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Office of Toxic Substances
US Environmental Protection Agency
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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 Dermal LD50 with Chlormephos Technical in Rabbits". 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 10, 20, 40, 70 and 100 mg/kg body weight. The dermal LD50 for males was 31 mg/kg with 95% confidence limits of 16.8 to 57.4 mg/kg and 62 mg/kg for females with 95% confidence limits of 36.5 to 105.4 mg/kg. Clinical signs included depression, dyspnea, trembling, salivation, ataxia, diarrhea, cyanosis, and convulsions (observed in only one moribund female). Except for convulsions, 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 DERMAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RABBITS

Study No. BCD0678

Report No. JCW 78:33

Toxicology-Pathology Laboratory
Rhodia Inc.
Ashland, Ohio 44805

July 26, 1978

ACUTE DERMAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RABBITS

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HESS & CLARK DIVISION
ASHLAND, OHIO 44805
Research Department



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Subject: Acute Dermal LD₅₀, Chlormephos Technical

Book No.: 5403 Pages 59-65
 5407 Pages 37-41, 45-50, 89, 90
 5409 Pages 54-72, 81-100

Study No. BCD0678

Dates 6-20-78 to 7-6-78

TITLE

Acute Dermal LD₅₀ with Chlormephos Technical in Rabbits

PURPOSE

To determine the single dermal LD₅₀ dose of chlormephos technical to rabbits when conducted according to the EPA proposed guidelines of April, 1978; 162.81-2.

LOCATION

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

SPONSOR

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

SUMMARY

Chlormephos Technical was applied topically to the skin of rabbits at levels of 10, 20, 40, 70 and 100 mg/kg body weight. The animals were observed for a 14-day observation period following treatment. Toxic symptoms included depression, dyspnea, tremors, salivation, ataxia, diarrhea, cyanosis and convulsions.

Observed mortality was 33, 17, 50, 83 and 100% in the males and 0, 0, 33, 50 and 100% in the females, respectively. An LD₅₀ for each sex was calculated according to the procedure of Litchfield and Wilcoxon (J. Pharm. Exp. Pharm., Exp. Therap. 96 (2) 99-113, 1949). The calculated LD₅₀ for the males was 31 mg/kg with 95% confidence limits of 16.8 to 57.4 mg/kg. The female LD₅₀ was calculated to be 62 mg/kg with 95% confidence limits of 36.5 to 105.4 mg/kg.



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EXPERIMENTAL

MATERIALS AND METHODS

ANIMALS

Sixty (60) New Zealand albino rabbits, 30 males and 30 females, weighing 1.63 to 2.63 kg., and 8 to 10 weeks of age were obtained from Davidson's Mill Farm, Jamesburg, New Jersey. They were examined by a veterinarian with respect to their general health and suitability as test animals.

HOUSING

For the quarantine period 3 animals from each shipping case were placed into large stainless steel animal cages, 71 x 86 x 71 cm. The rabbits were held for a period of 2 weeks prior to the start of the studies for acclimation to laboratory conditions and close observation for any signs of disease.

The feeders, waterers and cage floor racks were cleaned once per week and the waste pans flushed once or twice daily as required. The rooms were maintained at a temperature of $69^{\circ}\text{F} \pm 1^{\circ}$, with a humidity of 50%. Room lights were automatically controlled with a 14 hour light, 10 hour dark cycle and conventional disease control was practiced throughout the quarantine and test periods.

For the test period, the rabbits were housed in individual suspended wire bottom rabbit cages, 46 x 51 x 33 cm. Liquid litter from Pharmacal, Westport, Conn., was used in the litter pans and changed twice weekly.

DIET

The rabbits were maintained on Wayne Rabbit Ration, a nutritionally balanced standard laboratory diet manufactured by Allied Mills, Fort Wayne, Indiana with the following analysis: 2% crude fat, 17% crude protein, 15% crude fiber and 0.025% sulfaquinoxaline. Feed and tap water were provided ad libitum. For 5 days after arrival the rabbits received 5 g/gallon of Pfizer's Neo-Terramycin soluble in the drinking water to prevent illness from diet change.



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IDENTIFICATION

Following the quarantine period the rabbits were moved to their test rooms and randomly distributed according to the Standard Operating Procedures, among study and treatment groups as follows:

LD₅₀ Study

Six males and 6 females were placed into each of 5 treatment groups. The animals were identified by a number tattooed in the right ear as follows:

Rabbit Number				Treatment Level (mg/kg)*	
Male		Female		Theoretical	Actual
Intact	Abraded	Intact	Abraded		
101-103	104-106	151-153	154-156	10	10.2
201-203	204-206	251-253	254-256	20	20.4
301-303	304-306	351-353	354-356	40	40.8
401-403	404-406	451-453	454-456	70	70.2
501-503	504-506	551-553	554-556	100	101.2

Cages were tagged with an identifying color coded label bearing study and animal number and dose level.

* The actual purity was not available until after the study was completed. The minimum purity of 93% was used for calculations. A density of 1 gm/ml was assumed.

TEST SUBSTANCE

The test substance was Chlormephos Technical P.O.X. 150, Batch No. DA 109, a clear liquid supplied by Rhodia Inc., Agricultural Division, Monmouth Junction, New Jersey, shipped from Rhodia Inc., Agricultural Division, St. Joseph, Missouri, and received April 26, 1978. Purity as determined by GLC was 94.4% and the pH was 3.01.



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TEST PROCEDURE

The test substance was diluted in acetone to provide the proper concentration and volume to insure coverage of what would constitute 10% of the total body surface. Dose levels were determined from a pilot study.

Twenty four hours prior to the start of the study, the trunks of the rabbits were carefully clipped free of hair, the shaved area constituting at least 10% of the entire body surface. On day 0 prior to dosing the animals were weighed on a Toledo scale for dose volume calculation. The dose volume was 2 ml/kg.

Three males and three females from each dose group had skins abraded with a firm nylon brush so as to penetrate the stratum but not the dermis. Skins of the other rabbits were left intact.

The rabbits were placed in an impervious rubber cloth sleeve and the test material was applied directly to the skin using a glass syringe equipped with a 16 gauge x 3" straight dosing needle. The rabbits were immobilized in stocks for 24 hours and observed frequently. The day of dosing was designated day 0. The following day the rabbits were removed from stocks, dressings removed and skins wiped with a damp cloth. Their skins were evaluated for irritation according to Draize. They were returned to their cages and observed at least twice daily early AM and late PM of the normal working day for 14 days. Skin reactions were scored again at 72 hours and at necropsy. Survivors were sacrificed on day 15 of the study.

OBSERVATIONS

A study record book was maintained according to the Standard Operating Procedures and included the following:

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



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DATA ANALYSIS

An analysis of the mortality data was made by the method of Litchfield and Wilcoxon, J. Pharm. Exp. Therap. 96 (2), 99-113, 1949.

Skin irritation was scored using Draize procedure. Draize, J. H., 1959 - The Appraisal of Chemicals in Foods, Drugs and Cosmetics, Association of Food & Drug Officials of the U.S.

STORAGE OF DATA

All raw data generated by this study and the final report are on file in the archives at Rhodia Inc., Toxicology-Pathology facility in Ashland, Ohio.

