.	Test Day					
	0	1	4		7	10	14		1	4	7	10	14	
501	198	D ^a	-	-	-	-	551	159	D	-	-	-	-	-
502	164	D	-	-	-	-	552	165	D	-	-	-	-	-
503	175	D	-	-	-	-	553	154	D	-	-	-	-	-
504	161	D	-	-	-	-	554	166	D	-	-	-	-	-
505	187	D	-	-	-	-	555	153	D	-	-	-	-	-
506	180	D	-	-	-	-	556	157	D	-	-	-	-	-
507	144	D	-	-	-	-	557	168	D	-	-	-	-	-
508	179	D	-	-	-	-	558	149	D	-	-	-	-	-
509	172	D	-	-	-	-	559	176	D	-	-	-	-	-
510	178	D	-	-	-	-	560	174	D	-	-	-	-	-
Average	174	-	-	-	-	-	Average	162	161	-	-	-	-	-

a D = Dead

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 4

Individual Clinical and Necropsy Observations

KEY TO SYMBOLS

D	-	Died
FD	-	Found Dead
TS	-	Termination Sacrifice
Dp	-	Depression
Tr	-	Trembling
Sl	-	Salivation
Lc	-	Lacrimation
WB	-	Wet Belly
At	-	Ataxia
Pr	-	Prostration
+	-	Mild
++	-	Moderate
+++	-	Severe
NS	-	Nothing Significant

NOTE: This was a 14 day study. All survivors were sacrificed on the morning of day 15. No clinical observations were recorded for day 15.

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 4

Individual Clinical and Necropsy Observations

Animal No.	Day of Death	Observations	
		Clinical	Necropsy
Dose Group: 15 mg/kg Males			
101	D, 0	Dp++, Tr, S1 day 0	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - sloughed
102	TS, 15	Dp+ days 0-1 WB days 1-2 NS days 3-14	NS
103	TS, 15	Dp+ day 0 NS days 1-14	NS
104	TS, 15	Dp++ days 0-1 Tr day 0 WB days 1-2 NS days 3-14	NS
105	TS, 15	S1, Lc, Tr day 0 Dp++ days 0-1 WB days 1-2 NS days 3-14	NS
106	TS, 15	Dp+, Tr, S1 day 0 NS days 1-14	NS
107	TS, 15	Tr, S1 day 0 Dp+ days 0-1 WB days 1-2 NS days 3-14	NS
108	TS, 15	Dp+, Tr, S1, Lc day 0 Dp++ day 1 WB days 1-2 NS days 3-14	NS
109	TS, 15	Tr, S1, Lc day 0 Dp+ days 0-1 WB days 1-2 NS days 3-14	NS
110	FD, 7	Tr day 0 Dp+ day 0,5 WB days 1-2 NS days 2-4,6	Lungs, upper lobes - consolidated with many 2-4 mm dia. yellowish nodules which contain caseous material; Lungs, lower lobes - hemorrhagic, contain caseous material

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 4 (Cont'd)

Individual Clinical and Necropsy Observations

Animal No.	Day of Death	Observations	
		Clinical	Necropsy
Dose Group: 15 mg/kg		Females	
151	TS, 15	Tr, Dp+ day 0 Dp+++ day 1 WB days 1-2 NS days 3-14	NS
152	FD, 4	Tr, Dp+, S1 day 0 Dp+++ , WB days 1-3	Liver and kidneys - dark; Stomach, mucosa - sloughed
153	TS, 15	Tr, Dp+ day 0 Dp+++ days 1-2 Dp+ day 3 WB days 1-2 NS days 3-14	NS
154	TS, 15	Tr, Dp+ day 0 Dp+++ days 1-2 Dp+ day 2 WB days 1-2 NS days 3-14	NS
155	TS, 15	Tr, Dp+ day 0 Dp+++ days 1-2 Dp+ day 2 WB days 1-2 NS days 3-14	NS
156	TS, 15	Tr, S1, Dp+ day 0 Dp+++ days 1-2 Dp+ days 2-3 WB days 1-2 NS days 4-14	NS
157	FD, 1	Tr, Dp+++ , Lc, S1 day 0	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - sloughed
158	TS, 15	Dp+ days 0, 2-3 Dp+++ days 1-2 WB days 1-2 NS days 4-14	NS

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 4 (Cont'd)

Individual Clinical and Necropsy Observations

Animal No.	Day of Death	Observations	
		Clinical	Necropsy
<u>Dose Group: 15 mg/kg</u>			
<u>Females (Cont'd)</u>			
159	TS, 15	Dp+ days 0, 2-3 Dp+++ days 1-2 WB days 1-2 NS days 4-14	NS
160	TS, 15	Dp+ days 0, 2-3 Dp+++ days 1-2 WB days 1-2 NS days 4-14	NS
<u>Dose Group: 25 mg/kg - Males</u>			
201	FD, 1	Dp++, Tr, S1, Lc day 0	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - sloughed
202	TS, 15	Tr, S1, Dp++ day 0 Dp+++ days 1-2 Dp++ day 3 Dp+ days 4-6 WB days 1-5 NS days 7-14	NS
203	TS, 15	Tr, S1, Lc, Dp++ day 0 Dp+++ days 1-2 Dp++ day 3 Dp+ days 4-6 WB days 1-6 NS days 7-14	NS
204	D, 1	Dp+++ , Lc, Tr day 0 Dp+++ , At day 1	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - sloughed
205	TS, 15	Dp++ days 0, 2-3 Dp+++ day 1 WB days 1-2 NS days 4-14	NS
206	D, 0	Tr, S1, Dp++ day 0	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - sloughed

