3/22/94

MRID No. 429186-19

DATA EVALUATION RECORD

1. **CHEMICAL:** MB 46030 (Fipronil).
Shaughnessey Number: 129121.

2. **TEST MATERIAL:** EXP 60655A; CAS No. 120068-37-3; Reference No. 46LEHX-92; 1.6% active ingredient (fipronil); brown-colored granules.

3. **STUDY TYPE:** 71-1A. Avian Single Dose Oral LD_{50} Test.
Species Tested: Bobwhite Quail (Colinus virginianus).

4. **CITATION:** Pedersen, C.A. and D.R. DuCharme. 1993. EXP 60655A: 21-Day Acute Oral LD_{50} Study in Bobwhite Quail. Study performed by Bio-Life Associates, Ltd., Neillsville, Wisconsin. Laboratory Project No. 108-018-03. Submitted by Rhone-Poulenc Ag Company, Research Triangle Park, North Carolina. EPA MRID No. 429186-19.

5. **REVIEWED BY:**

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Signature: 2/18/94 **Date:**

6. **APPROVED BY:**

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Signature: 3/10/94 **Date:**

James J. Goodyear, Ph.D.
Project Officer, EEB/EFED
USEPA

Signature: **Date:** 3 21 94

7. **CONCLUSIONS:** The study is scientifically sound but does not meet the guideline requirements for an avian oral LD_{50} test. Based on nominal concentrations, the LD_{50} was 1065 mg/kg (17.0 mg ai/kg). This classifies the formulated product as slightly toxic to bobwhite quail. The NOEL was 175 mg/kg (2.8 mg ai/kg).

8. **RECOMMENDATIONS:** N/A.

9. **BACKGROUND:**

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5. **REVIEWED BY:**

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Project Officer, EEB/EFED
USEPA

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Date:

7. **CONCLUSIONS:** The study is scientifically sound ~~and fulfills~~ as but does not fulfill the requirements for an avian oral LD_{50} test.* Based on nominal concentrations, the LD_{50} was 1065 mg/kg (17.0 mg ai/kg). This classifies the formulated product as slightly toxic to bobwhite quail. The NOEL was 175 mg/kg (2.8 mg ai/kg). as

*Test chemical was the formulated product.

8. **RECOMMENDATIONS:** N/A.

9. **BACKGROUND:**

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10. **DISCUSSION OF INDIVIDUAL TESTS:** N/A.

11. **MATERIALS AND METHODS:**

A. **Test Animals:** The birds used in the study were 35-week-old bobwhite quail (Colinus virginianus) obtained from Oak Ridge Game Farm, Gravette, Arkansas. All birds were from the same hatch and were phenotypically indistinguishable from wild birds. The quail had been under dim lights for 24 hours per day all of their lives. The birds were placed on a 92-day quarantine period when they were received from the supplier. Thirty-two pairs of birds were selected for the study seven days prior to dosing. The birds were moved to a new building when they were selected and were allowed to acclimate to the testing conditions for seven days. All birds appeared to be in good health at initiation of the test.

B. **Test System:** The birds were housed indoors in pens constructed of wire mesh which were maintained over steel pans. The pens measured 61.0 x 53.3 x 38.1 cm.

The photoperiod was ten hours of natural daylight spectrum light per day during the acclimation period and throughout the test. The temperature averaged 76°F with relative humidity averaging 46%.

C. **Dosage:** Twenty-one-day single dose oral LD_{50} test. Based on preliminary studies and a failed 14-day study, the dosages selected for testing were 87.5, 175, 350, 700, and 1400 milligrams of the formulated product per kilogram of body weight (mg/kg).

D. **Design:** Ten birds (five female and five male) were randomly assigned to each of five treatment groups and one control group. The birds were housed separately by sex. The birds were fasted for approximately 20 hours prior to dosing.

The test substance was dispensed directly into gelatin capsules. The birds in the control group were given an empty gelatin capsule. Each bird was individually weighed and dosed on the basis of milligrams of formulated product per kilogram of body weight.

All birds were fed Purina Custom Game Bird Layena. Food was supplied ad libitum, except for the fasting period prior to dosing. Water was available to the birds at all times.

