US EPA ARCHIVE DOCUMENT

DATA EVALUATION RECORD

1. CHEMICAL: Brodifacoum

2. FORMULATION:

3. CITATION: Savarie, Peter J. and LaVoie, G. Keith, (1979). Secondary Toxicity Hazards of the Anticoagulent Brodifacoum to American Kestrels (Falco sparverius) Cooperative agreement between ICI and Denver Wildlife Research Center (FWS) Acc #245704

4. REVIEWED BY: Russel Farringer
   Wildlife Biologist
   EEB/HED

5. DATE REVIEWED: 11/13/81

6. TEST TYPE: Secondary Toxicity

   A. Test Species: American Kestrel (Falco sparverius)

7. REPORTED RESULTS:

   a) Chronic three day LC_{50} (95% C.L.) of brodifacoum to voles was 1.4 (0.77-2.0) ppm, slope ± standard error of the slope = 4.1 ± 1.2 Acute oral LD_{50} (95% C.L.) of brodifacoum to voles: 0.20 (0.11-0.32 mg/kg; slope ± S.E. of slope = 1.8 ± 0.4. entered in Database

   b) 4 out of 10 kestrels that feed for 6 days upon brodifacoum-treated voles died. No mortalities in kestrels that fed for 2 days upon brodifacoum - treated voles.

   c) At 71 days postreatment the mean prothrombin time in kestrels that consumed brodifacoum-treated voles for either 2 or 6 days was higher than the control group. At 100 days posttreatment 2 kestrels that fed upon brodifacoum-treated voles for 2 days had prothrombin times of greater than 300 seconds each, and 1 kestrel that fed upon brodifacoum-treated voles for 6 days had a prothrombin time of greater than 600 seconds. Statistical analysis of this data has not been completed.

8. Reviewer's Conclusions: EEB calculations of the LD_{50} and LC_{50} for voles was close to identical to those of the registrants. This study with kestrels indicates that mortality to these birds could occur if the birds fed on Brodifacoum killed voles for more than two days. However, this mortality data may not reflect the actual mortality pattern. The bird were administered a diet containing menadione sodium bisulfite complex (Vitamin K type compound) which could of biased the results.

Materials/Methods

Test Procedure

The LC_{50} and LD_{50} for voles was determined. Six dose levels and a control was use in each test. The LD_{50} dose levels ranged from 0.045 to 1.0 mg/kg. The LC_{50} dose levels ranged from 1 to 50 ppm. PEG 400 was use as the carrier in the LD_{50} study at a rate of 0.1 ml/20g body weight. Controls received an equivalent amount of PEG 400. The LC_{50} voles were given 40 g of treated bait in a no choice situation for 3 days, then observed for 21 days or until death. No control mortality occurred in either test.

American kestrels were live trapped in Sacromento, CA and shipped to Denver, CO. They were individually caged in outdoor pens for a minimum of 30 days before testing. They had free access to water and were fed daily (except Sunday). Twenty-one days before treatment and 21 days posttreatment each kestrel was fed approximately 75g of 25% Zu Preem Birds of Prey diet and 75% horsemeat. Kestrels were then maintained on a ration of approximately 45g. of horsement. Two groups of 10 kestrels were used for the treatment groups. Control birds were indicated but the number of control birds was not given. One group of treatment birds was exposed for two days and the other group for 6 days. Vole used for exposure to the kestrels were offered 30 grams of ICI Brodifacoum (Talon) 3/16 inch pelletized bait containing 50 ppm brodifacoum for days. After 3 feeding days the voles were killed by cervical dislocation, and kept frozen until fed to the kestrels. Ten voles were randomly selected for whole body residue analysis (not with this report), and sent to ICI, Labs. Teh amount of brodifacoum consumed by each vole was calculated and there was a stratified randomization of each vole to the kestrels. That is, voles consuming the highest amount of brodifacoum were fed to the heaviest kestrels. Each of the birds in the 2-day treatment group was offered one treated vole a day for two days and the 6-day treatment group was offered one treated vole per day for 6 days.

Statistical Analysis

The LC_{50} and LD_{50} for the voles was estimated by the probit analysis described by Finney as programed for the computer by Daum and Killcreas.

Discussion/Results

A) 3-day Chronic LC_{50} for voles = 1.4 (0.77-2.0) ppm

B) LD_{50} for voles = 0.20 (0.11-0.32) mg/kg

C) There were no mortalities in kestrels that fed for 2 days upon brodifacoum-treated voles or in the kestrels that fed upon untreated voles. Four of ten kestrels that fed for 6-days upon brodifacoum-trated voles died.