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 4 (Cont'd)

Individual Clinical and Necropsy Observations

Animal No.	Day of Death	Observations	
		Clinical	Necropsy
Dose Group: 25 mg/kg - Males (Cont'd)			
207	TS, 15	Dp+++ , S1 day 0 Dp+++ day 1 Dp++ days 2-3 WB days 1-2 NS days 4-14	NS
208	TS, 15	Tr, S1, Dp++ day 0 Pr day 1 WB days 1-2 Dp++ days 2-3 NS days 4-14	NS
209	FD, 2	Dp+++ , S1, Lc, Tr day 0 Dp+++ , WB day 1	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - inflamed appearing
210	TS, 15	Tr, Dp++ , S1 day 0 Dp+++ day 1 Dp++ day 2 Dp+ day 3 WB days 1-2 NS days 4-14	NS
Dose Group: 25 mg/kg - Females			
251	FD, 1	Dp++ day 0	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - sloughed
252	D, 1	Dp++ , S1 day 0 Pr, WB day 1	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - inflamed
253	FD, 1	Dp+++ , Lc, S1, Tr day 0	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - inflamed and eroded
254	TS, 15	Pr, S1, Tr day 0 Pr day 1 Dp++ days 2-3 Dp+ days 4-6 WB days 1-5 NS days 7-14	NS

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 4 (Cont'd)

Individual Clinical and Necropsy Observations

Animal No.	Day of Death	Observations	
		Clinical	Necropsy
Dose Group: 25 mg/kg			
Females (Cont'd)			
255	FD, 2	Dp+++ , Tr, S1 day 0 Pr, WB day 1	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - sloughed
256	D, 0	Dp+++ , S1, Tr day 0	Liver and kidneys - dark; Bladder - hemorrhagic; Stomach, mucosa - inflamed
257	FD, 1	Dp+++ , Tr, Lc, S1 day 0	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - sloughed
258	FD, 2	Dp+++ , S1, Tr day 0 Pr, WB day 1	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - sloughed
259	FD, 1	Dp+++ , S1, Tr, Lc day 0	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - inflamed and eroded
260	D, 0	Dp+ , S1, Tr day 0	Liver and kidneys - dark; Lungs hemorrhagic; Stomach, mucosa - sloughed
Dose Group: 35 mg/kg — Males			
301	TS, 15	Dp++ , S1, Tr day 0 Pr day 1 WB days 1-5 Dp++ days 2-3 Dp+ days 4-6 NS days 7-14	NS
302	FD, 2	Dp++ , Tr, S1 day 0 Pr, WB day 1	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - sloughed
303	D, 0	Dp++ , Tr, S1 day 0	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - sloughed
304	D, 0	Tr, Dp+ day 0	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; Stomach, mucosa - sloughed

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 4 (Cont'd)

Individual Clinical and Necropsy Observations

Animal No.	Day of Death	Observations	
		Clinical	Necropsy
<u>Dose Group: 35 mg/kg - Males (Cont'd)</u>			
305	D, 0	Tr, Dp+ day 0	Liver and kidneys - dark; lungs - hemorrhagic; stomach, mucosa - sloughed
306	D, 0	Tr, Dp+ day 0	Liver and kidneys - dark; lungs - hemorrhagic; stomach, mucosa - sloughed
307	FD, 3	Dp+++ , Tr, Sl, Lc day 0 Pr days 1-2 WB days 1-2	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
308	FD, 1	Dp+++ , Tr, Sl, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach mucosa - inflamed and eroded
309	FD, 1	Dp+++ , Tr, Sl, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach mucosa - sloughed
310	TS, 15	Tr, Dp++ day 0 Pr day 1 WB days 1-2 Dp++ day 2 DP+ day 3 NS days 4-14	NS
<u>Dose Group: 35 mg/kg - Females</u>			
351	FD, 1	Dp+++ , Lc, Tr day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed
352	FD, 2	Dp++ , Lc, Sl, Tr day 0 Pr, WB day 1	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed and eroded
353	D, 0	Dp+ , Lc day 0	Liver and kidneys - dark; bladder hemorrhagic; stomach, mucosa - inflamed

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 4 (Cont'd)