Inspections were made twice daily (except on weekends) for mortalities and clinical signs of toxicity. Daily inspections were made for abundance of food and water, and food spillage.

Birds were weighed individually at test initiation, days 3, 7, 14, and at test termination (day 21). Group food consumption values were recorded on test days 3, 7, 14, and 21.

All birds that died during the study were subjected to gross pathological examinations. Four arbitrarily selected birds (two male and two female) from the control group and four lowest dosage treatment groups were subjected to gross pathological examinations on test day 21. The one surviving bird from the highest treatment group was also examined for pathological abnormalities.

E. **Statistics:** The LD_{50} was determined and body weight data were analyzed using a commercial statistical package which employed probit analysis.

12. **REPORTED RESULTS:** No clinical signs of toxicity were noted in the control or the three lowest-dosage treatment groups.

Signs of toxicity were observed in birds at the two highest treatment levels. The clinical signs included: chalky excreta, chalky diarrhea, lethargy, noticeable weight loss, and noticeable feather loss on the head and back (one male only) in the 700 mg/kg (11.2 mg ai/kg) treatment group; chalky excreta, chalky diarrhea, lethargy, loss of righting reflexes (lying on the back), dyspnea, convulsions, being sprawled out with the wings outstretched, and death in the 1400 mg/kg (22.4 mg ai/kg) treatment group (Table 5, attached).

Statistically significant weight depressions were reported for the 700 and 1400 mg/kg treatment groups on days 3 and 7 and again in the 700 mg/kg treatment group on test days 14 and 21 (Table 6, attached).

Dose-correlated food consumption depressions were noted during the first three test days in the 350 mg/kg treatment group, during the first seven days in the 700 mg/kg treatment group, and during the first 14 days in the 1400 mg/kg treatment group. The birds in the 1400 mg/kg treatment group apparently did not eat any feed from day 4 through day 14 (Table 7, attached).

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Nine birds in the 1400 mg/kg treatment group died during the study. The deaths occurred between test days 7 and 16 (Table 3, attached). Gross pathological examinations of these birds revealed abnormal findings in all nine birds. Seven birds had a crop which was void of contents and/or air-filled. Emaciation was noted for five birds and their gizzards were empty. Three birds had gizzards that were green inside and green contents were found in the gizzards of four other birds.

Gross pathological examinations of the 21 arbitrarily selected survivors revealed abnormal findings in three birds. One 350 mg/kg bird had a friable liver, one 700 mg/kg bird had gaseous intestines, and the one surviving 1400 mg/kg bird was emaciated and had a pale liver.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The acute oral LD_{50} for the formulated product was 1079 mg/kg (17.3 mg ai/kg) with 95% confidence limits of 844 and 1329 mg/kg (13.5 and 21.3 mg ai/kg). The no-observed-effect-level (NOEL) was 175 mg/kg (2.8 mg ai/kg).

Quality Assurance and Good Laboratory Practice statements were included in the report indicating conformance with GLP regulations as set forth in 40 CFR Part 160.

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

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

The birds were only acclimated to the testing conditions for seven days. The SEP recommends that birds be acclimated to testing conditions for a minimum of 15 days.

The concentrations of the dosing solutions were not confirmed by chemical analysis. This is recommended, but not required.

B. **Statistical Analysis:** The reviewer used EPA's Toxanal computer program to calculate the LD_{50} value (attached printout). The reviewer's calculated LD_{50} (1065 mg/kg) was slightly lower than the author's value (1079 mg/kg) and will therefore be reported.

C. **Discussion/Results:** The study is scientifically sound but does not meet the guideline requirements of an avian acute oral LD_{50} study. Based on nominal concentrations,

the LD_{50} was 1065 mg/kg. This classifies the formulated product as slightly toxic to bobwhite quail. The NOEL for the formulated product was 175 mg/kg (2.8 mg ai/kg).

D. **Adequacy of the Study:**

(1) **Classification:** Supplemental.

(2) **Rationale:** SEP states that "routine tests must be conducted with the technical grade of the active ingredient (a.i.)".

(3) **Repairability:** N/A.

15. **COMPLETION OF ONE-LINER:** Yes; January 13, 1994.

Fifra 10 denied

Page _____ is not included in this copy.

Pages 7 through 12 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

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