RESULTS AND DISCUSSION

Results of a pilot study indicated that the dermal LD₅₀ of Chlormephos Technical was approximately 50 mg/kg. Therefore rabbits were given dermal doses ranging between 10 and 100 mg of Chlormephos/kg in an LD₅₀ study.

The individual and average fasting body weights, dose volumes and days to death are presented in Table 1. Individual and average body weights for days 1, 4, 7, 10 and 14 are presented in Table 2. Individual clinical and necropsy observations are presented in Table 3. Skin irritation scores at 24 and 72 hours and at necropsy are presented in Table 4, and skin irritation scoring system is presented in Table 5. Figures 1 and 2 are graphical illustration of the calculated LD₅₀ according to the procedure of Litchfield & Wilcoxon (J. Pharm. Exp. Therap. 96 (2) 99-113, 1949) using the theoretical dose levels.

Based on the results of this study the dermal dose LD₅₀ of Chlormephos Technical in rabbits is calculated to be 31 mg/kg body weight with 95% confidence limits of 16.8 to 57.4 mg/kg for the males and 62 mg/kg body weight with 95% confidence limits of 36.5 to 105.4 for the females. Theoretical values were used for the calculation.

Body weight data revealed a weight loss by day 1. This weight loss was not unexpected as the rabbits were without food and water during the 24 hours in stock. Most of the rabbits had regained weight loss by day 7.

Clinical symptoms of toxicity were seen in all dose groups and included depression and dyspnea and diarrhea at 10 mg/kg and at higher doses tremor, salivation, cyanosis and convulsions were also noted in



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one animal. Signs of toxicity were essentially the same in both males and females at each dose level abraded and non-abraded. However, among all dose groups toxic symptoms at the higher doses were of greater severity.

Mortality in the different dose groups was as follows:

<u>Dose Group (mg/kg)</u>	<u>M</u>	<u>F</u>
10	2	0
20	1	0
40	3	2
70	5	3
100	6	6

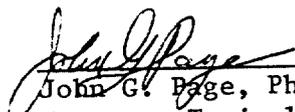
In the 10 mg/kg males one animal died day 0 and one death occurred on day 5. Deaths in all other dose levels occurred on day 0.

In the female 40 mg/kg group one rabbit died on day 0 and one on day 1. Deaths at 70 and 100 mg/kg occurred day 0. There did not appear to be any difference in abraded vs non-abraded animals.

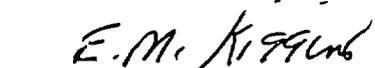
Necropsy observations for those rabbits dying within a few hours revealed no significant findings. Those rabbits in the higher dose group living approximately 12-24 hours had hemorrhagic and/or enlarged thymus and hemorrhagic lungs. Three rabbits in the 100 mg/kg dose group had inflamed areas in the stomach and mucosal sloughing. Three abraded females in the 20 mg/kg group had mottled or hemorrhagic and fibrous kidneys. Other necropsy findings were incidental in nature and not considered related to administration of Chlormephos Technical.

Skin irritation scores were zero in all rabbits for all time periods.


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 Toxicologist


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 Director of Research
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ACUTE DERMAL LD₅₀ IN RABBITS WITH CHLORMEPHOS TECHNICAL

TABLE 1

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

Males				Females			
Animal No.	Body Wt (gm)	Dose Volume * (ml)	Days to Death	Animal No.	Body Wt (gm)	Dose Volume (ml)	Days to Death
<u>Dose Group: 10 mg/kg</u>							
101	2425	4.8	5	151	2632	5.2	14
102	2175	4.4	14	152	2013	4.0	14
103	2155	4.4	14	153	1626	3.3	14
104	2055	4.2	14	154	2389	4.8	14
105	2057	4.2	0	155	2105	4.2	14
106	1790	3.6	14	156	2455	5.0	14
Average	2110	4.3	10.2	Average	2203	4.4	14.0
<u>Dose Group: 20 mg/kg</u>							
201	2177	4.4	14	251	2454	5.0	14
202	2215	4.4	14	252	2260	4.6	14
203	2256	4.6	14	253	2131	4.2	14
204	2051	4.2	14	254	2615	5.2	14
205	2122	4.2	0	255	2211	4.4	14
206	2293	4.6	14	256	2565	5.2	14
Average	2186	4.4	11.7	Average	2373	4.8	14.0
<u>Dose Group: 40 mg/kg</u>							
301	2391	4.8	14	351	2354	4.8	14
302	2190	4.4	0	352	2160	4.4	0
303	2161	4.4	14	353	2624	5.2	14
304	2184	4.4	14	354	2310	4.6	1
305	2511	5.0	0	355	2402	4.8	14
306	2259	4.6	0	356	2445	4.8	14
Average	2283	4.6	7.0	Average	2383	4.8	9.5

* Dose volumes were calculated to the nearest 0.1 kg.

ACUTE DERMAL LD₅₀ IN RABBITS WITH CHLORMEPHOS TECHNICAL

TABLE 1 (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: 70 mg/kg</u>							
401	2244	4.4	0	451	2160	4.4	14
402	2280	4.6	0	452	2436	4.8	14
403	2001	4.0	0	453	2160	4.4	14
404	2095	4.2	0	454	2176	4.4	0
405	2213	4.4	14	455	2476	5.0	0
406	2166	4.4	0	456	2087	4.2	0
Average	2167	4.3	2.3	Average	2249	4.5	7.0
<u>Dose Group: 100 mg/kg</u>							
501	2212	4.4	0	551	2061	4.2	0
502	2292	4.6	0	552	2257	4.6	0
503	1931	3.8	0	553	2210	4.4	0
504	2370	4.8	0	554	2220	4.4	0
505	2131	4.2	0	555	2143	4.2	0
506	2258	4.6	0	556	2373	4.8	0
Average	2199	4.4	0	Average	2211	4.4	0

* Dose volumes were calculated to the nearest 0.1 kg.

ACUTE DERMAL LD₅₀ IN RABBITS WITH CHLORMEPHOS TECHNICAL

TABLE 2

Individual and Average Body Weights (gm)