Individual Clinical and Necropsy Observations

Animal No.	Day of Death	Observations	
		Clinical	Necropsy
<u>Dose Group: 35 mg/kg - Females (Cont'd)</u>			
354	FD, 1	Dp+, Lc, S1, Tr day 0	Liver and kidneys - dark; Lungs and bladder - hemorrhagic; stomach, mucosa - inflamed and eroded
355	FD, 2	Dp+++, S1, Lc, Tr day 0 Dp+++. Pr, WB day 1	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed and eroded
356	D, 2	Dp++, Tr, S1 day 0 Pr, WB days 1-2	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
357	D, 1	Dp++, Tr, S1 day 0 Dp+++, WB day 1	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed and eroded
358	FD, 1	Pr, Lc, S1, Tr day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed and eroded
359	D, 0	Tr, Dp+ day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
360	D, 1	Dp+++, S1, Tr day 0 Pr, WB day 1	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed and eroded

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 4 (Cont'd)
Individual Clinical and Necropsy Observations

Animal No.	Day of Death	Observations	
		Clinical	Necropsy
<u>Dose Group: 50 mg/kg - Males</u>			
401	TS, 15	Dp+++ , Tr, S1 day 0 Dp+++ day 1 Dp++ days 2-3 Dp+ days 4-6 WB days 1-5 NS days 7-14	NS
402	TS, 15	Dp+++ , Lc, S1, Tr day 0 Dp+++ days 1-2 Dp+ day 3 WB days 1-3 NS days 4-14	NS
403	D, 2	Dp+++ , S1, Tr day 0 Dp+++ , WB days 1-2	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
404	D, 0	Dp++ , S1, Tr day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
405	TS, 15	Dp++ , S1, Tr day 0 Dp+++ day 1 WB days 1-2 Dp+ days 2-3 NS days 4-14	NS
406	D, 4	Dp+++ days 1-3 Pr day 4 WB days 1-3	Liver - dark; lungs - hemorrhagic; stomach, mucosa - sloughed
407	D, 0	Dp+ , Tr, S1 day 0	Liver and kidneys - dark; lungs - hemorrhagic; stomach, mucosa - sloughed
408	FD, 1	Dp+++ , S1, Lc, Tr day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 4 (Cont'd)

Individual Clinical and Necropsy Observations

Animal No.	Day of Death	Observations	
		Clinical	Necropsy
<u>Dose Group: 50 mg/kg - Males (Cont'd)</u>			
409	D, 0	Dp+, S1, Tr day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
410	FD, 2	Dp++, S1, Tr day 0 Dp+++ , WB day 1	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
<u>Dose Group: 50 mg/kg - Females</u>			
451	FD, 1	Dp+++ , Tr, Lc, S1 day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed and eroded
452	FD, 2	Dp+++ , S1, Tr day 0 Dp+++ , Tr, WB day 1	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
453	FD, 1	Dp+++ , S1, Tr, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
454	D, 1	Pr, S1, Tr, Lc day 0 Pr, WB day 1	Liver and kidneys - dark; stomach, mucosa - inflamed
455	FD, 1	Dp+++ , S1, Tr, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed and eroded
456	FD, 1	Dp+++ , S1, Tr, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed and eroded
457	FD, 2	Dp+++ , Tr, S1 day 0 Dp+++ , WB day 1	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 4 (Cont'd)

Individual Clinical and Necropsy Observations

Animal No.	Day of Death	Observations	
		Clinical	Necropsy
<u>Dose Group: 50 mg/kg - Females (Cont'd)</u>			
458	FD, 2	Dp+++ , Tr, Sl day 0 Pr, WB day 1	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed; Rt. lobe of lungs - a 5 mm. dia. caseous yellow nodule
459	D, 2	Dp+++ , Tr, Sl day 0 Dp+++ , WB, day 1-2 At day 1	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed and eroded
460	FD, 1	Dp+++ , Lc, Sl, Tr day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed; Rt. lobe of lungs - a 5 mm. dia. caseous yellow nodule
<u>Dose Group: 75 mg/kg - Males</u>			
501	FD, 1	Dp+++ , Lc, Sl, Tr day 0	Liver and kidneys - dark; lungs hemorrhagic; stomach, mucosa - inflamed
502	D, 0	Dp++ , Sl, Tr, Lc day 0	Liver and kidneys - dark; lungs hemorrhagic; stomach, mucosa - sloughed
503	D, 0	Dp++ , Sl, Tr, Lc day 0.	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
504	D, 0	Dp++ , Sl, Tr, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
505	D, 0	Dp++ , Sl, Tr, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

