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

3 NOV 1982

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: William Miller
Product Manager # 16
Insecticide
Registration Division (TS-767)

THRU: David Coppage
Section Head
Section 3, Ecological Effects Branch (TS-769)

THRU: Clayton Bushong
Branch Chief
Ecological Effects Branch (TS-769)

SUBJECT: EEB Request for Mammalian Acute Oral LD50 Data

In the conclusions of an EEB review for a conditional registration of terbufos for use on soybeans dated 2/11/82, Thomas Johnston requested the submission of the raw data for a mammalian acute oral LD50 test by Consultan (1972). The information was requested so that the dose response data could be used to calculate the LD10 values needed to make a hazard assessment on endangered mammalian species potentially exposed to terbufos granules applied to soybeans. Appended are the data obtained from Accession Number 247983. Note: The calculated LD10 values usually were greater than the lowest dose level which had 1 out of 5 deaths (20 percent mortality, not 10 percent).

The mammalian acute oral LD50 values ranging from 1.6 to 11.7 mg per kg body weight, which indicates that terbufos is slightly more toxic to small mammals than to birds as indicated by the 28.6 mg/kg LD50 for bobwhite quail. In general the toxicity level of concern for endangered mammals calculated as 1/10th of the LD50 versus 1/5th of the LD10 were similar and with only one exception the LD10/5 value was more conservative than the respective value calculated as 1/10th of the LD50.

The mammalian margin of safety values calculated as 1/5th of the LD10 ranged from 0.16 to 1.37 mg terbufos per kg of body weight. Given the terbufos content in 15 G Counter granules, consumption of less than one granule per gram of body weight (9 to 80 granules/kg of body weight) would exceed the margin of safety for endangered mammals. The only two endangered mammals identified as occurring in soybean or sorghum fields which are also small enough to be threatened by consumption of granules are the Delmarva fox squirrel (0.6 - 1.36 kg body weight and the Morro Bay kangaroo rat (50 - 94 g). Extrapolating from the available mammalian data on rats and mice, the safety margin values for smaller individuals of these two species would be equivalent to about 5.4 and 0.5 granules for each species, respectively. Knife-in, in-furrow, and band treatments of 8 - 16 oz. per 1000 feet proposed by the registrant are equivalent to 2 to 3.9 lb a. i./acre which average 183 to 357 granules/sq. ft. Despite treatment techniques designed to cover exposed granules, the toxicity

of terbufos is such that the safety margins for these two endangered mammals would easily be exceeded by spilled or exposed granules.

William S. Rabert

William S. Rabert, Biologist
Ecological Effects Branch

APPENDIX

Test Species	Percent Active	LD50 (mg/kg)	NOEL (mg/kg)	LD10 (mg/kg)	Level of Concern for Endangered Species LD50/10 vs. LD10/5 (mg/kg)	
Acute Oral LD50 Test						
Rat (Male)	96.7 %	4.5 (2.6- 7.7)	<1.75	1.78	0.45	0.36
Rat (Female)	96.7 %	9.0 (5.2-15.3)	<3.5	3.55	0.90	0.71
Mouse (Male)	96.7 %	3.5 (1.9- 6.6)	<1.57	1.34	0.35	0.27
Mouse (Female)	96.7 %	9.2		a	0.92	a
Rat (Male)	85.8 %	1.6 (1.2- 1.9)	0.4	0.81	0.16-0.4	0.16
Mouse (Female)	85.8 %	5.0 (4.0- 6.3)	2.5	b	0.5	b
Rat (Male)	15 % G	11.7 (9.0-15.3)	3.13	6.86	1.17	1.37
Acute Dermal LD50 Test						
Rabbit (Male)	96.7 %	1.1		a	0.11	a
Rabbit	85.8 %	1.0 (0.07- 1.3)	0.4	b	0.10	b
Rabbit (Male)	15 % G	10.2 (7.7-13.4	1.02	b	1.02	b

a No raw data available from which to calculate a LD10.
b Insufficient partial mortality points from which to calculate a LD10.

These studies have not been validated. Higher LD50 values may be due to absence of pre-testing fasting according to Tox Branch reviewer.