Animal No.	Males							Females						
	Test Day			Dose Group: 10 mg/kg				Test Day			Test Day			
	0	1	4	7	10	14	Animal No.	0	1	4	7	10	14	
101 I	2425	2237	2341	-	2546	2651	151 I	2632	2492	2618	2800	2808	3082	
102 I	2175	2114	2341	2425	2546	2651	152 I	2013	1785	1936	2069	2185	2373	
103 I	2155	2114	2081	2234	2287	2400	153 I	1626	1415	1502	1660	1688	1916	
104 A	2055	1756	1941	2119	2250	2463	154 A	2389	2188	2421	2430	2521	2671	
105 A	2057	-	-	-	-	-	155 A	2105	1976	2122	2052	2168	2306	
106 A	1790	1613	1991	2082	2275	2378	156 A	2455	2274	2532	2706	2805	2956	
Average	2110	1967	2139	2215	2340	2473	Average	2203	2022	2189	2286	2363	2551	
	Dose Group: 20 mg/kg							Dose Group: 40 mg/kg						
201 I	2177	1945	1877	2000	2024	2190	251 I	2454	2247	2334	2515	2700	2880	
202 I	2215	2176	2361	2560	2677	2661	252 I	2260	2085	2284	2388	2610	2749	
203 I	2256	2076	2203	2365	2479	2604	253 I	2131	1927	2229	2439	2697	2980	
204 A	2051	1797	2006	2096	2147	2297	254 A	2615	2353	2431	2462	2451	2650	
205 A	2122	-	-	-	-	-	255 A	2211	1996	2071	2265	2261	2502	
206 A	2293	2118	2262	2340	2452	2639	256 A	2565	2401	2600	2687	2697	2882	
Average	2186	2022	2142	2272	2356	2478	Average	2373	2168	2325	2459	2569	2774	
	Dose Group: 40 mg/kg							Dose Group: 40 mg/kg						
301 I	2391	2106	2251	2480	2450	2668	351 I	2354	2168	2396	2395	2640	2908	
302 I	2190	-	-	-	-	-	352 I	2160	-	-	-	-	-	
303 I	2161	2058	2242	2377	2500	2681	353 I	2624	2440	2486	2590	2747	2936	
304 A	2184	2065	2071	2168	2394	2531	354 A	2310	-	-	-	-	-	
305 A	2511	-	-	-	-	-	355 A	2402	2093	2347	2505	2580	2774	
306 A	2259	-	-	-	-	-	356 A	2445	2226	2265	2444	2500	2771	
Average	2283	2076	2188	2342	2448	2627	Average	2383	2232	2374	2484	2617	2847	

(-) = Dead

ACUTE DERMAL LD₅₀ IN RABBITS WITH CHLORMEPHOS TECHNICAL

TABLE 2 (Cont'd)

Individual and Average Body Weights (gm)

Animal No.	Males							Females						
	Test Day			Dose Group: 70 mg/kg	Animal No.	Test Day			Dose Group: 100 mg/kg	Animal No.	Test Day			
	0	1	4			7	10	14			0	1	4	7
401 I	2244	-	-	-	-	-	451 I	2160	1950	1951	1976	2056	2247	
402 I	2280	-	-	-	-	-	452 I	2436	2194	2336	2514	2650	2611	
403 I	2001	-	-	-	-	-	453 I	2160	1830	2111	2201	2363	2550	
404 A	2095	-	-	-	-	-	454 A	2176	-	-	-	-	-	
405 A	2213	2007	2115	2280	2430	2571	455 A	2476	-	-	-	-	-	
406 A	2166	-	-	-	-	-	456 A	2087	-	-	-	-	-	
Average	2167	2007	2115	2280	2430	2571	Average	2249	1991	2133	2230	2356	2469	
501 I	2212	-	-	-	-	-	551 I	2061	-	-	-	-	-	
502 I	2292	-	-	-	-	-	552 I	2257	-	-	-	-	-	
503 I	1931	-	-	-	-	-	553 I	2210	-	-	-	-	-	
504 A	2370	-	-	-	-	-	554 A	2220	-	-	-	-	-	
505 A	2131	-	-	-	-	-	555 A	2143	-	-	-	-	-	
506 A	2258	-	-	-	-	-	556 A	2373	-	-	-	-	-	
Average	2199	-	-	-	-	-	Average	2211	-	-	-	-	-	

(-) = Dead

ACUTE DERMAL LD₅₀ IN RABBITS WITH CHLORMEPHOS TECHNICAL

TABLE 3

Individual Clinical and Necropsy Observations

SYMBOLS

At	-	Ataxia
Cv	-	Convulsions
Cy	-	Cyanotic
D	-	Died
Dp+	-	Mild depression
Dp++	-	Moderate depression
Dp+++	-	Severe depression
Dr	-	Diarrhea
Dy	-	Dyspnea
FD	-	Found dead
HT	-	Head tilt
Lc	-	Lacrimation
Mb	-	Moribund
NS	-	Nothing Significant
S1+	-	Mild salivation
S1++	-	Moderate salivation
S1+++	-	Severe salivation
Tr	-	Trembling

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 DERMAL LD₅₀ IN RABBITS WITH CHLORMEPHOS TECHNICAL

TABLE 3 (Cont'd)

Individual Clinical and Necropsy Observations

Dose Group: 10 mg/kg

Animal No.	Manner & Day of Death	Observations	
		Clinical	Necropsy
<u>Males</u>			
101	FD, 5	Dp+ day 0 Dr days 1-4 At days 2, 3	Abdominal cavity filled with green fluid; Lungs - hemorrhagic
102	TS, 15	Dp+ day 0 NS days 1-14	NS
103	TS, 15	Dp+ day 0 NS days 1-14	NS
104	TS, 15	Dp+ day 0 Dy day 0 At days 1, 2 NS days 3-14	NS
105	D, 0	Dy day 0	Lungs - hemorrhagic; Stomach - few hemorrhagic areas, mucosa sloughed
106	TS, 15	Dp+ day 0 Dy day 0 Dr days 1, 2 NS days 3-14	NS
<u>Females</u>			
151	TS, 15	Dp+ day 0 NS days 1-14	NS
152	TS, 15	Dp+ day 0 NS days 1-14	NS
153	TS, 15	Dp+ day 0 Dy day 0 NS days 1-14	NS
154	TS, 15	Dp+ day 0 Dy day 0 Dr days 2-7 NS days 1, 8-14	NS
155	TS, 15	Dy day 0 NS days 1-14	NS
156	TS, 15	Dp+ day 0 NS days 1-14	NS

ACUTE DERMAL LD₅₀ IN RABBITS WITH CHLORMEPHOS TECHNICAL

TABLE 3 (Cont'd)

Individual Clinical and Necropsy Observations

Dose Group: 20 mg/kg

Animal No.	Manner & Day of Death	Observations	
		Clinical	Necropsy
<u>Males</u>			
201	TS, 15	Dp+ day 0 Dr days 1-3 NS days 4-14	NS
202	TS, 15	Dp+ day 0 NS days 1-14	Many parasites in cecum
203	TS, 15	Dp+ day 0 NS days 1-14	NS
204	TS, 15	Dp+ day 0 Dy day 0 NS days 1-14	NS
205	D, 0	Tr day 0 Dp+ day 0 Dy day 0 S1++ day 0	NS
206	TS, 15	Dp+ day 0 Dy day 0 Tr day 0 NS days 1-14	NS
<u>Females</u>			
251	TS, 15	Tr day 0 Dp+ day 0 Dy day 0 NS days 1-14	NS
252	TS, 15	Dp+ day 0 Dy day 0 NS days 1-14	NS
253	TS, 15	Dp+ day 0 NS days 1-14	NS
254	TS, 15	NS days 0-14	Kidneys - mottled, fibrous and small
255	TS, 15	Dy day 0 Dp+ day 0 Dr days 1-3 NS days 4-14	Kidneys - small, hemorrhagic, mottled and fibrous
256	TS, 15	Dp+ day 0 NS days 1-14	Kidneys - hemorrhages on surface, fibrous

ACUTE DERMAL LD₅₀ IN RABBITS WITH CHLORMEPHOS TECHNICAL

TABLE 3 (Cont'd)

