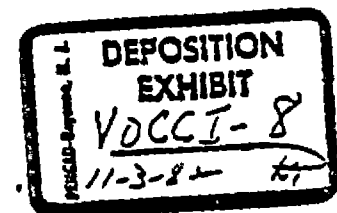


Tentative Agenda
For Meeting of the PSC
The Pentagon, Washington, D. C.

9 May 1963



0900	Opening Remarks	Dr. Gardner
0910	Army Objectives and Plans	Gen Ryder
0920	Navy Objectives and Plans	Navy Speaker
0930	Air Force Objectives and Plans	Air Force Speaker
0940	Defoliation	
	a. Opening Remarks	Gen Delmore
	b. Terminology 10-15'	Dr. Mohanara
	c. Long Term Anticipation	Dr. Minarik
1040-1050	Break	
1050	IS Program and Plans Including Offense and Defense	Dr. Housewright
1130	Overall CS Program and Plans Including Offense and Defense	Dr. Silver
1230	Defensive Program	CDC
1230-1400	Lunch --	
1400	Topics	
	a. IS	Dr. Housewright
	b. .IS	Dr. Silver
1430	CS Implementation Programs Including AT and Others	Dr. Silver and Col Bauer
1500	Extra Territorial Tests	Gen Hollett
1530	Close	

Try Run for Gen Ryder on 6 May 1963, Room 1B-1005.

Briefing to President's Scientific Advisory Committee 9 May 1963
by CBR Agency Personnel on

POSSIBLE HEALTH HAZARD OF PHENOXYACETATES AS RELATED TO DEFOLIATION OPERATIONS
IN VIETNAM

This report summarizes the briefing given 9 May 1963 by members of the CBR Agency to the President's Scientific Advisory Committee.

Formulas - Figure 1 shows the formulas for 2,4-D dichlorophenoxy-acetic acid and 2,4,5-T trichlorophenoxyacetic acid. These substances are used as the acids, salts, esters, and other chemical forms. The mixture, "Purple", consists of fifty per cent n-butyl 2,4-D, thirty per cent n-butyl 2,4,5-T, and twenty per cent isobutyl 2,4,5-T.

Estimated Possible Dose of "Purple" - Table 1 illustrates an attempt to estimate the dose of "Purple" which might have reached men who were exposed to the spray. The maximum quantity of "Purple" delivered in any area was twenty-four pounds per acre. This quantity was delivered in two places on two separate days. Twenty-four pounds per acre is equal to 250 mg per square foot. The size of these droplets would minimize inhalation and favor body surface contamination. Information of other chemical agents shows that the amount of agent falling on a man per unit of area is about seventy-five per cent of that falling on an equal area of the ground. A one-hundred-ten pound man would have about 16.2 square feet of body surface. Only half of this, 8.1 square feet, would be exposed to the spray. Thus, the maximum quantity of spray which could reach the man would be 30 mg/kg. If the man were in an area of maximum contamination on two days of spraying.

The Toxicity of Phenoxyacetates - Table 2 shows LD50 doses for phenoxyacetates in various species of animals by various routes of administration. Most of the published data refer to the parent acids or salts. However, this information

pertinent since the toxicity of the various forms can be interrelated. [NOTE: the values given in the column under "Purple" are different from those given in the meeting of 26 April 1963, because of further work at CRDL. Work done after the meeting of 9 May 1963 is given in a later report.]

In toxic doses all forms of the compounds produce muscle stiffness, ataxia, paralysis, coma, and death. These effects are similar in all animal species. In very high dosage acute ventricular fibrillation may occur.

Note that all forms of 2,4-D and 2,4,5-T have roughly similar toxicities, in all animal species, and by all routes of administration, other than the percutaneous route. "Purple" is much less toxic percutaneously than by the other routes of administration. Clothing gives additional protection and it has not been possible to kill clothed rats with applications of 12.5 mg/kg. Dogs may be more sensitive than other species to the parent compounds.

Table 3 shows lethal doses in mg/kg as calculated from published data by the Bliss method. Where more than one author is shown combined data were used. Three columns predict the doses which might kill - 1/100, 1/1000, or 1/10000 - if all of the compound entered the body by the intraperitoneal or the oral route. The predicted values were obtained by extending the dose-response regression line to the LD 0.1 and LD 0.01 values on log-probit graph paper. Note that all of these values are higher than the 30 mg/kg, which is the greatest dose which could have reached the man in maximal spray contamination. Remember also that toxic doses by the percutaneous route would be three to ten times higher than those shown here for bare skin and perhaps thirty times greater for clothed skin.

Safety Record of Phenoxyacetates - The outstanding safety record established

y these substances during more than fifteen years of extensive operational use is germane to this discussion.

Since 1947 more than three-hundred million pounds have been produced and used to control vegetation on more than four-hundred million acres of land in the United States. Rates of application range from one-sixteenth to one-hundred-sixty pounds per acre. The annual production is estimated to exceed fifty million pounds and fifty million acres are treated annually.

These herbicides are registered by the US Department of Agriculture which means they are considered to be (1) nonpoisonous, (2) noncorrosive, (3) noninflammable, (4) available in quantity, (5) economical, and (6) effective. The Department of Agriculture maintains constant control in areas where herbicides are applied. During fifteen years of extensive use the Department of Agriculture has not received a single complaint of injury to humans, livestock, wildlife, or soil from the phenoxy herbicides. Major manufacturers have certified that none of the workmen in their factories have shown any ill effects. Commercial spray operators report no adverse effects except for a very few allergic skin reactions. These companies report very few claims for damage to livestock and none of these have been proven. Only five suspected human intoxications have appeared in the literature in all of the years that these herbicides have been used.

The use of these herbicides is not restricted to the United States. The Russian scientific publication, "Protection of Plants from Pests and Diseases, pp 55-57, 1961", reports that in the recent years five million hectares of grain crops in the Soviet Union have been treated annually with 2,4-D. Further, systematic treatment for three or four generations has not affected the quality of the grain.

Another publication, "Problems in Economics, Moscow, No 11, pp 86-90, 1961", states that it is planned to use thirty-nine thousand seven-hundred-fifty tons of phenoxyacetates on thirty million hectares in an effort to increase food production.

A third publication, "Problems in Nutrition", by the Medical State Publishing House, Moscow, No 4, 1961, states the toxicity and carcinogenicity of agricultural chemicals was investigated by the Interdepartmental Committee for the Study and Regulation of Toxic Chemicals at the State Sanitary Inspection Office, USSR. The phenoxyacetates were among eighteen approved for application. It was stated that crops treated as prescribed with 2,4-D present no danger when consumed as food.

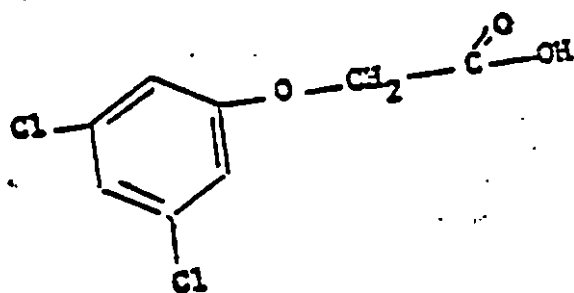
Friday, 26 April 1963, a committee of American experts on herbicides met at Edgewood Arsenal, Maryland, to consider the use of phenoxyacetates in Vietnam. They concluded that no hazard to health was incurred as a result of the quantity or the method of use in that operation.

