US EPA ARCHIVE DOCUMENT

415633-03
MRID No.

112701
Shaughnessy No.

Data Evaluation Record

BRODIFACOUM

Avian Oral Acute Toxicity Test

1. TEST MATERIAL: Brodifacoum.

2. STUDY MATERIAL - Brodifacoum, technical grade.

[3-(3-[4'-bromo- (1,1'-biphenyl) -4-yl]1,2,3,-4-tetrahydro-1-naphtalenyl)-4-hydroxy-2H-1- benzopyran -2-one	97.6% W/W
Inert ingredients	2.4
	100%

3. STUDY TYPE - Avian Dietary Single-dose Oral LD_{50}.

   Species tested- Mallard duck *Anas platyrhynchos*

4. STUDY IDENTIFICATION:

   Ross, D.B., N.L. Roberts and C. Fairley. 1980. Brodifacoum: The acute oral toxicity (LD_{50}) of Broadifacoum to the Mallard duck. Huntingdon Research Centre, Huntingdon, Cambridgeshire, UK. Submitted by ICI Americas, Inc., Agricultural Products, Wilmington, Delaware 19897. ICI's Study No. ICI 308 WL/791275. EPA MRID 415633-03.

5. REVIEWED BY:

   James J. Goodyear
   Biologist, Section 1
   Ecological Effects Branch
   Environmental Fate and Effects Division (H7507C)

   Signature: James Goodyear
   Date: Jan 4, 1991

6. APPROVED BY:

   Leslie W. Touart
   Acting Head, Section 1
   Ecological Effects Branch
   Environmental Fate and Effects Division (H7507C)

   Signature: L W T
   Date: 1-9-91

7. CONCLUSIONS:

   ICI used lumped values to make the calculations; this is not statistically acceptable. Therefore, EEB recalculated the LD_{50} based upon the larger single series of nine concentrations. The results are accepted as "Core." LD_{50} = 0.26 mg/kg (95% CI, 0.0 -0.8 mg/kg); NOEL <0.2 mg/kg.

8. RECOMMENDATIONS- N/A.

9. BACKGROUND:

The study was submitted to meet the requirements for the reregistration of Brodifacoum and its TEPs.

10. DISCUSSION OF INDIVIDUAL TEST- N/A.

11. MATERIALS AND METHODS:

A. TEST ANIMALS:

Sixty female and 63 male Mallards were obtained from a local game farm. The birds were given adequate food and shelter before (14 days), during and after the test. "A normal daylight pattern was followed." Therefore, the 16 hour light and 8 hour dark pattern was not followed.

B. DOSE:

The dosage levels in the food with a corn oil vehicle were 0 (control), 0.20, 0.80, 1.4, 2.00, 2.60, 3.20, 3.80, 4.40, and 5.00 mg/kg by oral gavage. Twenty-one days after the original group was dosed, "Extra groups were added to improve the spread of mortalities." These groups were dosed with 0.10 and 0.25 mg/kg. EEB regards these sets of dosage groups as two separate studies.

C. DESIGN:

The subjects were assigned to experimental groups of 5 males and 5 females by an unknown method. "The post dose observation period lasted for 28 days and the following observations were made: Mortalities (daily), bird health (daily), bodyweight (... Days -14, -7, 0, 3, 7, 14, 21 and 28), Food consumption by groups [in weekly intervals] and gross *postmortem* at death or at the termination of the study."

D. STATISTICS:

Litchfield and Wilcoxon, 1949. The data from the two studies was pooled.

12. REPORTED RESULTS:

LD_{50} = 0.31mg/kg (95% CI, 0.19-0.50), $LD_{50♂}$ = 0.36 mg/kg (0.19-0.67), $LD_{50♀}$ = 0.30 (0.17-0.53). The NOEL was not given.

13. STUDY AUTHORS' CONCLUSIONS/QA MEASURES:

"This report has been accepted by the QA Unit as being an accurate presentation of the findings of the study." * * *

"The LD_{50} value for male and female birds for brodifacoum to the Mallard duck was calculated to be 0.31 mg/kg (95% confidence limits 0.19 - 0.50 mg/kg)."

14. REVIEWER'S DISCUSSION AND INTERPRETATION OF THE STUDY:

A. TEST PROCEDURES:

There were a few minor errors in the housing, photoperiod, etc., but none of these are enough to invalidate the results of the study.

The two test groups did not experience the same environmental factors or have physiological condition. The relationship of the two test groups to their respective controls is not the same (in fact, it isn't clear if the second study had a control). Therefore, their data can not be lumped.

EEB recalculated the LD_{50} using only the original, single series data.

B. STATISTICAL ANALYSIS:

EEB used C.E. Stephen's computer method to confirm the LD_{50} calculations.

LD_{50} = 0.26mg/kg (95% CI, 0.0-0.8 mg/kg) NOEL <0.2 mg/kg.

C. DISCUSSION/RESULTS:

The original tests used a range of concentrations that were too high. Additional tests were done, but the data generated cannot be lumped with the previous data. It isn't clear if the second study had a control group.

EEB used the original, single series data to recalculate the LD_{50}. The result was not as satisfactory as EEB would have liked, but it was acceptable. This method had no "zero mortality" experimental group and too few "partial mortality" groups.

The last death occurred on day-23 of the 28 day study. There were no more birds in this group, so no more could have died. There were no mortalities in the other groups for the last ten days.

D. ADEQUACY OF THE STUDY:

Classification- Core.

Rational- The data was recalculated to meet statistical standards.

Repair- None.

15. COMPLETION OF ONE-LINER FOR STUDY- Yes.

16. CBI APPENDIX- N/A.

LITERATURE CITATIONS

Litchfield, J.T., Jr and F. Wilcoxon. 1949. A simplified method of evaluating dose-effect experiments. J. Pharmacology and Experimental Therapeutics. 96:99-113. MRID 84753.

Stephen, C.E. 1977. Methods for calculating an LC_{50}. *in*, Aquatic toxicology and hazard evaluation. ASTM STP 634. F.L. Mayer and J.L. Hamelink, Eds. American Society for Testing and Materials. pp. 65-84.

James J Goodyear Brodifacoum Avian Acute (Duck)

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
5	10	10	100	9.765625E-02
4.4	10	10	100	9.765625E-02
3.8	10	10	100	9.765625E-02
3.2	10	10	100	9.765625E-02
2.6	10	10	100	9.765625E-02
2	10	10	100	9.765625E-02
1.4	10	10	100	9.765625E-02
.8	10	9	90	1.074219
.2	10	4	40	37.69531

THE BINOMIAL TEST SHOWS THAT 0 AND .8 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 .257483

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
1	.7206815	.257483	1.448439E-02	.4713845

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
6	.3102319	1	.9997458

SLOPE = 3.011968
95 PERCENT CONFIDENCE LIMITS = 1.334348 AND 4.689589

LC50 = .2505594
95 PERCENT CONFIDENCE LIMITS = .1070089 AND .4012199

LC10 = 9.489858E-02
95 PERCENT CONFIDENCE LIMITS = 1.439299E-02 AND .1786748

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