Individual Clinical and Necropsy Observations

Dose Group: 40 mg/kg

Animal No.	Manner & Day of Death	Observations	
		Clinical	Necropsy
<u>Males</u>			
301	TS, 15	Dp+ days 0-1 Dr days 2, 3 Tr day 1 At day 1 NS days 4-14	NS
302	D, 0	Dp+ day 0 Tr day 0 Dy day 0	NS
303	TS, 15	Dp+ days 0-1 Tr day 1 At day 1 Dr days 1-7 NS days 8-14	NS
304	TS, 15	Dy day 0 Dp+ day 0 Tr day 0 S1++ day 0 At days 1, 2 NS days 3-14	NS
305	D, 0	Dy day 0 Dp+ day 0 Tr day 0 S1++ day 0	NS
306	D, 0	S1+ day 0 Dy day 0 Dp+++ day 0	Liver - several white foci on one lobe
<u>Females</u>			
351	TS, 15	Dy day 0 Dp+ day 0 Tr day 0 NS days 1-14	NS
352	D, 0	NS day 0	NS

ACUTE DERMAL LD₅₀ IN RABBITS WITH CHLORMEPHOS TECHNICAL

TABLE 3 (Cont'd)

Individual Clinical and Necropsy Observations

<u>Dose Group: 40 mg/kg</u>			<u>Observations</u>	
<u>Animal No.</u>	<u>Manner & Day of Death</u>	<u>Clinical</u>	<u>Necropsy</u>	
<u>Females (Cont'd)</u>				
353	TS, 15	Dp+ day 0 Lc day 0 Dy day 0 Tr day 0 NS days 1-14	Gallbladder - distended	
354	D, 1	Dp+ day 0	Lungs - congested and hemorrhagic; Thymus - slightly enlarged and hemorrhagic	
355	TS, 15	Dp+ days 0-1 NS days 2-14	NS	
356	TS, 15	Dp+ day 0 Dp++ day 1 At day 1 Tr day 1 Dr days 2, 3 NS days 4-14	Kidneys - mottled, hemorrhagic and fibrous	
<u>Dose Group: 70 mg/kg</u>			<u>Males</u>	
401	D, 0	Dp+ day 0 S1++ day 0 Tr day 0	NS	
402	D, 0	Dp+ day 0 S1++ day 0 Tr day 0	Lungs - hemorrhagic; Thymus - enlarged and hemorrhagic	
403	D, 0	Dy day 0 Cy day 0	Liver - dark	
404	D, 0	Dy day 0 Dp+++ day 0 Tr day 0 S1++ day 0	Spleen - enlarged	
405	TS, 15	Dy days 0-2 Dp+ days 0-4 S1++ days 0-2 Tr days 0-2 At days 1, 2 Dr days 3, 4 NS days 5-14	NS	
406	D, 0	Dy day 0 Dp+ day 0	NS	

ACUTE DERMAL LD₅₀ IN RABBITS WITH CHLORMEPHOS TECHNICAL

TABLE 3 (Cont'd)

Individual Clinical and Necropsy Observations

Dose Group: 70 mg/kg

Animal No.	Manner & Day of Death	Observations	
		Clinical	Necropsy
		<u>Females</u>	
451	TS, 15	Dy day 0 Dp+ days 0-4 S1++ day 0 Tr days 0, 1 At days 1-4 HT days 2-8 NS days 9-14	NS
452	TS, 15	Dy day 0 Dp+ days 0-1 Tr days 0, 1 S1++ day 0 S1+ day 1 At days 1, 2 NS days 3-14	NS
453	TS, 15	Dy day 0 Dp+ days 0-1 Tr days 0, 1 S1++ day 0 Dr days 1, 2 NS days 3-14	Spleen - enlarged and mottled, 8 x 2 x 1.5 cm
454	D, 0	Dp+ day 0 S1+ day 0 Tr day 0 Dy day 0	NS
455	D, 0	Dp+ day 0 Tr day 0 Dy day 0 S1+ day 0	Lungs - hemorrhagic; Thymus - enlarged and hemorrhagic
456	D, 0	Dp+ day 0 Dy day 0 Cv day 0 S1++ day 0	NS

ACUTE DERMAL LD₅₀ IN RABBITS WITH CHLORMEPHOS TECHNICAL

TABLE 3 (Cont'd)

Individual Clinical and Necropsy Observations

Dose Group: 100 mg/kg

Animal No.	Manner & Day of Death	Observations	
		Clinical	Necropsy
		<u>Males</u>	
501	D, 0	Dy day 0 Dp+ day 0 S1++ day 0 Cy day 0 Tr day 0	Lungs - hemorrhagic; Thymus - enlarged and hemorrhagic
502	D, 0	Dp+ day 0 Dy day 0 Tr day 0 S1+ day 0 Cy day 0	NS
503	D, 0	Dy day 0 Dp+ day 0 Tr day 0 S1+ day 0 Cy day 0	NS
504	D, 0	Dy day 0 Dp+ day 0	Thymus - enlarged
505	D, 0	Dy day 0 Dp+ day 0 S1++ day 0 Tr day 0	NS
506	D, 0	Dy day 0 Dp+++ day 0 S1+++ day 0 Tr day 0	Thymus - enlarged; Stomach - few inflamed areas

ACUTE DERMAL LD₅₀ IN RABBITS WITH CHLORMEPHOS TECHNICAL

TABLE 3 (Cont'd)

Individual Clinical and Necropsy Observations

Dose Group: 100 mg/kg

Animal No.	Manner & Day of Death	Observations	
		Clinical	Necropsy
<u>Females</u>			
551	D, 0	Tr day 0 S1++ day 0 Dy day 0 Dp+ day 0	Thymus - petechiae
552	D, 0	Dy day 0 Dp+ day 0 Tr day 0 S1++ day 0	Thymus and lungs - hemorrhagic; Stomach - many inflamed areas, mucosa sloughed
553	D, 0	Dy day 0 Dp+ day 0 Tr day 0 S1++ day 0	NS
554	D, 0	Dp+ day 0 S1+ day 0 Tr day 0	Stomach - slightly inflamed, some sloughing of mucosa
555	D, 0	Dp++ day 0 Dy day 0 Tr day 0 S1++ day 0	NS
556	D, 0	Dy day 0 Dp+ day 0 Cy day 0 S1+ day 0 Mb day 0	NS

ACUTE DERMAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RABBITS

TABLE 4

Individual Skin Irritation Scores

<u>Males</u>				
<u>Animal No.</u>		<u>24 Hrs.</u>	<u>72 Hrs.</u>	<u>Necropsy</u>
<u>Dose Group: 10 mg/kg</u>				
<u>Erythema and Eschar</u>				
101	I ^a	0	0	0
102	I	0	0	0
103	I	0	0	0
104	A	0	0	0
105	A	-	-	0
106	A	0	0	0
<u>Edema Formation</u>				
101	I	0	0	0
102	I	0	0	0
103	I	0	0	0
104	A	0	0	0
105	A	-	-	0
106	A	0	0	0
<u>Females</u>				
<u>Erythema and Eschar</u>				
151	I	0	0	0
152	I	0	0	0
153	I	0	0	0
154	A	0	0	0
155	A	0	0	0
156	A	0	0	0
<u>Edema Formation</u>				
151	I	0	0	0
152	I	0	0	0
153	I	0	0	0
154	A	0	0	0
155	A	0	0	0
156	A	0	0	0

a - the skin of the rabbits was intact (I) or abraded (A)