Cacodylic Acid (Fig 2) - In some of the operations in Vietnam cacodylic acid was used. The maximum dosage applied was four pounds per acre.

Detailed data on cacodylic acid are more sparse than that for the 2,4-D and 2,4,5-T. What is available (Table 4) indicates that the arsenical is only one-third as toxic as the phenoxyacetates. Moreover, the amount of cacodylic acid per acre was only one-sixth that for the phenoxyacetates.

FIGURE 1

2,4-D



2,4,5-T

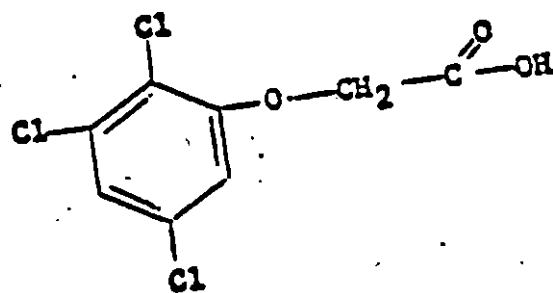


TABLE 1

POSSIBLE DOSE OF "PURPLE" BY DELIVERY METHOD

Ground Dosage

24 lbs (10.9 kg)/acre (43560 sq ft)
250 mg/sq ft

Ground/Man Dosage Ratio

1 mg/sq ft on ground = 0.75 mg/sq ft on man

Available Body Area on Prone Man (naked)

0.75 sq meters (8.1 sq ft)

(250 mg/sq ft) x (0.75) x (8.1 sq ft) = 1519 mg
(ground dosage) x (man/ground ratio) x (available body area) = 1519 mg

$$\frac{1519 \text{ mg/man}}{50 \text{ kg (body weight)}} = 30 \text{ mg/kg}$$

TABLE 2

TOXICITY OF PHENOXYACETATES

Species	Route	LD50 mg/kg					
		2,4-D			2,4,5-T		"Purple" (4)
		Acid	Salt	Mixed Butyl Esters	Acid	Mixed Butyl Esters	
Rat	ip		512(2)-589(2)				436
	ig	375(1)	666(2)-805(1)	620(1)	527(1)	481(1)	448
	it						543
	pc						3809
	pcc						>12500
Rabbit	iv		400(2)				573
	ip						438
	ig		800(2)	424(1)		712(1)	501
	it						1351
	pc						-
Dog	pcc						-
	ip						358
	ig		100(3)		100(3)		-
	it						305
Mouse	pc						>1250
	ip		269(2)-426(2)				
Guinea Pig	ig	368(1)	375(1)	713(1)	399(1)	940(1)	
	ip		576(2)-600(2)				
Chicks	ig	469(1)	551(1)-1000(2)	858(1)	331(1)	750(1)	
	ig	541(1)		2050(1)	310(1)		

(1) Roto & Hyman, Am J Vet Med, Vol XV, No 57: p 622, 1954

(2) Hill & Christle, J Ind Hyg & Tox, 29:85, 1947

(3) Drill & Hratzka, Arch Ind Hyg & Occup Med, 7:61, 1953

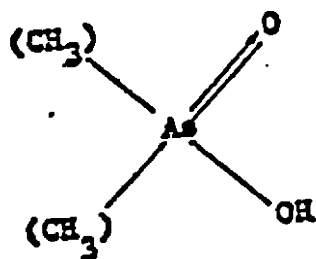
(4) CRDL

TABLE 3

LETHAL DOSES FOR PHENOXYACETATES

Species	Route	No of Animals	LD50	LD1	LD0.1	LD0.01	Reference
			mg/kg	mg/kg	mg/kg	mg/kg	
			<u>2,4-D</u>				
Rat	ip	72	512	228	170	133	Hill, 1947
Guinea Pig	ip	48	590	296	235	195	Hill, 1947
Mouse	ip	200	369	200	165	140	Hill, Fitzhugh
Rat	ig	90	637	240	130	133	Hill, (Na & Na ₂)
Rat	ig	166	630	231	170	130	Hill, Rowe, Fitzhugh, (Na)
Guinea Pig	ig	18	461	390	375	340	Rowe, 1954
Mouse	ig	30	357	237	205	135	Rowe, 1954
			<u>2,4,5-T</u>				
Rat	ig	40	527	285	230	195	Rowe, 1954
Guinea Pig	ig	20	389	252	220	195	Rowe, 1954
Mouse	ig	27	373	156	118	93	Rowe, 1954

FIGURE 2



CACODYLIC ACID

TABLE 4

LETHAL SINGLE DOSES OF CACODYLIC ACID IN RATS

Number of Rats	-	48
Route	-	Intragastric
LD50	-	1350 mg/kg
LD1	-	700 mg/kg
LD0.1	-	565 mg/kg
LD0.01	-	480 mg/kg
Time to Death	-	<24 hours

I wish to discuss information concerning the ^{possible} hazards of phenoxyacetic acids to man and his domestic animals. Most of the literature refers to the parent acids or their salts. Less special interest is in the butyl esters of 2,4 D and 2,4,5 T. However, much of the published information is pertinent since the acids, salts and esters can be inter-related.

- 1 (a) All forms of the compounds produce "muscle stiffness, ataxia, paralysis and coma. In sufficiently high dosage ^{acute} ventricular fibrillation occurs. The peripheral muscular effects are similar in all animal species.

ii. salts. V.N. question used to make interrelates form of compound and toxicity in different species.

1. Acute Oral Toxicities (Rowe & Hyman)

~~a. all species react alike~~

b. for a given form of compound doses are ^{roughly} similar in varying species

① Dog may be more sensitive

② Chickens may be less sensitive

c. acid more toxic than salt;
salt more toxic than ^{butyl} esters.

d. 24D & 245T are similar

Consequently, the butyl esters are the safest form.

13

For purposes of inter-relationships we discussed LD50s. From a standpoint of hazard we are interested in LD1 or "no effect" doses. This slide shows LD50s and LD1 doses which have been calculated from published (and unpublished) reports. The slide also shows the lower 95% confidence limits of the LD1 doses. I hasten to add that such values ^{are published data are not always suitable for statistical analysis} can be very misleading. ^{When statistical analysis is inappropriate} and ^{resistant} animals which survive very large doses can decrease the slope of the regression line and produce very low confidence limits around the LD1. This is illustrated on the slide - the highest LD50 has the lowest LD1 values because of a ^{few} 100 which survived large doses.