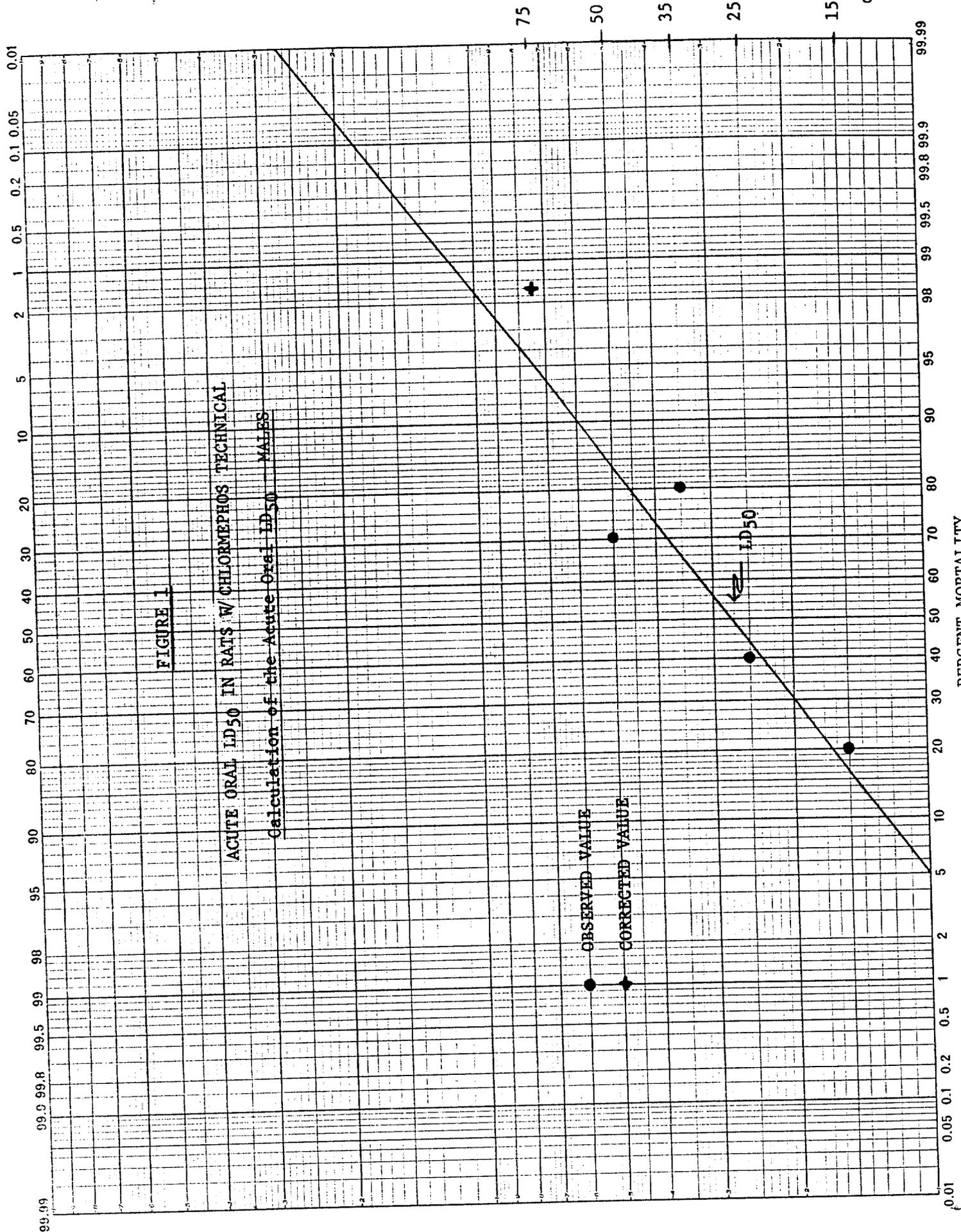
TABLE 4 (Cont'd)
Individual Clinical and Necropsy Observations

Animal No.	Day of Death	Observations	
		Clinical	Necropsy
<u>Dose Group: 75 mg/kg - Males (Cont'd)</u>			
506	D, 0	Dp++, Sl, Tr, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
507	D, 0	Dp++, Sl, Tr, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
508	FD, 1	Dp+++, Sl, Lc, Tr day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed and eroded
509	D, 0	Dp++, Sl, Tr, Lc day 0	Liver and kidneys - dark; lungs hemorrhagic; stomach, mucosa - sloughed
510	D, 0	Dp++, Sl, Tr, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
<u>Dose Group: 75 mg/kg - Females</u>			
551	D, 0	Dp++, Sl day 0	Liver and kidneys - dark; lungs hemorrhagic; stomach, mucosa - sloughed
552	FD, 1	Dp++, Sl, Tr, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed and eroded
553	D, 0	Dp++, Sl, Tr day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed
554	D, 0	Dp++, Sl, Tr day 0	Liver and kidneys - dark; lungs hemorrhagic; stomach, mucosa - sloughed

ACUTE ORAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RATS

TABLE 4 (Cont'd)
Individual Clinical and Necropsy Observations

Animal No.	Day of Death	Observations	
		Clinical	Necropsy
<u>Dose Group: 75 mg/kg - Females (Cont'd)</u>			
555	D, 0	Dp+ day 0	Liver and kidneys - dark; lungs - hemorrhagic; stomach, mucosa - sloughed
556	FD, 1	Pr, Lc, Sl, Tr day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed, sloughed and eroded
557	FD, 1	Dp+++ , Sl, Tr, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - inflamed, sloughed and eroded
558	FD, 1	Dp+++ , Sl, Tr, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed and eroded
559	FD, 1	Dp+++ , Sl, Tr, Lc day 0	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed and eroded
560	FD, 2	Dp+++ , Sl, Tr, Lc day 0 Pr, WB day 1	Liver and kidneys - dark; lungs and bladder - hemorrhagic; stomach, mucosa - sloughed and eroded