(-)= dead

ACUTE DERMAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RABBITS

TABLE 4 (Cont'd)

Individual Skin Irritation Scores

Males				
Animal No.		24 Hrs.	72 Hrs.	Necropsy
<u>Dose Group: 20 mg/kg</u>				
<u>Erythema and Eschar</u>				
201	I	0	0	0
202	I	0	0	0
203	I	0	0	0
204	A	0	0	0
205	A	-	-	0
206	A	0	0	0
<u>Edema Formation</u>				
201	I	0	0	0
202	I	0	0	0
203	I	0	0	0
204	A	0	0	0
205	A	-	-	0
206	A	0	0	0
<u>Females</u>				
<u>Erythema and Eschar</u>				
251	I	0	0	0
252	I	0	0	0
253	I	0	0	0
254	A	0	0	0
255	A	0	0	0
256	A	0	0	0
<u>Edema Formation</u>				
251	I	0	0	0
252	I	0	0	0
253	I	0	0	0
254	A	0	0	0
255	A	0	0	0
256	A	0	0	0

(-)= dead

ACUTE DERMAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RABBITS

TABLE 4 (Cont'd)

Individual Skin Irritation Scores

Males				
Animal No.		24 Hrs.	72 Hrs.	Necropsy
<u>Dose Group: 40 mg/kg</u>				
<u>Erythema and Eschar</u>				
301	I	0	0	0
302	I	-	-	0
303	I	0	0	0
304	A	0	0	0
305	A	-	-	0
306	A	-	-	0
<u>Edema Formation</u>				
301	I	0	0	0
302	I	-	-	0
303	I	0	0	0
304	A	0	0	0
305	A	-	-	0
306	A	-	-	0
<u>Females</u>				
<u>Erythema and Eschar</u>				
351	I	0	0	0
352	I	-	-	0
353	I	0	0	0
354	A	-	-	0
355	A	0	0	0
356	A	0	0	0
<u>Edema Formation</u>				
351	I	0	0	0
352	I	-	-	0
353	I	0	0	0
354	A	-	-	0
355	A	0	0	0
356	A	0	0	0

(-) = dead

ACUTE DERMAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RABBITS

TABLE 4 (Cont'd)

Individual Skin Irritation Scores

<u>Males</u>			
Animal No.	24 Hrs.	72 Hrs.	Necropsy
<u>Dose Group: 70 mg/kg</u>			
<u>Erythema and Eschar</u>			
401 I	-	-	0
402 I	-	-	0
403 I	-	-	0
404 A	-	-	0
405 A	0	0	0
406 A	-	-	0
<u>Edema Formation</u>			
401 I	-	-	0
402 I	-	-	0
403 I	-	-	0
404 A	-	-	0
405 A	0	0	0
406 A	-	-	0
<u>Females</u>			
<u>Erythema and Eschar</u>			
451 I	0	0	0
452 I	0	0	0
453 I	0	0	0
454 A	-	-	0
455 A	-	-	0
456 A	-	-	0
<u>Edema Formation</u>			
451 I	0	0	0
452 I	0	0	0
453 I	0	0	0
454 A	-	-	0
455 A	-	-	0
456 A	-	-	0

(-) = dead

ACUTE DERMAL LD₅₀ WITH CHLORMEPHOS TECHNICAL IN RABBITS

TABLE 4 (Cont'd)

Individual Skin Irritation Scores

Males				
Animal No.		24 Hrs.	72 Hrs.	Necropsy
<u>Dose Group: 100 mg/kg</u>				
<u>Erythema and Eschar</u>				
501	I	-	-	0
502	I	-	-	0
503	I	-	-	0
504	A	-	-	0
505	A	-	-	0
506	A	-	-	0
<u>Edema Formation</u>				
501	I	-	-	0
502	I	-	-	0
503	I	-	-	0
504	A	-	-	0
505	A	-	-	0
506	A	-	-	0
<u>Females</u>				
<u>Erythema and Eschar</u>				
551	I	-	-	0
552	I	-	-	0
553	I	-	-	0
554	A	-	-	0
555	A	-	-	0
556	A	-	-	0
<u>Edema Formation</u>				
551	I	-	-	0
552	I	-	-	0
553	I	-	-	0
554	A	-	-	0
555	A	-	-	0
556	A	-	-	0