However, the point of note is that all of the LD1 values are far above

Note also that the

ACUTE ORAL TOXICITIES 2,4 D

es	Form	No. Animals	LD50	LD1	LD1 Lower 95%	Reference
			mg/kg	mg/kg		
	Purified Na	24	670	311	162	Hill - Table 2, 1947
	Purified Na	18	612	158	44	Hill - Table 3, 1947
	Purified Na	12	697	324	155	Hill - Table 4, 1947
	Crude Na	18	677	167	45	Hill - Table 3, 1947
*	Combined all Salts	90	637	240	164	Hill - Total data, com- bined Na + NH ₄
	Na	44	665	379	271	Rowe - 1954
	Acid	60	375	187	129	Rowe - 1954
	Na	20	489	193	90	Fitzhugh
*	Na	166	630	231	174	Hill-Rowe-Fitzhugh
e	Acid	29	357	237	164	Rowe - 1954
nea Pigs	Acid	18	481	390	273	Rowe - 1954
icks	Acid	30	401	135	53	Rowe - 1954
gs	Acid	12	100	59	11570	Drill- 1953

Slide 2 - The comments on the I.P. doses apply also to the oral dosage. The LD₅₀ values are well over the 40 mg/kg dose, except for the dog. The later data ~~was~~ consisted of 4 dose levels, the two upper responses were 100%, the lowest was zero percent. Such data is not adaptable to computation as shown by the ridiculous 95% confidence limits.

The data marked by * can be considered statistically reliable. In these cases - note that despite the fact that different workers ~~used~~ measured the values are remarkably alike.

5-5
Shows that 2,4,5T is very similar to 2,4D on a statistical basis and again the LD1 values are above the 40 mg/kg value.

ORAL TOXICITIES OF 2,4,5 T

Species	Form	No of Animals	LD50	LD1	LD1 Lower 95%	Reference
			mg/kg	mg/kg		
Rats	Acid	40	527	285	280	Rowe
Guinea Pigs	Acid	20	389	252	171	Rowe
Mice	Acid	27	373	156	69	Rowe
Chicks	Acid	33	312	144	83	Rowe

Slide 6

Toxicity studies on the mixed sample used in V.N. have been initiated within the past week. Consequently, a few more deaths may occur.

The species, doses, routes of administration and number of deaths to date are shown

An analysis of this data will be shown on the next slide. However, it is pointed out ~~that certain areas shown are~~ that ppt data in rabbits and that the data on dogs is not applicable to statistical analysis because of lack of deaths.

ACUTE TOXICITY OF PURPLE

	Gm/kg	Deaths									
		Rats				Rabbits			Dogs		
		Oral	ip	it	oc	ip	it	oc	ip	it	oc
10/100	12.5		4/4								
8	7.5				5/6						
6.25	6.25				5/8						
4.0	5.0				3/6						
	3.75				0/6						
2.5	3.13		6/6			3/6		2/8			4/4
2.0	2.50		6/6		0/6	8/10		0/6			4/4
1.5	1.88		7/7			2/6		0/6			2/2
	1.25		10/10		0/6	3/8		1/6			0/2
	0.94		8/10								
	0.75	4/10									0/4
.5	0.63	5/10	6/10			0/6	1/5	0/6			1/6
.40	0.50	5/10		2/6					3/4	2/4	
.375	0.47		6/10				0/6				
.30	0.38	0/10		2/6							
.25	0.31		1/10			0/6	0/6	0/6			
.20	0.25	1/10		0/6					0/4	1/4	0/4
.125	0.16		2/10				0/6				
.10	0.125	0/10	0/10	0/6		0/2			0/4	0/4	
.0625	0.08						0/6				
.0125			0/2			0/2					

ACUTE TOXICITY OF PURPLE

Route & Doses mg/kg	Rats	Rabbits	Dogs
<u>Oral</u>			
LD50	566		
LD1	213		
LD1 (95)	124		
<u>ip</u>			
LD50	586	1994	≈250
LD1	121	363	> 850
LD1 (95)	64	178	
<u>ic</u>			
LD50	569		≈ 500
LD1	244		> 250
LD1 (95)	107		
<u>pc</u>			
LD50	5562	12034	
LD1	3178	493	>1250
LD1 (95)	2034	40	

Slide 7

40 mg/kg.

You can see from this slide that the maximum possible contamination — if it enters lung, peritoneum, etc would not likely kill.

This dose is not reached at LD1 by any route

Not likely that pc LD1 is less than i.p. LD1 (95). Low 95% is due to the very few deaths (3-3 rabbits).

Lowest pc death in rabbit was at 1250 mg/kg.

Purple

Toxicity in rats (oral, i.p., i.t.) like that for salts.

Toxicity in rabbits much less than that for salts.

$$\text{i.p.} \quad \frac{\text{Est. LD}_{50}}{\text{salt LD}_{50}} = \frac{7574}{400-800}$$

Dog - no unusual sensitivity to esters

P.C. Toxicity at least 6-10% higher; failure high for dogs (adult-rat)

Particularly not rabbit p.c. only 3 scattered deaths at high doses — but this influences lower 95% confidence limit

Note rat i.p. (one death at 250 mg influences lower 95%)

145 animals by all routes to death 80-125 mg/kg.

	Reto	Pollo	Disco
LD50	536 (429 - 664)	1470 (843 - 2562)	350
LD1	137 (77 - 243)	57 (5 - 598)	123

LD50	421 (352 - 502)	< 625
LD1	155 (91 - 234)	

LD50	549 (338 - 891)	2555 (22 - 569,990)	358 (232 - 552)
LD1	191 (72 - 508)	16 (03 - 6940)	123 (42 - 365)

LD50	> 12,500	مس
LD1	> 12,500	مس

LD50	5138 (423 - 6172)	1935 (1004 - 3728)	> 1250	مس
LD1	2203 (1233 - 3940)	41 (3 - 1367)	> 1250	مس

	Rock	Form	No Exposures	LDSD	LDI	units 95%	Reference
<u>2,4D</u>							
Rat	1P	Salts	72	512	228	156	Lind 19
GP	1P	Salts	48	590	296	172	Hill
Mice	1P	Salts	200	369	200	190	Hill & Fitzhugh
Rat	1G	NAUPL Salts	90	637	240	164	Hill
Rat	1G	NA Salts	166	630	231	174	Hill-Know-Fitz
GP	1G	Acid	18	481	390	273	Zone
Mice	1G	Acid	30	357	237	164	Zone
<u>4,5T</u>							
Rat	1G	Acid	40	527	285	280	Zone
GP	1G	Acid	20	389	252	171	Zone
Mice	1G	Acid	27	373	156	69	Zone
Rat	1P	Pyrite	94	536	137	77	
Reddish	1P	"	46	1470	57	5	
Dark	1P	"	12	350	123		
Rat	1G	"	60	421	155	91	
"	1G	"	30	625			
"	1G	"	—				
Rat	1P	"	24	549	191	72	
"	1P	"	27	500	—	—	

LETHAL DOSES OF 2, 4 D IN ANIMALS
(Given in saline)

Species	Route	LD50 mg/kg	LD1 mg/kg	LD1 Lower 95 Ratios			Reference
				LD50/LD1	LD50/LD1(95%)		
Rat	Sodium Salt Sodium Purified ip	589	257	127	2.3	4.6	Hill & Carlisle - Table 3 JIN&T 29, p 88, 1947
Guinea Pig	Sodium Purified ip	576	413	309	1.4	1.86	Hill & Carlisle - Table 3 JIN&T 29, p 88, 1947
Guinea Pig	Sodium Crude ip	600	160	15	3.7	40	Hill & Carlisle - Table 3 JIN&T 29, p 88, 1947 Low LD1 because resistant animal flattened slope.
Rat	Sodium Purified oral	612	158	44	3.9	14	Hill & Carlisle - Table 3 JIN&T 29, p 88, 1947
	Sodium Crude oral	677	167	45	4.0	15	
Rat	Sodium Salt oral	697	324	155	2.2	4.5	Hill & Carlisle - Table 4 JIN&T 29, p 89, 1947
Mouse	Pure Ammonium Salt ip	42 396	263	191	1.5	2.1	Hill & Carlisle - Table 5 JIN&T 29, p 89, 1947
	Crude NH Salt ip	42 426	178	99	2.4	4.3	Hill & Carlisle - Table 5 JIN&T 29, p 89, 1947
Rat	oral	670	311	162	2.2	4.2	Hill & Carlisle - Table 2 JIN&T 29, p 88, 1947

