9-27-89 ✓

Accession No. 409958-01

DATA EVALUATION RECORD

1. **CHEMICAL:** Ametryn.
Shaughnessey Number: 80801.

2. **TEST MATERIAL:** Ametryn Technical. FL # 862730. 99.0% active ingredient.

3. **STUDY TYPE:** Avian Single-Dose Oral LD50 Test.
Species Tested: Bobwhite quail (Colinus virginanius).

4. **CITATION:** Grimes, J., and M. Jaber. 1988. Ametryn: An Acute Oral Toxicity Study with the Bobwhite. Submitted by Ciba-Geigy Corporation, Greensboro, North Carolina. Study performed by Wildlife International Ltd., Easton, Maryland. Laboratory Study No. 108-291. EPA Accession No. 409958-01.

5. **REVIEWED BY:**

Michael L. Whitten, M.S.
Wildlife Toxicologist
KBN Engineering and
Applied Sciences, Inc.

Signature: Michael L. Whitten
Date: 4-14-89

6. **APPROVED BY:**

James R. Newman, Ph.D.
Project Manager/
Principal Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: James R. Newman
Date: 4/14/89

Henry T. Craven, M.S.
Supervisor, EEB/HED
USEPA

Signature: 9-26-89
Date: Henry T. Craven 9/27/89

7. **CONCLUSIONS:** The acute oral LD50 of ametryn was determined to be greater than 2250 mg/kg, the highest dosage tested. This value classifies ametryn as practically non-toxic to bobwhite quail. The no-observed effect dosage was 486 mg/kg, based on signs of toxicity, body weight loss, and reduced food consumption at 810 mg/kg. The study is scientifically sound and meets the requirements for an avian single dose oral LD50 test.

8. **RECOMMENDATIONS:** N/A

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9. BACKGROUND:

10. DISCUSSION OF INDIVIDUAL TESTS: N/A.

11. MATERIALS AND METHODS:

A. **Test Animals:** The birds used in the study were 17-week old Bobwhite quail (Colinus virginanius), obtained from Fritts' Quail Farm, Phillipsburg, New Jersey. All birds were acclimated to the facilities for 15 days prior to initiation of the study. Birds exhibiting abnormal behavior or physical injury during acclimation were not used in the test.

B. **Test System:** All birds were housed indoors in 78 cm x 51 cm wire pens. Floors were sloped resulting a ceiling height of 20 to 25 cm. Fluorescent lights provided eight hours of light per day. The temperature averaged 19°C ± 2°C with an average relative humidity of 52%.

C. **Dosage:** 14-day single dose oral LD50 test. Based on "known toxicity data" nominal dosages selected for the definitive study were 292, 486, 810, 1350, and 2250 milligrams of ametryn per kilogram of body weight.

D. **Design:** Groups of ten birds (five males and five females) were randomly assigned to each of the five treatment groups and the control group. Each group was assigned two pens. One pen contained five males and the other five females. The birds were fed a game bird ration formulated to Wildlife International Ltd.'s specifications. Food and water were supplied ad libitum except for a period of "at least 15 hours" prior to dosing when the birds were fasted, with water allowed. At test initiation, a single dose of test material in diluent (corn oil) was orally intubated into the crop or proventriculus of each bird using a stainless steel catheter. Each bird was individually weighed and dosed on the basis of milligrams of test substance per kilogram of body weight. The control birds received diluent only. All treatment and control birds received a constant dosage volume of 6 milliliters per kilogram of body weight. The birds were individually weighed at test initiation and by group on days 3, 7, and 14. Group food consumption was recorded on test days 3, 7, and 14. Observations were conducted at least twice daily for potential clinical signs indicative of test material effect.

E. **Statistics:** The LD50 was not calculated, since less than half of the birds died in the 2250 mg/kg group. No statistical analyses of body weight or food consumption were reported.

12. **REPORTED RESULTS:** There were no mortalities in the control group, or in the 292, 486, and 810 mg/kg groups. Three of 10 birds died at the 1350 mg/kg dosage and 2 of 10 died at the 2250 mg/kg dosage.

Two birds were found dead in the 1350 mg/kg group on the morning of Day 1, and one on the morning of Day 2. The two mortalities from the 2250 mg/kg group were noted on the morning of Day 1.

All birds in the control, 292, and 486 mg/kg groups were normal in appearance and behavior throughout the study.

Behavioral abnormalities attributed to ametryn intoxication were noted in the 810, 1350, and 2250 mg/kg groups. Symptoms included lethargy, depression, ruffled appearance, wing droop, reduced reaction to external stimuli, lower limb weakness and loss of coordination. At 810 mg/kg, signs of toxicity were first noted 45 minutes after dosing and continued through the afternoon of Day 6. At 1350 mg/kg, signs of toxicity were first noted 35 minutes after dosing and continued through the morning of Day 8. At 2250 mg/kg, signs of toxicity were first noted 30 minutes after dosing. Most birds in this group had recovered by the morning of Day 10, but one bird displayed symptoms of toxicity through the morning of Day 12.