103 Toxicological Properties

Test	Species	Material	LD/LC50	Validation Status	Source
Oral LD50	Rat (Male)	96.7 % a.i.	4.5 (2.6- 7.7) mg/kg		Acc.247983
	Rat (Female)	96.7 % a.i.	9.0 (5.2-15.3) mg/kg		Acc.247983
	Mouse (Male)	96.7 % a.i.	3.5 (1.9- 6.6) mg/kg		Acc.247983
	Mouse (Female)	96.7 % a.i.	9.2 mg/kg		Acc.247983
	Rat	86 % a.i.	1.5 mg/kg		
	Rat	86 % a.i.	1.7 mg/kg		
	Rat (Male)	85.8 % a.i.	1.6 (1.2- 1.9) mg/kg		Acc.247983
	Mouse (Female)	85.8 % a.i.	5.0 (4.0- 6.3) mg/kg		Acc.247983
	Dog (Male)	Tech.	4.5 mg/kg		
	Dog (Female)	Tech.	6.3 mg/kg		
	Rat (Male)	15 % G	11.7 (9.0-15.3) mg/kg		Acc.247983
Dermal LD50	Rabbit (Male)	96.7 % a.i.	1.1 mg/kg		Acc.247983
	Rabbit (Male)	85.8 % a.i.	1.0 (0.07- 1.3) mg/kg		Acc.247983
	Rabbit (Male)	15 % G	10.2 (7.7-13.4 mg/kg		Acc.247983
	Rabbit	15G (paste)	29- 34 mg/kg		
	Rabbit	15G (dry)	900-1425 mg/kg		
Dietary Effects					
30 days	Rat	Tech.	Marked CHE depression at 2.0 ppm.		
30 days	Beagle Dog	Tech.	Depressed body weights at 0.25 ppm.		
31 days	Mice	Tech.	Significant body weight depression at 16.0 ppm		
Acute Oral LD50	Bobwhite	89.6 % a.i.	28.6 (22.2-57.2) mg/kg		Core
8-Day Dietary LC50	Pheasant	96.7 % a.i.	145 ppm		IBT
	Bobwhite	86 %	140 (107-183) ppm		Core
	Mallard	96.7 % a.i.	185 ppm		IBT
	Mallard	86 % a.i.	160 (131-195) ppm		Invalid
	Mallard	86 % a.i.	520 (400-676) ppm		Core (food rejection)
Avian Reprod.	Bobwhite	? % a.i.	Sign. diff. at 2.0 and 20 ppm		
	Mallard	? % a.i.	No sign. diff.		
Simulated Field Tests	Pheasants	1.03 and 5.15 lb/A	No acute or chronic effects		
	Pheasants	Simulated spill	2 out 3 hens died within 12 hours of exposure		

96.7 %

NOEL < 1.75 mg/kg

RABERT TERBUFOS ALBINO RAT LD50 MALE

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CONC.	NUMBER EXPOSED	NUMBER OEAD	PERCENT OEAD	BINOMIAL PROB.(PERCENT)
14	5	5	100	3.125
7	5	4	80	18.75
3.5	5	1	20	18.75
1.75	5	1	20	18.75

THE BINOMIAL TEST SHOWS THAT 0 AND +INFINITY CAN BE USEO AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATEO WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 4.949747

RESULTS CALCULATED USING THE MOVING AVERAGE METHOO

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
3	0.4919916	4.361198	1.764255	8.436509

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOOONESS OF FIT PROBABILITY
6	0.5172167	1	0.4503647

SLOPE = 3.425349
95 PERCENT CONFIOENCE LIMITS = 0.961914 AND 5.888784

LC50 = 4.172828
95 PERCENT CONFIOENCE LIMITS = 2.040969 AND 7.699532

LC10 = 1.77691
95 PERCENT CONFIDENCE LIMITS = 0.1514464 ANO 3.020601

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96.7%

RABERT TERBUFOS ALBINO RAT LD50 FEMALE

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
28	5	5	100	3.125
14	5	4	80	18.75
7	5	1	20	18.75
3.5	5	1	20	18.75

THE BINOMIAL TEST SHOWS THAT 0 AND +INFINITY CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 9.899495

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
3	0.4919917	8.722397	3.528509	16.87302

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
6	0.5172168	1	0.4503642

SLOPE = 3.425348
95 PERCENT CONFIDENCE LIMITS = 0.9619136 AND 5.888783

LC50 = 8.345655
95 PERCENT CONFIDENCE LIMITS = 4.081938 AND 15.39906

LC10 = 3.553818
95 PERCENT CONFIDENCE LIMITS = 0.3028923 AND 6.041201

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96.7%

RABERT TERBUFOS ALBINO MOUSE (MALE) LO50

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CONC.	NUMBER EXPOSED	NUMBER OEAD	PERCENT OEAD	BINOMIAL PROB.(PERCENT)
12.5	5	5	100	3.125
6.25	5	4	80	18.75
3.13	5	2	40	50
1.57	5	1	20	18.75

THE BINOMIAL TEST SHOWS THAT 0 AND +INFINITY CAN BE USEO AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIOENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 3.697956