ACUTE INTRAPERITONEAL TOXICITIES 2,4 D

Species	Form	No. Animals	LD50 mg/kg	LD 50 LD1 mg/kg	LD1 Lower 95%	Reference
Rat	Purified Na	24	589	257	127	Hill - Table 3
*	Na + NH ₄	72	512	228	156	Hill - Combined data
Guinea Pig	Crude Na	24	600	160	15	Hill - Table 3
	Purified Na	24	576	413	309	Hill - Table 3
*	Na + NH ₄	36	590	296	172	Hill - Combined data
Mice	Pure NH ₄	40	396	263	191	Hill - Table 5
	Crude NH ₄	40	426	178	99	Hill - Table 5
*	Na + NH ₄	200	369	200	190	Hill & Fitzhugh

ACUTE ORAL TOXICITIES 2,4 D

Species	Form	No. Animals	LD50	LD1	LD1 Lower 95%	Reference
			mg/kg	mg/kg		
Rats	Purified Na	24	670	311	162	Hill - Table 2, 1947
	Purified Na	18	612	158	44	Hill - Table 3, 1947
	Purified Na	12	697	324	155	Hill - Table 4, 1947
	Crude Na	18	677	167	45	Hill - Table 3, 1947
	* Combined all Salts	90	637	240	164	Hill - Total data, combined Na + NH ₄
Rats	Na	44	665	379	271	Rowe - 1954
	Acid	60	375	187	129	Rowe - 1954
	Na	20	489	193	90	Fitzhugh
*	Na	166	630	231	174	Hill-Rowe-Fitzhugh
Mice	Acid	29	357	237	164	Rowe - 1954
Guinea Pigs	Acid	18	481	390	273	Rowe - 1954
Chicks	Acid	30	401	135	53	Rowe - 1954
Dogs	Acid	12	100	59	11570	Drill - 1953

ACUTE ORAL TOXICITIES

V.K. Rowe & T.A. Hyman
Am J Vet Med, Vol XV, No 57; p 622, 1954

Species	LD50 - mg/kg					
	2,4 D			2,4,5 T		50:50
	Acid	Na Salt	Mixed Butyl Esters	Acid	Mixed Butyl Esters	Brush Killer
						27% - 2,4 D 27% - 2,4,5 T
Rats	375	805 666 (2)	620	500	481	1070
Mice	368	375 (2)	713	389	940	800
Guinea Pigs	469	551 1000 (2)	848	381	750	1160
Rabbits		800 (2)	424		712	1420
Dogs	100 (4)			100 (4)		
Chicks	541		2000	310		4000

(2) Hill & Carlisle - J Ind Hyg & Tox; 29:85, 1947

(3) Bjorn & Northen - Science; 108:479, 1948

(4) Drill & Hiratzka - Arch Ind Hyg & Occup Med, 7:61, 1953

ORAL TOXICITIES OF 2,4,5 T

Species	Form.	No of Animals	LD50	LD1	LD1 Lower 95%	Reference
			mg/kg	mg/kg		
Rats	Acid	40	527	235	280	Rowe
Guinea Pigs	Acid	20	389	252	171	Rowe
Mice	Acid	27	373	156	69	Rowe
Chicks	Acid	33	312	144	83	Rowe

TOXICITY OF 2,4 D IN FISH

Reference	Dosage	Effects
Gerking, 1948	100 ppm	No damage to invertebrates
Hanson, 1952	1 lb/acre	No damage to wild life in marshes
Harrison & Rees, 1946	2000 ppm	LD50 for catfish, minnows
King & Penfound, 1946	100 ppm	Some deaths in breams and bass
	65 ppm	Some deaths in carp
	675-850 ppm	24-hour, LD50 for minnows
	830 ppm	No deaths in bluegills or minnows in 29 days
100 lbs/acre in 3-ft pond		

EFFECTS OF REPEATED DOSES OF PHENOXYACETATES

Compound	Animal	Route	Dosage	Effects	Reference
2,4 D	Rats	Oral	10 mg/kg, 3 times/week, 4 weeks	No effects	Rowe & Hymas Am J Vet Med, 19
			30 mg/kg, 3 times/week, 4 weeks	No effects	
			100 mg/kg, 3 times/week, 4 weeks	Decreased growth cloudy swelling of liver	
			300 mg/kg, 3 times/week, 4 weeks	Deaths	
2,4 D	Rats	Diet	100	100 ppm - 113 days	Ibid
			300	300 ppm - 113 days	
			1000	1000 ppm - 113 days	
			3000	3000 ppm - 12 days	
ron Brush Killer	Steers	Oral	100 mg/kg - 15 days	Some pathology of liver, kidney, & GI tract	Ibid
			500 mg/kg - 3 days	No effect	
			500 mg/kg - 2 days	Decreased appetite	
			1000 mg/kg - 3 days	Death	
2,4 D	Rabbits	Injected	50 mg/kg - 4-13 doses	Nothing remarkable some kidney degeneration hyperphasia of bone marrow, decreased hgb	Hill & Carlisle J-I Hyg & Tox, 19
			100 mg/kg - 3- 7 doses	Decreased hgb, degeneration of kidney, hyperphasia of spleen, lymphoid, & bone marrow	
2,4 D	Dogs	iv	25 mg/kg/day - 6 days	Bleeding gums, leg ulcers	Ibid
			50 mg/kg/day - 2,3 days	2/2 deaths	
2,4 D	Dogs	iv	10 mg/kg, 5 times/week-90 days	No effect	Drill & Hirsatzka Arch Y Hyg Occ Med,
2,3,5 T			20 mg/kg 5 times/week-90 days	Deaths	

CONCLUSIONS:

In summary and after careful review of toxicological data related to 2,4-D and 2,4,5-T plus the knowledge as to the manner these materials have been used for defoliation in military situations in Southeast Asia, no health hazard is or was involved to man or domestic animals from the amounts or manner these materials were used in the aforementioned exercise.