When compared to controls, there was a loss in body weight at 810, 1350, and 2250 mg/kg from Day 0 to Day 3. "A loss in body weight continued among females at 1350 mg/kg and among males and females at 2250 mg/kg through Day 7. A corresponding reduction in feed consumption was noted at 810, 1350, and 2250 mg/kg from Day 0 to Day 3. A reduction in feed consumption continued at 2250 mg/kg through Day 7."

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The acute oral LD50 of ametryn was determined to be greater than 2250 mg/kg a.i., the highest dosage tested. The no-observed effect dosage was 486 mg/kg, based on signs of toxicity, body weight loss, and reduced food consumption at 810 mg/kg.

The study was designed and conducted in conformance with Good Laboratory Practice regulations. The data were

inspected and the final report signed by the Quality Assurance Officer of Wildlife International Ltd.

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

A. Test Procedure: The test procedures were in accordance with SEP guidelines except for the following deviations:

Body weights were measured by group at the end of the study. According to the SEP, individual body weights should be measured.

Gross necropsies were not performed.

B. Statistical Analysis: The LD50 was not calculated due to the observed mortality pattern. The only deaths occurred in the two highest dosage groups and in each case was less than 50% (30 % at 1350 mg/kg and 20% at 2250 mg/kg). The LD50 is assumed to be greater than the highest dosage tested (2250 mg/kg).

C. Discussion/Results: An examination of Table 2 (attached) indicates reductions in body weight and food consumption in the 810, 1350, and 2250 mg/kg groups from Day 0 to Day 3. These effects continued through Day 7 in the 2250 mg/kg group.

The acute oral LD50 of ametryn was determined to be greater than 2250 mg/kg, the highest dosage tested. This value classifies ametryn as practically non-toxic to bobwhite quail. Weight loss and behavioral signs of toxicity were observed, however, in the 810, 1350, and 2250 mg/kg groups. Behavioral abnormalities were noted in the 810 mg/kg group for six days following dosing. These signs of intoxication indicate sublethal effects which could effect the birds' ability to survive in the wild. The no-observed effect dosage was 486 mg/kg.

The study is scientifically sound and meets the requirements for an avian single dose oral LD50 test.

D. Adequacy of the Study:

(1) Classification: Core

(2) Rationale: N/A

(3) Repairability: N/A

15. COMPLETION OF ONE-LINER: Yes; April 14, 1989.

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Shaughnessey No. 80801 Chemical Name Ametryn Chemical Class ____ Page 1 of 1

Study/Species/Lab/ Accession	Chemical % a.i.	Results	Reviewer/ Date	Validat Status
14-Day Single Dose Oral LD_{50}		LD50 = * mg/kg (* 95% C.L.) Contr. Mort.(%) = 0		
Species Bobwhite quail (Colinus virginianus)	99.0%	Slope = * # Animals/Level = 10 Age(Days) = 119 Sex = 5M, 5F	M L WHITTEN 4-14-89	CBI
Lab Wildlife International Ltd		14-Day Dose Level mg/kg/(% Mortality) 292 (0), 486 (0), 810 (0), 1350 (30%), 2250 (20%)		
Acc. 409958-01		Comments: *LD50 GREATER THAN HIGHEST DOSE TESTED (2250 mg/kg)		
14-Day Single Dose Oral LD_{50}		LD50 = mg/kg. (95% C.L.) Contr. Mort.(%) =		
Species ____		Slope = # Animals/Level = Age(Days) = Sex =	____	____
Lab		14-Day Dose Level mg/kg/(% Mortality) ( ), ( ), ( ), ( ), ( )		
Acc.		Comments:		
8-Day Dietary LC_{50}		LC50 = ppm (95% C.L.) Contr. Mort.(%) =		
Species		Slope = # Animals/Level = Age(Days) = Sex =		
Lab ____		8-Day Dose Level ppm/(%Mortality) ( ), ( ), ( ), ( ), ( )	____	____
Acc.		Comments:		
8-Day Dietary LC_{50}		LC50 = ppm (95% C.L.) Contr. Mort.(%) =		
Species		Slope = # Animals/Level = Age(Days) = Sex =		
Lab ____		8-Day Dose Level ppm/(%Mortality) ( ), ( ), ( ), ( ), ( )	____	____
Acc.		Comments:		
48-Hour L_{50}		LC50 = ___ (95% C.L.) Contr. Mort.(%) =		
Species		Slope = # Animals/Level = Sol. Contr. Mort.(%) =		
Lab ____		48-Hour Dose Level /(%Mortality) Temperature = ( ), ( ), ( ), ( ), ( )	____	____
Acc.		Comments:		
96-Hour LC_{50}		LC50 = pp___ (95% C.L.) Con. Mor.(%) =		
Species		Slope = # Animals/Level = Sol. Con. Mor.(%) =		
Lab ____		96-Hour Dose Level pp /(%Mortality) Temp. = ( ), ( ), ( ), ( ), ( )	____	____
Acc.		Comments:		
96-Hour LC_{50}		LC50 = pp___ (95% C.L.) Con. Mort.(%) =		
Species		Slope = # Animals/Level = Sol. Con. Mort.(%) =		
Lab ____		96-Hour Dose Level pp /(%Mortality) Temp. = ( ), ( ), ( ), ( ), ( )	____	____
Acc.		Comments:		