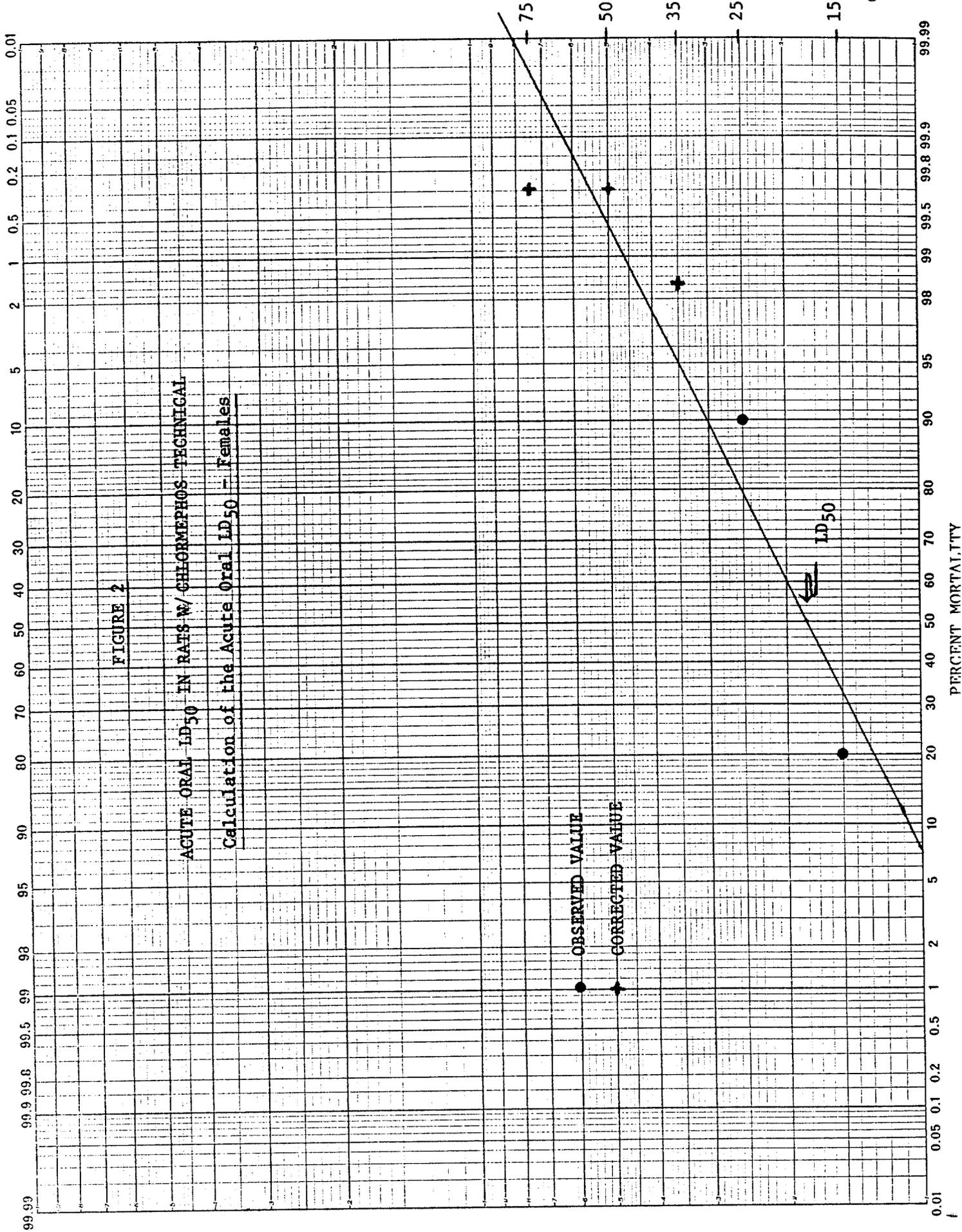


FIGURE 2

ACUTE ORAL LD₅₀ IN RATS W/ CHLORMEPHOS TECHNICAL

Calculation of the Acute Oral LD₅₀ - Females

OBSERVED VALUE

CORRECTED VALUE

LD₅₀

Front Sheet

Study No. RCP0478x, RCP0478
Project No. Acute Oral LD₅₀ in Rats
Sponsor Agricultural Div., Rhodia Inc.
Start Date 6-8-78
Duration 7 Days - PILOT 5-24 to 5-31-78
14 Days - LD₅₀
Finish Date 6-22-78
Study Director S. E. Hastings
Study Personnel BF, JCW

Chemical Chlormephos Technical
Purity 94.4%
Animal Rat
No. M 80 F 80
Start Weight
M 150-200 gm
F 150-200 gm
Route Oral

<u>Animal No.</u>	<u>Treatment Level mg/kg</u>	<u>Tag Color</u>
<u>PILOT STUDY</u>		
	7	45
	15	60
	30	100
<u>LD 50 STUDY</u>		
101-110	15	white tag
151-160		
201-210	25	blue tag
251-260		
301-310	35	green tag
351-360		
401-410	50	pink tag
451-460		
501-510	75	yellow tag
551-560		

Assays or Special Procedures

OBSERVATIONS:

1. Body weights - Days 0, 1, 4, 7, 10 and 14
2. Clinical observations - Day 0 frequently. Days 1-14, twice daily (a.m. and p.m.)
3. Gross necropsy on all rats.