ACUTE TOXICITY OF PURPLE

Route & Doses mg/kg	Rats	Rabbits	Dogs
<u>Oral</u>			
LD50	566		
LD1	213		
LD1 (95)	124		
<u>ip</u>			
LD50	586	1994	@ 500
LD1	12/ 24	363	500 > 250
LD1 (95)	64	178	
<u>it</u>			
LD50	569		@ 500
LD1	244		250
LD1 (95)	107		
<u>pc</u>			
LD50	5562	12034	
LD1	31784	493	> 1250
LD1 (95)	2034	40	

EFFECTS OF REPEATED DOSES OF PHENOXYACETATES

Compound	Animal	Route	Dosage	Effects	Reference
2,4 D Na	Mice	sc	1/3 LD50 (90 mg/kg/day) for 3 months	No effects	Bucher, Proc Soc Exp Biol & Med, 19/
2,4 D salts	Rats	Feed	About 6 mg/kg/day-24 days	No effects	Hill & Carlisle, 19/
2,4 D Na	Rats	Feed	95 mg/kg/day-100 weeks	No effects	Fitzhugh
2,4 D Na	Dogs	Feed	12.5 mg/kg/day-100 weeks	No effects	Fitzhugh
2,4 D alkylamine	Chicks	Oral	200 mg/kg, 3 times/week, 4 weeks (acute oral LD50 = 390-765 mg/kg)	No effects	Bjorn & Northen Science, 1948
2,4 D	Sheep Cows	Pasture	About 2.77 lbs/acre for 12 days	No effects	Hitchell, et al. J Animal Sci, 1946
2,4 D salt isopropylester	Horses Cattle	Pasture	4 lbs/acre)	No effects	Grigoby & Farwell Mich Agr Exp Sta Qt Bull, 1950
2,4 D isopropylester	Sheep Swine Chicks		3.3 lbs/acre) - for 12 days 3.3 lbs/acre)		
			3.3 lbs/acre)		
2,3,5 T					
2,4,5 T	8 Steers	Oral	16, 17, 52, 55, 114, & 161 mg/kg/day-78 days	No effects	Anderson, Arndt, Godbey, Jones JAVMA, 1949
	2 Steers	Oral	50, 58 mg/kg/day-154 days	No effects	

ACUTE TOXICITY OF PURPLE

Gm mg /kg	Deaths									
	Oral	Rats			Rabbits			Dogs		
		ip	ie	pc	ip	ie	pc	ip	ie	pc
12.5		4/4								
7.5				5/6						
6.25				6/8						
5.0				2/6						
3.75				0/8						
3.13		6/6			3/6		2/8			
2.50		6/6		0/6	8/10		0/6			
1.88		7/7			2/6		0/6			
1.25		10/10		0/6	3/8		1/6			0/4
0.94		7/10								
0.75	8/10									0/4
0.63	6/10	6/10			0/6	1/5	0/6			
0.50	4/10		2/6					2/4	2/4	
0.47		0/10				0/6				
0.38	0/10		1/6							
0.31		1/10			0/6	0/6	0/6			
0.25	1/10		0/6					0/4	0/4	0/4
0.16		2/10				0/6				
0.125		0/10	0/6					0/4	0/4	
0.09						0/6				

Toxicology

1- Hazard - 1.5 gm/man - 40mg/kg.

2- a) LD 50 Literature

b LD 1 Literature

No p.c. data of value.

seems
including
fish,
chickens.

3- In house data

Various routes including p.c.

PC - LD 1

S.P.
of 6000-8000
dog population.

No danger except initial. It
seems negated by prior experience
with human exposure in crop
operations - Viet Namese operation
Sensitive animal - dog.

4 - Chronic
Literature -

9 May - White House

6 May - 3 E 1065

$$454 \times 24 \text{ lbs/acre} = 10,896 \text{ gms/acre} = 10,896,000 \text{ mg/acre}$$

$$43,560 \text{ sq ft/acre}$$

$$\frac{10,896,000}{43,560} = 250 \text{ mg/sq ft}$$

$$\text{Poly area} - 1 \text{ m}^2 = 10.9 \text{ sq ft (Orlando)}$$

$$\text{Grass} 75\% \times 10.9 = 8.0 \text{ sq ft (Orlando)}$$

$$\text{Assume sq ft on ground} / 0.75 \text{ sq ft when } 1/4$$

$$250 \text{ mg/sq ft} \times 8 \text{ sq ft} = 2000 \text{ mg}$$

$$2000 \times 0.75 = 1500 \text{ mg/mean}$$

$$1500 \text{ mg}/40 \text{ kg mean} = 37.5 \text{ mg/kg}$$

↓
negligible information

Toxicity as related to question

Slide 1 - Formulae, Acids, salts, esters, butyls, purp

Slide 2 - illustrates - unit needed more or less approx to

- ① Max. quantity - 24 lb/acre - 2 prodos. - 2 days.
- ② 24 lb/acre = 250 mg/sq. ft.
- ③ 300 μ MHD - minimum inhibition - from today's
- ④ Ground / Man. 75%
- ⑤ 8.1 sq. ft.
- ⑥ $8.1 \times .75 \times 250 = 1500/50 = 30 \text{ mg/kg}$
- ⑦ (Max. qt. for max. contamination - 2 days / sp

Slide 3 - ① LD 50's. - various species - various routes

- ② Most data on acids - salts -
- ③ Potent - toxicities can be inter-related.
- ④ In toxic dose - all forms of both cause same effects - in all
- ⑤ all forms of both have roughly same tox. in all species - by
- ⑥ Except p.c. - p.c. - LD50's are 3-10 or more greater than
- ⑦ Clothing - added protection - > 30 fold.
- ⑧ Data on purple not adequate for LD1 - or other minimal
- ⑨ Adequate data on others
- ⑩ Based on slide 3 - what applies to acids - salts - esters

Slide 4

- ① Minimal lethal doses - calc. from published data - by Bliss
 - ② where more than one author is shown - combined data
 - * ③ 3 columns predict $1,000$, $1,0000$, $1/10,000$ — if all of the compound entered the body by i.p. or i.g. route
 - + ④ all values higher than 30 mg/kg - which is greatest dose which could reach man in 2 maximal sphi contaminations - or 2 separate doses
 - * ⑤ Remember doses by p.c. would be 3-10 times less than those shown for bare skin — and > 30 times higher for clothed skin.
-

- ① Safety record during 15 years is impressive
- ② Since 1947 - > 300 million lbs = > 400 million acres in U.S.
- ~~③ Commercial production~~
- ④ Yields to 160 lbs/acre.
- ⑤ Annual production > 50 million pounds - used to treat 50 million
- ⑥ Also wide spread use in other countries including USSR where it has state approval for use on food crops.
- ⑦ In U.S., Agriculture maintains control in areas where herbicide use is
- ⑧ 15 yrs Not one complaint for damage to man, livestock, wildlife
- ⑨ Refs. certify no harmful effect on employees
- ⑩ Spray operators state only rare case of allergic skin reactions
- ⑪ Refs. & spray operators have had few claims for damage to crops or property - none substantiated
- ⑫ Only 5 suspect findings in 7 yrs of medical literature.

Slide 4

- ① Animal lethal doses - calc. from published data - " by Bliss
 - ② When more than one author is shown - combined data
 - * ③ 3 columns predict Y_{100} , Y_{1000} , $1/10,000$ — of oil of the compound entered the body by i.p. or i.g. route
 - + ④ All values higher than 30 mg/kg - " which is greatest dose which could reach man in 2 maximal i.p. administrations - or 2 separate doses
 - * ⑤ Residue doses by p.c. would be 3-10 times higher than those shown for bare skin — and $> 30 \text{ t}$ higher for clothed skin.
-

- ① Safety record during 15 years in Germany
- ② Since 1947 - > 300 million lbs ≈ 7400 million acres in U.S.
- ~~③ Annual production~~
- ④ Y_{100} is 160 lbs acre.
- ⑤ Annual production > 50 million pounds - used to treat 50 million.
- ⑥ Also with approved use in other countries including USSR where it has state approval for use on food crops.
- ⑦ In the U.S. Dept. Agriculture maintains control in areas where pesticides are used.
- ⑧ 15 years not one complaint for damage to man, livestock, wildlife.
- ⑨ Refs. certify no harmful effect on employees.
- ⑩ Spray operators state only rare case of allergic skin reaction.
- ⑪ Refs. & spray operators have had few claims for damage to skin or property - none substantiated.
- ⑫ Only 5 suspect persons in ~~any~~ medical literature.