D) See attached tables (#'s 3+4) form report.

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Reviewer's Conclusion

A. Test Procedure

The test procedure raised a major question. The kestrels were being tested to see what effects brodifacoum had on then as a potential secondary hazard. The supplemental feed contained vitamin k-like compound (menadione sodium bisulfite complex). Vitamin k is antidotal to the toxicant. Thus, a masking of the effects of the compound could have occurred. For this type of test, the kestrels should of been maintained on voles pre-and post treatment.

B. Statistical Analysis

Our probit analysis of the vole data confirmed the LC_{50} and LD_{50} values reported by the reseacher. (See attached analysis)

Conclusions

Category: Invalid

Rationale: See that procedure in coclusions.

Repairability: None at this time subject to data showing that the use of a Vitamin K complex is not antidotal.

VOLES. LC50

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
50	10	10	100	0.09765625
30	10	10	100	0.09765625
15	10	10	100	0.09765625
5	10	10	100	0.09765625
3	10	9	90	1.074219
1	10	3	30	17.1875

THE BINOMIAL TEST SHOWS THAT 0.045 AND 3 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 LC_{50} FOR THIS SET OF DATA IS 1.409166

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
1	0.509802	1.409166	0.6021472	2.147129

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATINS	G	H	GOODNESS OF FIT PROBABILITY
7	0.3564675	1	0.9968676

SLOPE = 4.09327
95 PERCENT CONFIDENCE LIMITS + 1.649387 AND 6.537153

LC50 = 1.360264
95 PERCENT CONFIDENCE LIMITS = 0.772308 AND 1.990645

LC10 = 0.6658213
95 PERCENT CONFIDENCE LIMITS = 0.1608374 AND 1.037864

VOLES. LD50

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
1	10	9	90	1.074219
0.75	10	8	80	5.46875
0.37	10	8	80	5.46875
0.18	10	4	40	37.69531
0.09	10	2	20	5.46875
0.045	10	1	10	1.074219

THE BINOMIAL TEST SHOWS THAT 0.045 AND 1 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 0.214014

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
5	0.189172	0.2129989	0.1193247	0.3420593

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
4	0.1901451	1	0.900969

SLOPE = 1.956266
95 PERCENT CONFIDENCE LIMITS = 1.103224 AND 2.809308

LC50 = 0.2158203
95 PERCENT CONFIDENCE LIMITS = 0.129784 AND 0.3428208

LC10 =
95 PERCENT CONFIDENCE LIMITS = 0.01245027 AND 0.08909829

Table 4. Data on Kestrels Dying After Eating Voles Treated with Brodifacoum. Kestrels fed upon voles for 6 days.

Kestrel No.	Sex	Theoretical maximum mg/kg brodifacoum consumed	Initial wt (g)	Dead wt (g)	Days to death*
43	M	27.9	122	122	5
54	F	43.2	147	129	8
65	F	26.2	120	123	11
29	M	19.9	113	***	83
		29.3 ± 9.9**	125.5 ± 14.8	124.7 ± 3.8	26.8± 37.6

* After initial feeding on voles

** Mean ± standard deviation

*** Dead weight not obtained

Table 3. Theoretical Maximum Consumption of Brodifacoum by Kestrels Feeding upon Voles

Kestrel No.	Sex	Wt (g)	Amount of 50 ppm bait eaten by voles (g)	mg Brodifacoum eaten by voles	Theoretical maximum mg/kg brodifacoum consumed
			2-day feeding of voles to kestrels		
53	M	119	23	1.15	9.7
58	M	118	18	0.9	7.6
50	M	115	15	0.75	6.5
67	M	102	11	0.55	5.4
62	F	144	39	1.95	13.5
64	F	134	32	1.6	11.9
68	F	133	29	1.45	10.9
69	F	130	28	1.4	10.8
60	F	127	26	1.3	10.2
51	F	113	22	1.1	9.7
		123.5 ± 12.3*	24.3 ± 8.3	1.2 ± 0.4	9.6 ± 2.5
			6-day feeding of voles to kestrels		
43	M	122	74	3.4	27.9**
38	M	116	69	2.8	24.1
29	M	113	61	2.25	19.9**
37	M	107	52	1.5	14.0
54	F	147	129	6.35	43.2**
78	F	139	106	5.0	36.0
40	F	132	96	4.55	34.5
66	F	132	87	4.05	30.7
70	F	128	79	3.90	30.5
65	F	120	72	3.15	26.2**
		125.6 ± 12.3	82.5 ± 22.8	3.7 ± 1.4	28.7 ± 8.3

* Mean ± standard deviation

** Died - see Table 4