Special Handling

Handle with care - avoid all skin and eye contact. Use gloves. In case of accidental contact, wash affected areas with large amounts of water and then report the incident to the study director.



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PROTOCOL

TITLE

Acute Oral LD₅₀ in Rats with Chlormephos Technical.

PURPOSE

To determine the acute toxicity and lethality of Chlormephos Technical in rats according to the EPA proposed guidelines of April, 1978; 162.81-1.

LOCATION

This study will be conducted at the Rhodia, Inc., Toxicology-Pathology facility on the Hess & Clark Research Farm, Ashland, Ohio 44805.

SPONSOR

This study is sponsored by Rhodia, Inc., Agricultural Division, Monmouth Junction, New Jersey.

ANIMALS

Pilot Study - 60 Sprague Dawley derived outbred albino rats, 30 males and 30 females, from Flow Laboratories, Dublin, Virginia and weighing between 150 and 200 grams at the start of the study, will be divided into 6 dose groups of 5 males and 5 females each.

LD₅₀ Study - 100 Sprague Dawley derived outbred albino rats, 50 males and 50 females, from Flow Laboratories, Dublin, Virginia and weighing between 150 and 200 grams at the start of the study period, will be divided into 5 dose groups of 10 males and 10 females each.

HOUSING

Quarantine - the rats will be held in a quarantine room for a 1 to 2 week acclimation period depending on the age and weight of the rats. The rats will be randomly distributed from the shipping crates into the gang cages. The rats will be housed 3 to 4 per sex per cage in suspended 1.3 cm wire mesh cages, 43 x 18 x 25 cm. The rats will receive feed and water ad libitum. The feeders, water bottles, cages and racks will be changed once per week.



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The quarantine and test room will be temperature ($72^{\circ}\text{F} \pm 1^{\circ}$), humidity (50%) and light (12 hours on, 12 hours off) controlled.

During the quarantine-acclimation period the rats will be examined by a veterinarian with respect to their state of health and suitability as test animals. Conventional disease control will be practiced during the quarantine-acclimation and study period.

Study Room - At the end of the quarantine period, the cage racks containing the test animals will be moved to the test room. The rats will be randomly distributed from the quarantine racks to the test racks according to the Standard Operating Procedures, Manual #2. The rats will be weighed. If the mean body weights of any dose group varies significantly from any other group, the rats will be redistributed so that the mean body weights of all dose groups do not vary significantly. The rats will receive food and water ad libitum. The feeders, water bottles, cages and racks will be changed once per week. The rats will be housed individually in suspended stainless steel 1.3 cm wire mesh cages, 18 x 18 x 23 cm.

DIET

The rats will be maintained on a diet of Wayne Lab-Blox, manufactured by Allied Mills, Fort Wayne, Indiana and containing 24% crude protein, 4% crude fat and 4.5% crude fiber. Tap water will be provided by 8 oz. water bottles with sipper tubes.

IDENTIFICATION

The rats on the LD₅₀ study will be identified by ear notches. An identifying tag will be placed on each rat cage indicating the number of the rat in the cage and the treatment level. The tags are as follows:

101-110 M	15 mg/kg	white tag
151-160 F		
201-210 M	25 mg/kg	blue tag
251-260 F		
301-310 M	35 mg/kg	green tag
351-360 F		
401-410 M	50 mg/kg	pink tag
451-460 F		
501-510 M	75 mg/kg	yellow tag
551-560 F		



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TEST SUBSTANCE

The test substance will be Chlormephos Technical P.O.X. 150, Batch No. DA 109, a clear liquid organophosphorous insecticide supplied by Rhodia Inc., Agricultural Division, Monmouth Jct., New Jersey, shipped from Rhodia Inc., Agricultural Division, St. Joseph, Mo., and received April 26, 1978, with a theoretical purity of 93%.

Warning: Chlormephos Technical should be handled with care, avoid all skin and eye contact. Use gloves. In case of accidental contact, immediately wash affected areas with large volumes of water and then report the incident to the study director.

TEST PROCEDURE

For both the pilot and LD₅₀ studies the test substance will be suspended in corn oil to give the dose levels recorded in Tables 1 and 2. Each concentration will be mixed continuously on a magnetic stirrer during the dosing. Each rat will receive a dose volume of 10 ml/kg body weight of the concentration for that dose group. The dose schedule is recorded in Table 3. The rats will be orally gavaged one time with a curved 18 g x 2w/2½ mm bail dosing needle. The rats will be fasted from food 18 hours prior to dosing.