ORAL TOXICITIES OF 2,4,5 T

Species	Form.	No of Animals	LD50	LD1	LD1 Lower 95%	Reference
			mg/kg	mg/kg		
Rats	Acid	40	527	235	280	Rowe
Guinea Pigs	Acid	20	389	252	171	Rowe
Mice	Acid	27	373	156	69	Rowe
Chicks	Acid	33	312	144	83	Rowe

TOXICITY OF 2,4 D IN FISH

Reference	Dosage	Effects
Gerking, 1943	100 ppm	No damage to invertebrates
Hanson, 1952	1 lb/acre	No damage to wild life in marshes
Harrison & Reas, 1946	2000 ppm	LD50 for catfish, minnows
King & Penfound, 1946	100 ppm	Some deaths in breams and bass
	65 ppm	Some deaths in carp
	675-850 ppm	24-hour, LD50 for minnows
	830 ppm	No deaths in bluegills or minnows in 29 days
	100 lbs/acre in 3-ft pond	

EFFECTS OF REPEATED DOSES OF PHENOXYACETATES

Compound	Animal	Route	Dosage	Effects	Reference
2,4 D	Rats	Oral	10 mg/kg, 3 times/week, 4 weeks	No effects	Rowe & Hymas Am J Vet Med, 1954
			30 mg/kg, 3 times/week, 4 weeks	No effects	
			100 mg/kg, 3 times/week, 4 weeks	Decreased growth cloudy swelling of liver	
			300 mg/kg, 3 times/week, 4 weeks	Deaths	
2,4 D	Rats	Diet	100 100 ppm - 113 days	No effects	Ibid
			300 ppm - 113 days	No effects	
			1000 ppm - 113 days	Toxic effects & deaths	
			3000 ppm - 12 days	Toxic effects - sacrificed	
Iron Brush Killer	Steers	Oral	100 mg/kg - 15 days	Some pathology of liver, kidney, & GI tract	Ibid
			500 mg/kg - 3 days	No effect	
			500 mg/kg - 2 days	Decreased appetite	
			1000 mg/kg - 3 days	Death	
2,4 D	Rabbits	Injected	50 mg/kg - 4-13 doses	Nothing remarkable some kidney degeneration hyperphasia of bone marrow, decreased hgb	Hill & Carlisle J-I Hyg & Tox, 194
			100 mg/kg - 3- 7 doses	Decreased hgb, degeneration of kidney, hyperphasia of spleen, lymphoid, & bone marrow	
2,4 D	Dogs	iv	25 mg/kg/day - 6 days	Bleeding gums, leg ulcers	Ibid
			50 mg/kg/day - 2,3 days	2/2 deaths	
2,4 D 2,3,5 T	Dogs	iv	10 mg/kg, 5 times/week-90 days	No effect	Drill & Hiratska Arch I Hyg Occ Med,
			20 mg/kg 5 times/week-90 days	Deaths	

EFFECTS OF REPEATED DOSES OF PHENOXYACETATES

Compound	Animal	Route	Dosage	Effects	Reference
2,4 D Na	Mice	sc	1/3 LD50 (90 mg/kg/day) for 3 months	No effects	Bucher, Proc Soc Exp Biol & Med, 1946
2,4 D salts	Rats	Feed	About 6 mg/kg/day-24 days	No effects	Hill & Carlisle, 1946
2,4 D Na	Rats	Feed	95 mg/kg/day-100 weeks	No effects	Fitzhugh
2,4 D Na	Dogs	Feed	12.5 mg/kg/day-100 weeks	No effects	Fitzhugh
2,4 D alkylamine	Chicks	Oral	200 mg/kg, 3 times/week, 4 weeks (acute oral LD50 = 380-765 mg/kg)	No effects	Bjorn & Northen Science, 1948
2,4 D	Sheep Cows	Pasture	About 2.77 lbs/acre for 12 days	No effects	Mitchell, et al. J Animal Sci, 1946
2,4 D salt isopropylester	Horses Cattle	Pasture	4 lbs/acre)	No effects	Grigby & Farwell Mich Agr Exp Sta Qt Bull, 1950
2,4 D isopropylester	Sheep Swine		3.3 lbs/acre) - for 12 days		
	Chicks		3.3 lbs/acre)		
2,3,5 T					
2,4,5 T	8 Steers	Oral	16, 17, 52, 55, 114, & 161 mg/kg/day-78 days	No effects	Anderson, Arndt, Godbey, Jones JAVMA, 1949
	2 Steers	Oral	50, 58 mg/kg/day-154 days	No effects	

CONCLUSIONS:

In summary and after careful review of toxicological data related to 2,4-D and 2,4,5-T plus the knowledge as to the manner these materials have been used for defoliation in military situations in Southeast Asia, no health hazard is or was involved to man or domestic animals from the amounts or manner these materials were used in the aforementioned exercise.

ACUTE TOXICITY OF PURPLE

Route & Doses mg/kg	Rats	Rabbits	Dogs
<u>Oral</u>			
LD50	566		
LD1	213		
LD1 (95)	124		
<u>ip</u>			
LD50	586	1994	500
LD1	121	363	250
LD1 (95)	64	178	
<u>ic</u>			
LD50	569		@ 500
LD1	244		250
LD1 (95)	107		
<u>pc</u>			
LD50	5562	12034	
LD1	3178	493	> 1250
LD1 (95)	2034	40	

ACUTE TOXICITY OF PUPPLE

	Deaths									
	Rats			Rabbits			Dogs			
	Oral	ip	ie	sc	ip	ie	sc	ip	ie	sc
GA mg/kg										
12.5		4/4								
7.5				5/6						
6.25				6/8						
5.0				2/6						
3.75				0/8						
3.13		6/6			3/6		2/8			
2.50		6/6		0/6	8/10		0/6			
1.88		7/7			2/6		0/6			
1.25		10/10		0/6	3/8		1/6			0/4
0.94		7/10								
0.75	8/10									0/4
0.63	6/10	6/10			0/6	1/5	0/6			
0.50	4/10		2/6					2/4	2/4	
0.47		0/10				0/6				
0.38	0/10		1/6							
0.31		1/10			0/6	0/6	0/6			
0.25	1/10		0/6					0/4	0/4	0/4
0.16		2/10				0/6				
0.125		0/10	0/6					0/4	0/4	
0.09						0/6				

Toxicology

1- Hazard - 1.5 gm / man - 40 mg / kg.

2- a) LD 50 Literature

b LD 1 Literature

No p.c. data of value.

Specimens
including
fish,
chickens, etc.

3- In house data

Various routes including p.c.