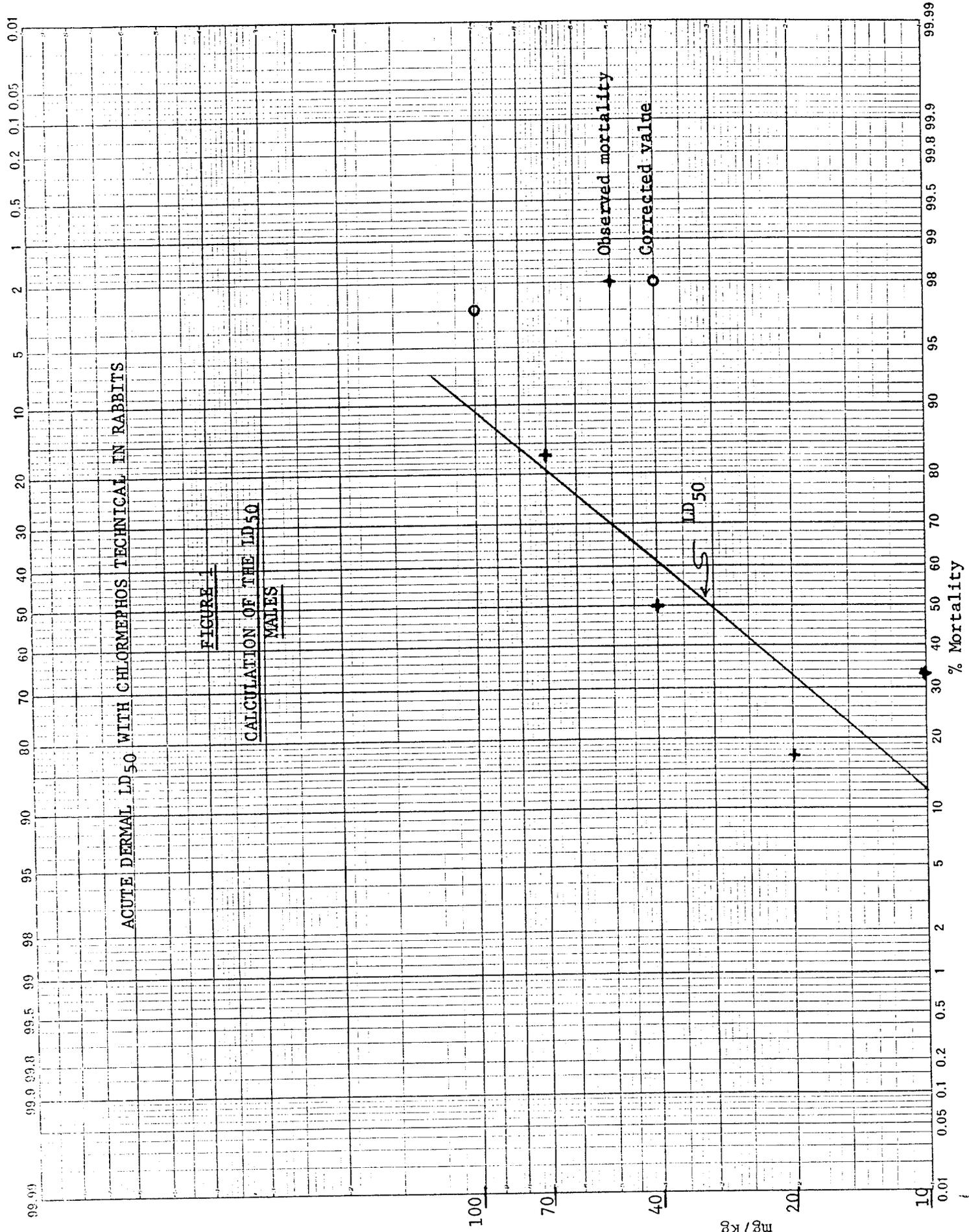
(-) = dead

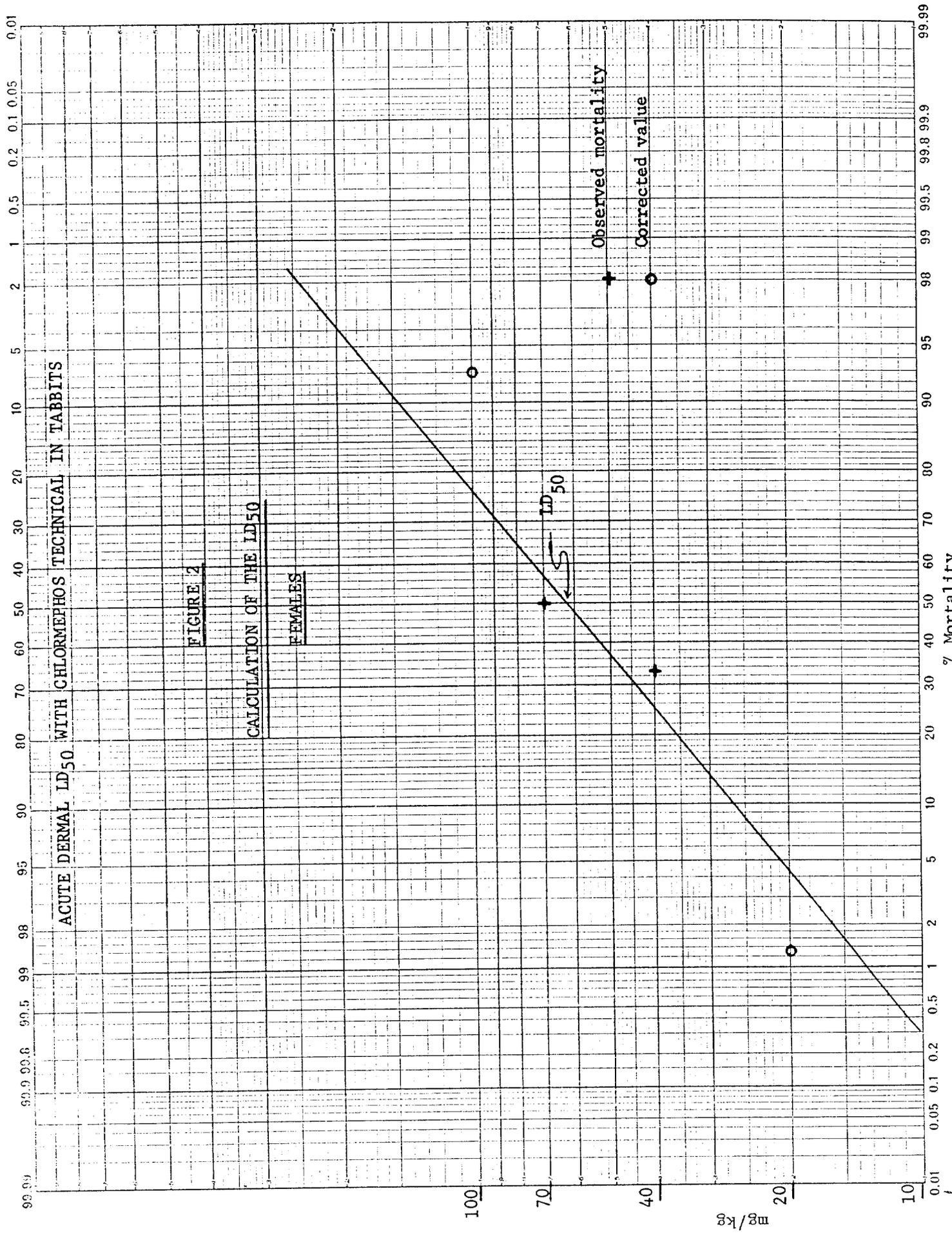
TABLE 5

Skin Reaction

	<u>Value</u>
Erythema and Eschar Formation:	
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Edema Formation:	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1 millimeter)	3
Severe edema (raised more than 1 millimeter and extending beyond the area of exposure)	4

Draize, J. H., 1959 - The Appraisal of Chemicals in Foods, Drug, and Cosmetics, Association of Food and Drug Officials of the U.S.





Front Sheet

Study No. <u>BCD0678X and BCD0678</u>	Chemical <u>Chlormephos Tech.</u>
Project No. <u>Pilot Study and Acute Dermal LD₅₀</u>	Purity <u>94.4%</u>
Sponsor <u>Ag. Div. Rhodia Inc.</u>	Animal <u>Rabbit</u>
Start Date <u>5-9-78</u> <u>7 days - Pilot</u>	No. <u>M 40 F 40</u>
Duration <u>14 days - LD₅₀</u>	Start Weight
Finish Date <u>7-6-78</u>	<u>M 2-3 kg</u>
Study Director <u>J. Winbigler</u>	<u>F 2-3 kg</u>
Study Personnel <u>SEH, CM and SK</u>	Route <u>Skin</u>

<u>Animal No.</u>	<u>Treatment Level</u> (mg/kg)	<u>Color Code</u>
<u>BCD0678X - PILOT STUDY</u>		
Male		
Female		
101-102	Low 25	white
201-202	2nd 50	blue
301-302	Mid 100	green
401-402	4th 200	pink
501-502	High 500	yellow
 <u>BCD0678 - DERMAL LD₅₀</u>		
Male		
Female		
101-106	Low 10	white
201-206	2nd 20	blue
301-306	Mid 40	green
401-406	4th 70	pink
501-506	High 100	yellow

Assays or Special Procedures

PREPARATIONS:

Shave all animal trunks.
Abrade all animals of pilot study.
Abrade 3 animals/sex/treatment group - LD₅₀ study

OBSERVATIONS:

Body weights - days 0, 1, 4, 7, 10 and 14.
Clinical observations - day 0 frequent, days 1-14 b.i.d.
Gross necropsy - all animals.
Skin irritation evaluation at 24 and 72 hours and at time of death or sacrifice.

Special Handling

Handle with care; avoid skin contact. Wash any contaminated areas with copious amounts of water, and then report the incident to the study director.