OBSERVATIONS

The animals will be weighed prior to dosing to determine the ml of dosing solution required. Survivors will be weighed on days 1, 4, 7, 10 and 14 of the 14 day observation period. The weighing will be performed on a Mettler electronic balance interfaced to a programmable calculator, HP 9815A. The day of dosing will be designated as day 0. The rats will be observed frequently during the first 8 hours post-treatment and then twice daily (a.m. and p.m.) for the remaining 14 days. All relevant clinical signs including the nature, onset, severity and duration of each toxic or pharmacological sign, and time of death will be recorded. For the pilot study, only deaths need to be recorded and no body weights after day 0 will be required.

GROSS NECROPSY

A gross necropsy will be performed on all rats in the LD₅₀ study. The examination will include: heart, lung, spleen, liver, kidney, stomach, small and large intestine and urinary bladder. Any lesions will be recorded.



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RECORDS TO BE MAINTAINED

A study record book will be maintained according to Manual #19 in the Standard Operating Procedures and will include the following records:

1. Pilot study
2. Body weights - days 0,1,4,7,10 and 14
3. Day 0 observations
4. Daily observations
5. Necropsy observations
6. Data analysis

DATA ANALYSIS AND FINAL REPORT

A final report will be issued and the data will be tabulated by sex and dose level and will include:

1. animals showing clinical signs
2. animals dead/animal dosed
3. time to death after dosing

The LD₅₀ with 95% confidence limits will be calculated for each sex according to Litchfield and Wilcoxon and dose response curves drawn.

STORAGE OF DATA

All raw data generated during this study and the final report will be stored in the archives at Rhodia, Inc., Toxicology-Pathology facility in Ashland, Ohio.

Prepared by:

S. E. Hastings
S. E. Hastings, B.S.
Study Director

Approved by:

John G. Page
John G. Page, Ph.D.
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Approved by:

E. M. Kiggins
E. M. Kiggins, Ph.D.
Director of Research
& Product Development



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TABLE 1

PILOT STUDY

Dose Level (mg/kg)	No. Rats		Volume of Test Substance	Volume of Diluent	Mg Test Substance per ml	
	M	F			Theoretical*	Actual
7	5	5	1 ml	qs to 132.9 ml	0.70	0.71
15	5	5	1 ml	qs to 62.0 ml	1.5	1.52
30	5	5	1 ml	qs to 31.0 ml	3.0	3.03
45	5	5	2 ml	qs to 41.4 ml	4.5	4.56
60	5	5	2 ml	qs to 31.0 ml	6.0	6.09
100	5	5	4 ml	qs to 37.2 ml	10.0	10.15

Theoretical purity of Chlormephos Technical was 93% or 930 mg/ml - Need a stock solution in corn oil of 93 mg/ml

Calculations

7 mg/kg/10 ml/kg = 0.7 mg/ml; dilute 1:132.9 ml
 15 mg/kg/10 ml/kg = 1.5 mg/ml; dilute 1:62 ml
 30 mg/kg/10 ml/kg = 3.0 mg/ml; dilute 1:31 ml
 45 mg/kg/10 ml/kg = 4.5 mg/ml; dilute 1:20.7 ml
 60 mg/kg/10 ml/kg = 6.0 mg/ml; dilute 1:15.5 ml
 100 mg/kg/10 ml/kg = 10.0 mg/ml; dilute 1:9.3 ml

* GLC analysis of Chlormephos Technical = 94.4%



RHODIA INC.
HESS & CLARK DIVISION
ASHLAND, OHIO 44805
Research Department



TABLE 2
LD₅₀ STUDY

Dose Level (mg/kg)	No. Rats		Volume of Test Substance	Volume of Diluent	Mg Test Substance per ml	
	M	F			Theoretical*	Actual
15	10	10	1 ml	qs to 62 ml	1.5	1.52
25	10	10	1.5 ml	qs to 55.8 ml	2.5	2.54
35	10	10	2 ml	qs to 53.2 ml	3.5	3.55
50	10	10	2.5 ml	qs to 46.5 ml	5.0	5.08
75	10	10	4 ml	qs to 49.6 ml	7.5	7.61

Theoretical purity of Chlormephos Technical was 93% or 930 mg/ml
Need a stock solution of 93 mg/ml in corn oil