PC - LD 1

No danger except intense ...
seems negated by ...
and human exposures in crop
operations - Viet Namese operation
Intensive animal - dog.

Q.P.
of 1000-2000
day 1

4 - Chronic
Literature -

5 -

9 May - White House

6 May - 3 E 1065

$$454 \times 24 \text{ lbs/acre} = 10,896 \text{ gms/acre} = 10,896,000 \text{ mg/acre}$$

$$43,760 \text{ sq ft/acre}$$

$$\frac{10,896,000}{43,760} = 250 \text{ mg/sq ft.}$$

$$\text{Avg area} - 1 \text{ m}^2 = 10.9 \text{ sq ft (Oriental)}$$

$$\text{Oriental } 75' \times 10.9 = 8.0 \text{ sq ft. (Oriental)}$$

$$\text{Assume } \text{sq. ft on ground} / 0.75 \text{ sq ft. = area } 1/92$$

$$\begin{aligned} 250 \text{ mg/sq ft.} \times 8 \text{ sq ft.} &= 2000 \text{ mg.} \\ 2000 \times 0.75 &= 1500 \text{ mg/area} \end{aligned}$$

$$1500 \text{ mg} / 40 \text{ Kg man} = 37.5 \text{ mg/Kg}$$

↓
negligible information

Slide 1

- Formulae, Acids, salts, esters, butyls, purple

Slide 2

① illustrates - unit used more or less approx to

- ② Max. quantity - 24 lb/acre - 2 passes. - 2 days.
- ③ 24 lb/acre = 250 mg/sq. ft.
- ④ 300 μ MMD - minimum inhibition - for being rep.
- ⑤ Ground / Man. 75%
- ⑥ 0.1 sq. ft.
- ⑦ $5 \times 0.1 \times .75 \times 250 = 1500/50 = 30 \text{ mg/kg}$
- ⑧ (Max. qt. for max. contamination - 2 days / sp)

Slide 3

- ① LD 50's. - various species - various routes

- ② Most data on acids - salts -
- ③ Potent - toxicities can be inter-related.
- ④ In toxic dose - all forms of both cause same effects - in all sp.
- ⑤ all forms of both have roughly same tox. in all species - by a ^{about}
- ⑥ Except p.c. - p.c. - LD50's are 3-10 or more greater than
- ⑦ Clothing - added protection - > 30 fold.
- ⑧ Data on purple not adequate for LD1 - or other amounts.
- ⑨ Purple data - others
- ⑩ Based on slide 3 - what applies to acids - salts - esters

Slide 4

- ① Animal lethal doses - calc. from published data - by Bliss
 - ② where more than one author is shown - combined data
 - * ③ 3 columns predict $1/100$, $1/1000$, $1/10,000$ — if all of the compound entered the body by i.p. or i.g. route
 - * ④ all values higher than 30 mg/kg - which is greatest dose which could reach man in 2 maximal sp. contaminations - or 2 separate doses
 - * ⑤ Remember doses by p.c. would be 3-10 times higher than those shown for bare skin - and $>30 \times$ higher for clothed skin.
-

- ① Safety record during 15 years is germane
- ② Since 1947 - >300 million lbs = >400 million acres in U.S.
- ~~③ Annual production~~
- ③ $1/10$ lb to 100 lbs acre.
- ④ Annual production >50 million pounds - used to treat 50 million
- ⑤ Also wide spread use in other countries including USSR where it has state approval for use on food crops.
- ⑥ In the U.S. Dept. Agriculture maintains control in areas where bituminous are used
- ⑦ No Not one complaint for damage to man, livestock, wildlife
- ⑧ Mfgs. certify no harmful effect on employees
- ⑨ Spray operators state only rare case of allergic skin res.
- ⑩ Mfgs. & spray operators have had few claims for damage to the property - none substantiated
- ⑪ Only 5 suspect references in ~~toxicology~~ medical literature

side 4

- ① Animal Lettles Ears - calc. from published data - by Bliss
 - ② when more than one author is shown - combined data
 - ③ 3 columns predict $1,000$, $1,000,000$, $1/10,000$ — of oil of the compound entered the body by i.p. or i.g. route
 - ④ all values higher than 30 mg/kg - which is greatest dose which could reach man in 2 maximal spray concentrations - or 2 separate doses
 - ⑤ Residue dose by p.c. would be 3-10 times higher than those shown for live skin — and >30 times higher for clothed skin.
-

- ① Safety record during 15 years is germane
 - ② since 1947 - >300 million lbs = >2000 million acres in U.S.
 - ~~③ Annual production~~
 - ④ $1/10$ to $1/100$ acre.
 - ⑤ Annual production >50 million pounds - used to treat 50 million
 - ⑥ Also wide spread use in other countries including USSR where it has state approval for use on food crops.
 - ⑦ In the U.S. Dept. Agriculture maintains control in areas where tobacco is used
 - ⑧ 15 yrs Not one complaint for damage to man, livestock, wildlife
 - ⑨ 24 yrs. certify no harmful effect on employees
 - ⑩ Spray operators state only rare case of allergic skin rashes
 - ⑪ 24 yrs. 2 spray operators have had few claims for damage to lungs
 - ⑫ 24 yrs. 100% - none obstructed
 - ⑬ Only 5 suspect fatalities in 24 yrs. medical literature.
-

POSSIBLE HEALTH HAZARD OF PHENOXYACETATES AS RELATED TO DEFOLIATION OPERATIONS IN VIET NAM

1. Formulas.

Figure 1 shows the formulas for 2,4-D, dichlorophenoxy-acetic acid and 2,4,5-T, trichlorophenoxyacetic acid. These substances are used as the acids, salts, esters, and other chemical forms. The mixture, "Purple," consists of 50% n-butyl 2,4-D; 30% n-butyl 2,4,5-T; and 20% isobutyl 2,4,5-T.

2. Estimated Possible Dose of "Purple."

Table 1 illustrates an attempt to estimate the dose of "Purple" which might have reached men who were exposed to the spray. The maximum quantity of "Purple" delivered in any area was 24 lbs per acre. Twenty-four pounds per acre is equal to 250 mg/sq ft. The size of these droplets would minimize inhalation and favor body surface contamination. Information of other chemical agents shows that the amount of agent falling on a man per unit of area is about 75% of that falling on an equal area of the ground. A 170-lb man would have about 16.2 sq ft of body surface. Only half of this, 8.1 sq ft would be exposed to the spray. Thus, the maximum quantity of spray which could reach the man would be 30 mg/kg.

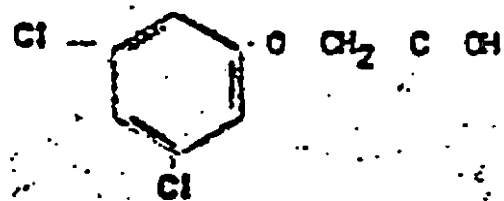
3. The Toxicity of Single Doses of Phenoxyacetates.

Table 2 shows LD50 doses of phenoxyacetates in various species of animals by various routes of administration. Most of the published data refer to the parent acids or salts. However, this information is pertinent since the toxicity of the various forms can be interrelated. In toxic doses, all forms of the compounds produce muscle stiffness, ataxia, paralysis, coma, and death. These effects are similar in all animal species. In very high dosages, acute ventricular fibrillation may occur.