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PROTOCOL

TITLE

Acute Dermal LD₅₀ with Chlormephos Technical in Rabbits

PURPOSE

To determine the single dermal LD₅₀ dose of chlormephos technical to rabbits when conducted according to the EPA proposed guidelines of April, 1978; 162.81-2.

LOCATION

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

SPONSOR

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

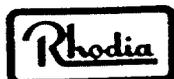
ANIMALS

Eighty (80) New Zealand white rabbits, 40 males and 40 females, weighing 2 to 3 kilograms, and 8 to 10 weeks of age will be obtained from Davidson's Mill Farm, Jamesburg, New Jersey. They will be examined by a veterinarian with respect to their general health and suitability as test animals.

HOUSING

For the quarantine period three animals from each shipping case will be placed into large stainless steel animal cages, 71 x 86 x 71 cm. The remaining rabbits will also be distributed three to a cage. The rabbits will be held for a period of 1 to 2 weeks prior to the start of the studies for acclimation to laboratory conditions and close observation for any signs of disease.

The feeders, waterers and cage floor racks will be cleaned once per week and the waste pans flushed once or twice daily as required. The rooms will be maintained at a temperature of 69°F ± 1°, with a humidity of 50%. Room lights will be automatically controlled with a 14 hour light, 10 hour dark cycle and conventional disease control will be practiced throughout the quarantine and test periods (see SOP Manual #2).



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For the test period, the rabbits will be housed in individual suspended wire bottom rabbit cages, 46 x 51 x 33 cm. Liquid litter from Pharmacal, Westport, Conn., will be used in the litter pans and changed twice weekly.

DIET

The rabbits will be maintained on Wayne Rabbit Ration, a nutritionally balanced standard laboratory diet manufactured by Allied Mills, Ft. Wayne, Indiana with the following analysis: 2% crude fat, 17% crude protein, 15% crude fiber and 0.025% sulfaquinoxaline. Feed and tap water will be provided ad libitum. For 5 days after arrival the rabbits will receive 5 g/gallon of Pfizer's Neo-Terramycin soluble in the drinking water to prevent illness from diet change.

IDENTIFICATION

Following the quarantine period the rabbits will be moved to their test rooms and randomly distributed according to the Standard Operating Procedures, Manual #2 among study and treatment groups as follows:

Pilot Study

Two males and 2 females will be placed into each of 5 treatment groups and identified by a number tattooed in the right ear as follows:

<u>Male</u>	<u>Level</u>	<u>Female</u>	<u>Level</u>
101, 102	25	151, 152	25
201, 202	50	251, 252	50
301, 302	100	351, 352	100
401, 402	200	451, 452	200
501, 502	500	551, 552	500

Cages will be tagged with an identifying color coded label bearing study and animal number and dose level. The skin of all rabbits in the pilot study will be abraded (see text).



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LD₅₀ Study

Six male and 6 females will be placed into each of 5 treatment groups. The animals will be identified by a number tattooed in the right ear as follows:

<u>Male</u>	<u>Female</u>	<u>Level (mg/kg)</u>
101-106	151-156	10
201-206	251-256	20
301-306	351-356	40
401-406	451-456	70
501-506	551-556	100

Cages will be tagged with an identifying color coded label bearing study and animal number and dose level. The skin of rabbits 4, 5 and 6 in each group will be abraded. Rabbits 1, 2 and 3 in each group will have skins left intact.

TEST SUBSTANCE

The test substance will be Chlormephos Technical P.O.X. 150, Batch No. DA 109, a clear liquid supplied by Rhodia, Inc., Agricultural Division, Monmouth Junction, N. J., shipped from Rhodia, Inc., Agricultural Division, St. Joseph, Mo., and received April 26, 1978.

Warning: Chlormephos is an organophosphate and should be handled with care. Wear gloves. Avoid all skin and eye contact. In case of accidental contact, immediately wash afflicted areas with large amounts of water and then report the incident to the study director.

The test substance will be diluted in acetone to provide the mg/ml concentration necessary for a 2 ml/kg dose volume. Each dilution will be mixed continuously on a magnetic stirrer during application.

TEST PROCEDURE

Pilot Study

Twenty-four hours prior to the start of the study, the rabbits will be prepared by clipping the skin of the trunk free of hair with electric clippers equipped with a #40 blade. The shaved area will constitute at least 10% of the total body surface. On day 0 prior to dosing, the animals will be weighed on a Toledo scale for proper dose calculations and the skin of all the rabbits will be abraded with a firm nylon brush. This treatment should penetrate the stratum corneum but not the dermis.



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Pilot Study (Cont'd)

The test material will be applied directly to the skin (treatment levels are shown in Table 1). Each animal will then be placed in an impervious rubber cloth sleeve to retard evaporation and to maintain skin contact with the test material. The rabbits will then be immobilized in stocks for 24 hours and observed frequently during this period. Following this period, the rabbits will be removed from the stocks, dressings removed and skins wiped with a damp cloth to remove excess material. They will be returned to their cages and observed at least twice daily, early a.m. and late p.m. of the normal working day for a period of seven days, and the time to death recorded. From the pilot study, doses for the LD₅₀ study will be determined. (Table 1)

Any survivors after 7 days will be euthanized with an i.v. injection of pentobarbital sodium.

LD₅₀ Study

Skins of all animals will be shaved as for the pilot study, 24 hours prior to application of the test material. The animals will be weighed on a Toledo scale and the dose to be applied will be determined from the dose schedule (Table 2)

Three males and 3 females, Nos. 4, 5 and 6 from each treatment level will have skins abraded with a stiff nylon brush as for the pilot study and the remainder will be left intact. After application of the test material and wrapping, the rabbits will be immobilized in stocks for 24 hours with frequent observations and recording of toxic symptoms. The day test material is applied will be designated as day 0. Following this period the rabbits will be removed from the stocks, unwrapped, wiped with a damp cloth and returned to their cages.

OBSERVATIONS

A study record book will be maintained according to the Standard Operating Procedures, Manual #19, and will include observations made day 0 and twice daily, a.m. and p.m. for 14 days, and records of body weights for day 0, and days 1, 4, 7, 10 and 14 after dosing. The nature, onset, severity and duration of all toxic and pharmacologic signs and the time of death will also be recorded.

A gross pathological examination of heart, kidney, lung, spleen, liver, stomach, small and large intestine, urinary bladder and skin will be made, and all abnormal findings recorded.

Skin irritation will be evaluated at 24 and 72 hours and at time of death or sacrifice for erythema eschar and edema (Table 3).

Survivors from the LD₅₀ study will be sacrificed on day 15 of the study by i.v. injection of pentobarbital sodium.



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DATA ANALYSIS AND FINAL REPORT

A final report will be issued according to Manual #15 of the SOP and in addition, an analysis of the mortality data will be made by the Litchfield & Wilcoxon method (J. Pharm., Exp. Therap. 96 (2) 99-113, 1949) to determine the acute dermal median lethal dose (LD_{50}) of Chlormephos Technical.

Primary irritation scores will be determined according to Draize.

STORAGE OF DATA

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

Prepared by:

J. C. Winbigler
 J. C. Winbigler, B.S., M.T.
 Study Director

Approved by:

John G. Page
 John G. Page, Ph.D.
 Manager, Toxicology-Pathology
 Rhodia, Inc.