RESULTS CALCULATEO USING THE MOVING AVERAGE METHOO

SPAN	G	LC50	95 PERCENT CONFIOENCE LIMITS	
3	0.4921612	3.3578	1.097752	6.02114

RESULTS CALCULATED USING THE PROBIT METHOO

ITERATIONS	G	H	GOOONESS OF FIT PROBABILITY
6	0.5570162	1	0.8267556

SLOPE = 3.275146

95 PERCENT CONFIDENCE LIMITS = 0.8307892 AND 5.719502

LC50 = 3.266208

95 PERCENT CONFIDENCE LIMITS = 1.382024 ANO 6.DO5924

LC10 = 1.337441

95 PERCENT CONFIDENCE LIMITS = 0.06226621 AND 2.366621

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85.8 %

RABERT TERBUFOS ALBINO RAT (MALE) LD50

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
6.9	20	20	100	9.536743E-05
3.5	20	19	95	0.002002716
1.7	20	12	60	25.17223
0.9	20	3	15	0.128414
0.4	20	0	0	9.536743E-05

THE BINOMIAL TEST SHOWS THAT 0.9 AND 3.5 CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 1.489559

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
4	0.04910519	1.518308	1.212481	1.877039

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
5	0.1342827	1	0.9897676

SLOPE = 4.713962
95 PERCENT CONFIDENCE LIMITS = 2.98655 AND 6.441375

LC50 = 1.513879
95 PERCENT CONFIDENCE LIMITS = 1.235259 AND 1.854012

LC10 = 0.8141016
95 PERCENT CONFIDENCE LIMITS = 0.5299627 AND 1.030914

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85.8%

RABERT TERBUFOS ALBINO MOUSE (FEMALE) LD50

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
20	10	10	100	0.09765625
10	10	10	100	0.09765625
5	10	5	50	62.30469
2.5	10	0	0	0.09765625

THE BINOMIAL TEST SHOWS THAT 2.5 AND 10 CAN BE USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 5

WHEN THERE ARE LESS THAN TWO CONCENTRATIONS AT WHICH THE PERCENT DEAD IS BETWEEN 0 AND 100, NEITHER THE MOVING AVERAGE NOR THE PROBIT METHOD CAN GIVE ANY STATISTICALLY SOUND RESULTS.

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105001

15% G

RABERT TERBUFOS ALBINO RAT (MALE) LD50

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
25	10	10	100	0.09765625
12.5	10	5	50	62.30469
6.25	10	1	10	1.074219
3.13	9	0	0	0.1953125

THE BINOMIAL TEST SHOWS THAT 6.25 AND 25 CAN BE
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 12.5

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
3	0.1191621	11.07458	8.493822	15.27602

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
7	0.3050242	1	0.687812

SLOPE = 5.679737
95 PERCENT CONFIDENCE LIMITS = 2.542875 AND 8.816598

LC50 = 11.48761
95 PERCENT CONFIDENCE LIMITS = 8.575358 AND 15.43294

LC10 = 6.864799
95 PERCENT CONFIDENCE LIMITS = 3.320959 AND 9.056415

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105001

85.8 %

RABERT TERBUFOS ALBINO RABBIT (MALE) OERMAL LO5O

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CONC.	NUMBER EXPOSEO	NUMBER OEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
3.5	5	5	100	3.125
1.7	5	5	100	3.125
0.9	5	2	40	50
0.4	5	0	0	3.125

THE BINOMIAL TEST SHOWS THAT 2.5 ANO +INFINITY CAN BE USEO AS STATISTICALLY SOUNO CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIOENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC5O FOR THIS SET OF OATA IS 0.9767707

WHEN THERE ARE LESS THAN TWO CONCENTRATIONS AT WHICH THE PERCENT OEAD IS BETWEEN 0 AND 100, NEITHER THE MOVING AVERAGE NOR THE PROBIT METHOD CAN GIVE ANY STATISTICALLY SOUND RESULTS.

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105001

15% G

RABERT TERBUFOS ALBINO RABBIT (MALE) OERMAL LO50

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CONC.	NUMBER EXPOSEO	NUMBER OEAD	PERCENT OEAD	BINOMIAL PROB.(PERCENT)
25	5	5	100	3.125
12.5	5	4	80	18.75
6.25	5	0	0	3.125
3.13	5	0	0	3.125

THE BINOMIAL TEST SHOWS THAT 6.25 ANO +INFINITY CAN BE USEO AS STATISTICALLY SOUNO CONSERVATIVE 95 PERCENT CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIOENCE LEVEL ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 10.03165

WHEN THERE ARE LESS THAN TWO CONCENTRATIONS AT WHICH THE PERCENT DEAD IS BETWEEN 0 ANO 100, NEITHER THE MOVING AVERAGE NOR THE PROBIT METHOD CAN GIVE ANY STATISTICALLY SOUND RESULTS.

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