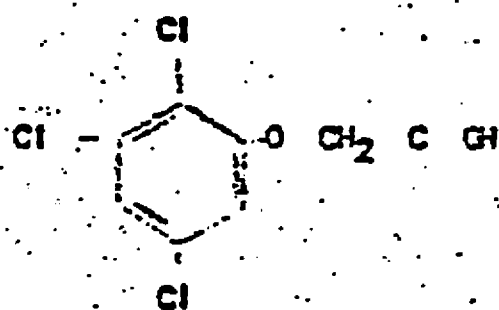
Note that all forms of 2,4-D and 2,4,5-T have roughly similar toxicities, in all animal species and by all routes of administration, other than the percutaneous route. "Purple" is much less toxic percutaneously than by the other routes of administration. Clothing gives additional protection and it has not been possible to kill clothed rats with applications of 12.5 gm/kg. Dogs may be more sensitive than other species to the parent compounds. However, even for dogs the intraperitoneal and the intratracheal LD50s are 358 and 305 mg/kg, respectively. The LD50 by the bare percutaneous route is greater than 1,25 gm/kg in this species.

4. The Toxicity of Repeated Intraperitoneal Doses of "Purple" in Dogs.

Table 3 shows that 5 daily doses of 30 mg/kg of "Purple" did not produce any toxic signs or cause death in any of 6 dogs. Lower doses, 100 mg/kg, did cause weakness and weight loss on the 4th day of compound administration. Deaths occurred on the 5th - 10th day of the test. The LD50 for "Purple" by the intraperitoneal route in dogs is 358 mg/kg.



2,4-D



2,4,5-T

FIGURE 1

TABLE 1-

POSSIBLE DOSE OF "PUPPLE" BY DELIVERY METHOD

Ground Dosage

24 lbs (10.9 kg/acre = 43560 sq ft)

250 mg/sq ft

Ground-Man Dosage Ratio

1 mg/sq ft on ground = 0.75 mg/sq ft on man

Available Body Area on Prone Man (Naked)

0.75 sq meters (8.1 sq ft)

(250 mg/sq ft) x (0.75) x 8.1 sq ft = 1519 mg

(ground dosage) x (man/ground ratio) x (available body area) = 1519 mg

$$\frac{1519 \text{ mg/man}}{50 \text{ kg (body weight)}} = 30 \text{ mg/kg}$$

TABLE 2

TOXICITY OF PHENOXYACETATES

Species	Route of Administration ^a	LD50 (mg/kg) 2,4-D			LD50 (mg/kg) 2,4,5-T		LD50 (mg/kg) "Purple" ⁽⁴⁾
		Acid	Salt	Mixed Butyl Esters	Acid	Mixed Butyl Esters	
Cat	lp		512(2)-599(2)				435
	lg	375(1)	666(2)-805(1)	620(1)	527(1)	491(1)	448
	lt						543
	pc						3909
	pcc						>12,500
Rabbit	lv		400 (2)				578
	lp						438
	lg		800 (2)	424(1)		712(1)	501
	lt						1351
	pc						-
Dog	pcc						-
	lp						350
	lg		100 (3)		100 (3)		-
	lt, pc						305
Mouse							>1250
	lp		369(2)-426(2)				
Guinea Pig	lg	368(1)	375(1)	713(1)	389(1)	940(1)	
	lp		576(2)-800(2)				
Chicks	lg	469(1)	551(1)-1000(2)	840(1)	301(1)	750(1)	
	lp	541(1)		2000(1)	310(1)		

(1) Rowe & Hynes, Am J. Vet Med, Vol XV, No. 57; p 662, 1954.

(2) Hill & Carlisle, J. Ind. Hyg & Tox, 29:85, 1947.

(3) Drill & Hratzke, Arch Ind Hyg & Occup Med, 7:61, 1953.

(4) CRDL

^a lp = Intraperitoneal; lg = Intra-gastric; lt = Intratracheal; pc = percutaneous, bare;

TABLE 3

TOXICITY OF FIVE DAILY INTRAPERITONEAL DOSES OF "PURPLE" IN DOGS

Daily Dose mg/kg	No. of Dogs	Remarks		
		Toxic Signs	Deaths	Day of Deaths
100	6	Weight loss and weakness on 4th day.	6/6	5,6,6,7,7,10
30	6	No toxic signs	0/6	

5. Safety Record of Phenoxyacetates.

The outstanding safety record established by these substances during more than 20 years of extensive operational use is also germane to this discussion.

From 1947-1963 more than three-hundred million pounds were produced and used to control vegetation on more than four-hundred million acres of land in the United States. Rates of application ranged from 1/16 - 160 lbs per acre. The annual production as of 1963 was estimated to exceed fifty million pounds and fifty million acres were treated.

These herbicides are registered by the US Department of Agriculture which means they are considered to be (1) non-poisonous, (2) non-corrosive, (3) non-inflammable, (4) available in quantity, (5) economical, and (6) effective. The Department of Agriculture maintains constant control in areas where herbicides are applied. During fifteen years of extensive use, the Department of Agriculture had not received a single complaint of injury to humans, livestock, wildlife, or soil from the phenoxy herbicides. Major manufacturers have certified that none of the workmen in their factories have shown any ill effects. Commercial spray operators report no adverse effects except for a very few allergic skin reactions. These companies report very few claims for damage to livestock and none of these have been proven. Only five suspected human intoxications have appeared in the literature in all of the years that these herbicides have been used (as of 1963).

The use of these herbicides is not restricted to the United States. The Russian scientific publication, "Protection of Plants from Pests and Diseases," 1961, pp 55-57, reports that in the recent years, five million hectares of grain crops in the Soviet Union have been treated annually with 2,4-D. Further, systematic treatment for three or four generations has not affected the quality of the grain.

Another publication, "Problems in Economics," Moscow, No. 11, pp 86-90, 1961, states that it is planned to use 39,750 tons of phenoxyacetates on thirty million hectares in an effort to increase food production.

A third publication, "Problems in Nutrition" by the Medical State Publishing House, Moscow, No. 4, 1961, states the toxicity and carcinogenicity of agricultural chemicals was investigated by the Interdepartmental Committee for the Study and Regulation of Toxic Chemicals at the State Sanitary Inspection Office, USSR. The phenoxyacetates were among 18 approved for applications. It was stated that crops treated as prescribed with 2,4-D present no danger when consumed as food.

Friday, 26 April 1963, a committee of American experts on herbicides met at Edgewood Arsenal, Maryland, to consider the use of phenoxyacetates in Viet Nam. They concluded that no hazard to health was incurred as a result of the quantity or the method of use in that operation.

man

Received Call from:

Lt. Col. Shadle

Headquarters, D.A.

OACSFOR-CM

Info ^{needed} for Gen. Hebler

Mr Mc provided data for
Gen. Hebler on herbicide range
Mr Mc also provided data on
to a Mr Denton, whom Gen. Hebl
gave a briefing for on Orange.

Mr Denton was not satisfied ^{with him} because
the data provided to Denton & Hebl
were different or ^{were} interpreted differently
Gen. Hebler would like to have
Dis. - D. P. 10 1.

send info to either

Gen. Hebler or Col. Shuck,

(Monday) 18 Dec 1967