Calculations

15 mg/kg/10 ml/kg = 1.5 mg/ml dilute 1:62 ml

25 mg/kg/10 ml/kg = 2.5 mg/ml dilute 1:37.2 ml

35 mg/kg/10 ml/kg = 3.5 mg/ml dilute 1:26.6 ml

50 mg/kg/10 ml/kg = 5.0 mg/ml dilute 1:18.6 ml

75 mg/kg/10 ml/kg = 7.5 mg/ml dilute 1:12.4 ml

* GLC analysis of Chlormephos Technical = 94.4%



RHODIA INC.
 HESS & CLARK DIVISION
 ASHLAND, OHIO 44805
 Research Department



TABLE 3

DOSE SCHEDULE

10 ml/kg body weight
 or 1 ml/100 gm body weight

Gram Body Weight	Dose Volume ml
100	1.0
110	1.1
115	1.2
120	1.2
125	1.3
130	1.3
135	1.4
140	1.4
145	1.5
150	1.5
155	1.6
160	1.6
165	1.7
170	1.7
175	1.8
180	1.8
185	1.9
190	1.9
195	2.0
200	2.0



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAR 30 1995

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EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan
Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12194A



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Triage of 8(e) Submissions

Date sent to triage: MAY 10 1995

NON-CAP

CAP

Submission number: 12194A

TSCA Inventory:

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Study type (circle appropriate):

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Contractor reviewer:	<u>PM</u>			Date:	<u>2/22/95</u>

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: 12194H Submission # SEHQ: 0992 - 12194H SEQ. #

TYPE: INT SUPP FLWP Rhone-Poulenc Inc

INFORMATION REQUESTED: FLWP DATE: 0501 NO INFO REQUESTED 0502 INFO REQUESTED (TECH) 0503 INFO REQUESTED (VOL. ACTIONS) 0504 INFO REQUESTED (REPORTING RATIONALE); DISPOSITION: REFER TO CHEMICAL SCREENING CAP NOTICE

SUB. DATE: 09/14/92 OTS DATE: 09/21/92 CSRAD DATE: 01/26/95

CHEMICAL NAME: Chlormephos Phosphorodithioate, S-(chloromethyl) O,O-diethyl

VOLUNTARY ACTIONS: 0401 NO ACTION REPORTED 0402 STUDIES PLANNED/IN PROGRESS 0403 NOTIFICATION OF WORK IN PROGRESS 0404 LABEL/MSDS CHANGES 0405 PROCESS/ANDLING CHANGES 0406 APP/USE DISCONTINUED 0407 PRODUCTION DISCONTINUED 0408 CONFIDENTIAL

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 ECO/AQUA TOX	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUREL/FATE	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQEST DELAY	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PROD/COMP/CHEM ID	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04
0211 CHR. TOX (HUMAN)	01 02 04	CONFIDENTIAL	01 02 04
0212 ACUTE TOX. (ANIMAL)	01 02 04	ALLERG (HUMAN)	01 02 04
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	ALLERG (ANIMAL)	01 02 04
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	METAB/PHARMACO (ANIMAL)	01 02 04
0215 CHRONIC TOX (ANIMAL)	01 02 04	METAB/PHARMACO (HUMAN)	01 02 04
		0241 IMMUNO (ANIMAL)	01 02 04
		0242 IMMUNO (HUMAN)	01 02 04
		0243 CHEM/PHYS PROP	01 02 04
		0244 CLASTO (IN VITRO)	01 02 04
		0245 CLASTO (ANIMAL)	01 02 04
		0246 CLASTO (HUMAN)	01 02 04
		0247 DNA DAM/REPAIR	01 02 04
		0248 PROD/USE/PROC	01 02 04
		0251 MSDS	01 02 04
		0299 OTHER	01 02 04

USE: PRODUCTION: R&D pesticide Imported from Europe

TRIAJE DATA: NON-CBI INVENTORY YES NO CAS SR NO (CONTINUE) MED HIGH (M MIMI) SPECIES: RAT TOXICOLOGICAL CONCERN: LOW MED HIGH AOX

-CPSS- 0929951235

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> <ID NUMBER>

8(e)-12194A

> <TOX CONCERN>

H

> <COMMENT>

ACUTE ORAL TOXICITY IN RATS IS HIGH CONCERN WITH MALE AND FEMALE LD50S OF 27 AND 16 MG/KG, RESPECTIVELY. DOSE (MG/KG) AND MORTALITY: 15 (2/10 M, 2/10 F), 25 (4/10 M, 9/10 F), 35 (8/10 M, 10/10 F), 50 (7/10 M, 10/10 F), AND 75 (10/10 M, 10/10 F). CLINICAL SIGNS INCLUDED MILD TO SEVERE DEPRESSION, TREMBLING, SALIVATION, LACRIMATION, WET BELLY, ATAXIA, AND PROSTRATION. NECROPSY OF DECEDENTS REVEALED DARK APPEARING LIVER AND KIDNEY, HEMORRHAGIC LUNGS, URINARY BLADDER, SLOUGHING AND/OR INFLAMMATION AND EROSION OF STOMACH MUCOSA. NO SIGNIFICANT FINDINGS WERE FOUND IN SURVIVORS. IN A PILOT STUDY, 60 RATS (5/DOSE/SEX) WERE DOSED WITH 7, 15, 30, 45, 60 AND 100 MG/KG OF TEST MATERIAL. THE APPROXIMATE LD50 WAS DETERMINED TO BE 35 MG/KG. NO MORTALITY DATA WAS GIVEN FOR THIS STUDY.

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