Approved by:

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

Draize, J. H., 1959 - The Appraisal of Chemicals in Foods, Drugs and Cosmetics, Association of Food and Drug Officials of the U.S.



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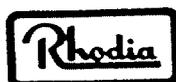


TABLE 1
 TREATMENT LEVELS

Pilot Study

Dose Level (mg/kg)		No. Rabbits		Volume of Test Substance	Volume of Diluent	Mg/ml Test Substance
Theoretical ^a	Actual ^b	M	F			
25	25.7	2	2	0.34	qs to 25 ml	12.6
50	50.6	2	2	0.67	qs to 25 ml	24.9
100	101.1	2	2	1.34	qs to 25 ml	49.8
200	203.1	2	2	2.69	qs to 25 ml	100.1
500	253.7	2	2	6.72	qs to 25 ml	249.9

LD₅₀ Study

Dose Level (mg/kg)		No. Rabbits		Volume of Test Substance	Volume of Diluent	Mg/ml Test Substance
Theoretical	Actual	M	F			
10	10.2	6	6	0.27	qs to 50 ml	5.02
20	20.4	6	6	0.54	qs to 50 ml	10.04
40	40.8	6	6	1.08	qs to 50 ml	20.08
70	70.2	6	6	1.86	qs to 50 ml	34.6
100	101.2	6	6	2.68	qs to 50 ml	49.8

a - based on 93% purity
 b - corrected doses for 94.4%

Formula: $\frac{\text{mg/ml dose} \times \text{ml of concentration desired}}{\text{mg of concentrate/ml}} = \text{ml of concentrate required}$



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TABLE 2
DOSE SCHEDULE

Body Weights (kg)	Dose Volume ^a 2 ml/kg
2.0	4.0
2.1	4.2
2.2	4.4
2.3	4.6
2.4	4.8
2.5	5.0
2.6	5.2
2.7	5.4
2.8	5.6
2.9	5.8
3.0	6.0
3.1	6.2
3.2	6.4
3.3	6.6
3.4	6.8
3.5	7.0
3.6	7.2
3.7	7.4
3.8	7.6
3.9	7.8
4.0	8.0

a - Dose (ml) = animal body weight (kg) x dose vol./kg

TABLE 3

Skin Reaction

Erythema and Eschar Formation:	<u>Value</u>
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Edema Formation:	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1 millimeter)	3
Severe edema (raised more than 1 millimeter and extending beyond the area of exposure)	4

Draize, J. H., 1959 - The Appraisal of Chemicals in Foods, Drugs, and Cosmetics, Association of Food and Drug Officials of the U.S.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Glenn S. Simon, Ph.D., DABT
Director of Toxicology
Rhône-Poulenc
P.O. Box 12014
2 T.W. Alexander Drive
Research Triangle Park, North Carolina 27709

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAR 20 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

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

12196A



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Triage of 8(e) Submissions

15

Date sent to triage: _____

NON-CAP

CAP

Submission number: 12196A

TSCA Inventory:

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Study type (circle appropriate):

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Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

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entire document	0	1	2	pages <u>1, 2</u>	pages <u>1, 2, 5</u>
Notes:					
Contractor reviewer:				Date:	<u>2/13/95</u>

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA: 12196
Submission # BEHQ: 0992 - ~~1412~~ SEQ. A

TYPE (INT. SUPP FLWP)
SUBMITTER NAME: Rhone-Poulenc Inc.

- VOLUNTARY ACTIONS:
- 0401 ACTION REPORT ID
 - 0402 STUDIES PLANNED/IN PROGRESS
 - 0403 NOTIFICATION OF WORKING ITEMS
 - 0404 LABEL/MSDS CHANGES
 - 0405 PROCESS/ANDING CHANGES
 - 0406 APPAUSE DISCONTINUED
 - 0407 PRODUCTION DISCONTINUED
 - 0408 CONFIDENTIAL

INFORMATION REQUESTED: FLWP DATE:

- 0501 NO INFO REQUESTED
- 0502 INFO REQUESTED (TECH)
- 0503 INFO REQUESTED (VOL ACTIONS)
- 0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:

- 0639 REFER TO CHEMICAL SCREENING
- 0678 CAP NOTICE

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

CASE#
24934-91-6
24934-91-6

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

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
ONCO (HUMAN)	01 02 04	EPICLIN	01 02 04	IMMUNO (ANIMAL)	01 02 04
ONCO (ANIMAL)	01 02 04	HUMAN EXPOS (PROD CONTAM)	01 02 04	IMMUNO (HUMAN)	01 02 04
CELL TRANS (IN VITRO)	01 02 04	HUMAN EXPOS (ACCIDENTAL)	01 02 04	CHEM/PHYS PROP	01 02 04
MUTA (IN VITRO)	01 02 04	HUMAN EXPOS (MONITORING)	01 02 04	CLASTO (IN VITRO)	01 02 04
MUTA (IN VIVO)	01 02 04	ECO/AQUA TOX	01 02 04	CLASTO (ANIMAL)	01 02 04
REPRO/TERATO (HUMAN)	01 02 04	ENV. OCCURREL/FATE	01 02 04	CLASTO (HUMAN)	01 02 04
REPRO/TERATO (ANIMAL)	01 02 04	EMER INCI OF ENV CONTAM	01 02 04	DNA DAM/REPAIR	01 02 04
NEURO (HUMAN)	01 02 04	RESPONSE REQEST DELAY	01 02 04	PROD/USE/PROC	01 02 04
NEURO (ANIMAL)	01 02 04	PROD/COMP/CHEM ID	01 02 04	MSDS	01 02 04
ACUTE TOX. (HUMAN)	01 02 04	REPORTING RATIONALE	01 02 04	OTHER	01 02 04
CHR. TOX. (HUMAN)	01 02 04	CONFIDENTIAL	01 02 04		
ACUTE TOX. (ANIMAL)	01 02 04	ALLERG (HUMAN)	01 02 04		
SUB ACUTE TOX (ANIMAL)	01 02 04	ALLERG (ANIMAL)	01 02 04		
SUB CHRONIC TOX (ANIMAL)	01 02 04	METAB/PHARMACO (ANIMAL)	01 02 04		
CHRONIC TOX (ANIMAL)	01 02 04	METAB/PHARMACO (HUMAN)	01 02 04		

USE:
R+D
pesticide

TOXICOLOGICAL CONCERN:
LOW
MED
HIGH

SPECIES:
R+T

TRIAJE DATA:

NON-CBI INVENTORY:
YES
NO

ONGOING REVIEW:
YES (DROP/REFER)
NO (CONTINUE)

LEFT-R:
IN IN MINI

12196A

H

Acute dermal toxicity in rabbits is of high concern. Single topical doses were administered to the intact and abraded skin of New Zealand albino rabbits (6/sex/dose) at levels of 10, 20, 40, 70, and 100 mg/kg. The LD₅₀ values for males and females were 31 and 62 mg/kg, respectively. Clinical signs of toxicity observed in animals surviving treatment as well as those that died from treatment included depression, dyspnea, trembling, salivation, ataxia, diarrhea, and cyanosis. In addition, one moribund female exhibited convulsions. Gastric mucosal inflammation, enlarged thymus, and hemorrhagic lungs were observed at the higher dose groups.