

US EPA ARCHIVE DOCUMENT

1-9-91

066942
MRID No.

112701
Shaughnessy No.

Data Evaluation Record
BRODIFACOUM
Avian Single Dose Oral LD₅₀

GUIDELINE NUMBER: 71-1 (a)

CITATION: Ross, D.B. 1978. The acute oral toxicity (LD₅₀) of Brodifacoum to the Mallard duck. Submitted by ICI Americas, Inc., Agricultural Products, Wilmington, Delaware 19897. Report No. ICI122WL/78507. Study No. ICI122WL. MRID 66942.

REASON FOR SUBMISSION:

FIFRA '88 Reregistration.

RESULTS-	Valid _____	Invalid <u> X </u> _____	Supplemental _____
GUIDELINE-	Satisfied _____	Partially Satisfied _____	Not Satisfied <u> X </u> _____

DISCUSSION:

The original DER (Turner, 1979) classified this study "Supplemental" because Vitamin K, an antidote for anticoagulants was used as a feed supplement. Later, Turner (1979) reclassified the study as "Core" because it was established that not enough Vitamin K was put into feed to make a difference and that the supplement was a different kind on Vitamin K. The study was then raised to "Core."

Examination of the data reveals that two (perhaps three) tests were run and the data combined in order to give a proper range of concentrations. This procedure is not statistically acceptable. EEB used Stephen's computer program to recalculate the LD₅₀ from ICI's data. The LD₅₀ was 1.42 mg/kg (CI 0.6 - 141.8 mg/kg).

The dosage column in the tables says, "Dose Volume" and "Mean dose level (mg/kg). A constant dose volume that produces a group mean dose concentration of Brodifacoum leads EEB to infer that the birds were dosed based upon the group's mean weight not their individual body weight. Therefore, each birds received a different dose of toxicant.

The observation period was extended to 5 weeks because of the time it takes anticoagulants to act. The mortality data is present in a table that lists deaths by the week of the study. It can not be determined when during the fourth week the last death occurred. The observation period after the last death should be longer than that for most anticoagulants.


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CONCLUSIONS:

The study must be reclassified as "Invalid." The requirement must be met, therefore, another study should be submitted.

REVIEWED BY:

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Date: Jan 7, 1991

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11/10/79

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VALIDATION SHEET

CRF # _____ PAGE _____ OF _____

FORMULATION:			IA	IB	T	FW	EC	R		
% a.i.	SC #	CHEMICAL NAME	Validator: Larry Turner				Date: 4/14/79			
technical		brodifacoum	Test Type: Avian acute oral LD ₅₀ mallard duck							
			Test ID.# ES-C1							

CITATION: Ross, David B., Nicholas L. Roberts, and David M. Cameron. 1978. The acute oral toxicity (LD₅₀) of PP581 to the mallard duck. 10p. Study conducted by Huntingdon Research Centre. Submitted by ICI Americas, 10182-26; Acc. #234655, report 6I; 8/15/78.

RESULTS: Mallard duck acute oral LD₅₀ = 2.0 mg/kg (95% c.i. 0.8-4.8 mg/kg). Mortality was 10% at the two lowest levels of 0.3 and 0.6 mg/kg; 100% mortality occurred at doses of 18.4 mg/kg, except that only 70% mortality occurred at 70.7 mg/kg. Toxic symptoms included weakness, lethargy, lack of coordination, and hemorrhage. Weight loss occurred in some birds dosed at 18.4 mg/kg and up, but did not become apparent until 14 days after treatment. One of ten control birds died, apparently (from symptoms and autopsy) from lead shot poisoning. Most experimental mortalities occurred 7-14 days after treatment.

VALIDATION CATEGORY: Supplemental

CATEGORY RATIONALE: The reported results appear to give an accurate estimation of the LD₅₀. However, different birds apparently were tested at different times, and 2 of 10 test groups were reported as being from a different batch of birds. The report identifies the test material as technical, but no % a.i. was given. In addition, it is unclear which birds and which time frames were used in the statistical computation of the LD₅₀ value.

reviewed
11/10/79
[Signature]

CATEGORY REPAIRABILITY: It is possible that this test could be upgraded to core if additional information is received. Specifically, Ecological Effects requires that the exact dates that various groups were dosed be reported, the % a.i. be identified, and complete information on the statistical analysis - including log-probit graphs - be furnished. Registrant should also justify why the test should not be considered unacceptable on the basis of a high chi square value indicating heterogeneous data.

ABSTRACT: Young adult mallards were given single oral doses of brodifacoum to determine the LD₅₀ values. An initial range-finding study used two birds per concentration at levels from 2-179 mg/kg. For the main study, 6 groups of 10 birds/concentration were tested at mean dose levels of 0 (control), 9.2, 18.4, 35.5, 70.7, and 141.8 mg/kg. Because mortality was higher than expected, four additional groups were tested at mean dose levels of 2.1, 3.4, 0.3, and 0.6 mg/kg. It is unclear if these four groups were tested concurrently, but the report did state that the 0.3 and 0.6 mg/kg groups were from a different batch of birds. Because mortality occurred mostly towards the end of 14 days, observations were continued to a total of 35 days.

Other than as noted above, procedures generally followed the proposed guidelines with respect to housing conditions, food and consumption, weights, necropsies, etc. However, dosing of birds was based on mean dose levels for each group, rather than dosing each individual bird at a precise level according to its individual weight. Also the percent a.i. was not given, although the test material was specified as technical.

Statistical analysis was reported to have followed Litchfield and Wilcoxon, but it is unclear how the different treatment times related to the analysis, ie. which test groups were analyzed. This reviewer, using Finney probit analysis, calculated an LD₅₀ of 1.6 mg/kg (1.0-2.7) for the four lowest dose levels that were reported as being tested subsequent to the initial six groups. A second LD₅₀ of 2.4 mg/kg (1.2-4.8) was calculated for all ten test groups. However, the chi square value for the latter analysis was 20.035 for 9 degrees of freedom, whereas a maximum value of 16.919 is allowable at the .05 level of probability.

0.3
1.
10.

0.6
1.
10.

2.1
7.
10.

all doses
considered
(see validation)

3.4
7.
10.

9.2
6.
10.

18.4
10.
10.

35.5
10.
10.

70.7
7.
10.

141.8
10.
10.

1.078 M
4.594 YINT
8.460 LW M
20.035 CHI²

2.378 LD50
1.178 LDCL
4.802 UPCL

0.154 LD10
0.037 LDCL
0.647 UPCL

36.737 LD90
13.015 LDCL
103.697 UPCL

← Mallard acute oral LD50
Talon tech (brodifacoum)
L. Turner 4/14/79

only "follow-up"
doses used
(see validation)

0.3
1.
10.

0.6
1.
10.

2.1
7.
10.

3.4
7.
10.

2.093 M
4.571 YINT
3.005 LW M
1.297 CHI²

1.603 LD50
0.967 LDCL
2.657 UPCL

0.391 LD10
0.167 LDCL
0.916 UPCL

6.570 LD90
2.378 LDCL
18.172 UPCL