3/11/94

MRID No. 429186-17

FILE COPY

DATA EVALUATION RECORD

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

2. **TEST MATERIAL:** M & B 46030 technical; Lot No. JJW-2127; approximately 96% purity; a white solid.

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

4. **CITATION:** Pedersen, C.A. 1990. M & B 46030 Technical: 21-Day Acute Oral LD_{50} Study in Bobwhite Quail. Study performed by Bio-Life Associates, Ltd., Neillsville, Wisconsin. Laboratory Project No. 89 QD 133. Submitted by Rhone-Poulenc Ag Company, Research Triangle Park, North Carolina. EPA MRID No. 429186-17.

5. **REVIEWED BY:**

Nicole U. Jurczyk, M.S.
Associate Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: Nicole U. Jurczyk
Date: 1/12/94

6. **APPROVED BY:**

Mark A. Mossler, M.S.
Associate Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: Mark A. Mossler
Date: 1/12/94

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

Signature: James J. Goodyear
Date: 3 11 94

2/23/94

3/9/94

7. **CONCLUSIONS:** The study is scientifically sound and fulfills the requirements for an avian oral LD_{50} test. Based on nominal concentrations, the LD_{50} was 11.3 mg/kg. This classifies the test material as highly toxic to bobwhite quail. An NOEL could not be determined.

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

9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** The birds used in the study were approximately 44-week old bobwhite quail (*Colinus virginianus*) obtained from Oak Ridge Game Farm, Gravette, Arkansas. All birds were phenotypically indistinguish-able from wild birds. The quail had been in egg production, but the lights were taken away from them 4 or 5 weeks prior to their shipment to the testing facility. The birds were acclimated to the testing conditions for 31 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 x 53 x 39 cm.

The photoperiod (maintained by a time clock) was eight hours of fluorescent light per day during the acclimation period and throughout the test. The temperature ranged from 62°F to 84°F with relative humidity between 53% and 82%.

C. **Dosage:** Twenty-one-day single dose oral LD_{50} test. Based on preliminary studies, the dosages selected for testing were 1, 4.64, 10, 21.5, and 46.4 milligrams of test substance per kilogram of body weight (mg/kg). The dosage concentrations were not adjusted for purity of the test substance which had a reported purity of approximately 96%.

D. **Design:** The birds were randomly assigned to five treatment groups and one control group. Ten birds (five female and five male) were assigned to each pen. The birds were fasted for 18 hours prior to dosing.

The test substance was mixed with acetone and dispensed into gelatin capsules. The acetone was allowed to evaporate before the capsules were closed. The control group was given gelatin capsules containing evaporated acetone only. Each bird was individually weighed and dosed on the basis of milligrams of test substance per kilogram of body weight.

All birds were fed Purina Duck Grower W/O. Food was supplied *ad libitum*, except for the 18 hour fasting period prior to dosing. Water was available to the birds at all times.

Daily inspections were made throughout the study for mortalities, clinical signs of toxicity, 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 three lowest dosage treatment groups were subjected to gross pathological examinations on test day 21.

E. **Statistics:** The LD_{50} was determined using the Litchfield and Wilcoxon method. Body weight data were analyzed using one-way analysis of variance ($p< 0.05$).

12. **REPORTED RESULTS:** All control birds and 1 mg/kg dosage level birds were normal in appearance and behavior for the duration of the test.

Signs of toxicity were observed in the four highest treatment level groups. The clinical signs included: lethargy, moving the head from side to side when disturbed, chalky diarrhea, anorexia, stumbling, ataxia, tremors, tachypnea, wing-beat convulsions, tetany, spasms, loss of balance, piloerection, sitting, failure to respond to external stimuli, gasping for breath, noticeable weight loss, the appearance of weakness or listlessness, and death. Total remission was achieved by test day 18. Deaths occurred from test day 3 through test day 18. Three deaths were recorded in the 10 mg/kg treatment group and all of the birds in the two highest treatment level groups died (Table 4, attached).

Statistically significant weight depressions were reported for the 4.64 and 10 mg/kg treatment groups on days 3,7, and 14. Significantly depressed body weights were also recorded for the two highest treatment level groups before the birds died. Body weights for surviving treatment groups on test day 21 of the study were statistically comparable to the control group's values (Table 6, attached).

Dose-correlated food consumption depressions were noted during the first three test days in all of the treatment groups. The depressions continued through test day 7 in the

4.64 mg/kg treatment group, and through test day 14 in the 10 and 21.5 mg/kg treatment groups (Table 6, attached).

Gross pathological examinations revealed abnormal findings in 18 of the 23 birds that died during the study. A complete description of all abnormal findings was included in the report. The abnormal findings in the 10 mg/kg treatment group included severe emaciation, an intestinal tract impacted with food, and gaseous intestines. Pathological findings in the 21.5 mg/kg treatment level birds included severe emaciation, friable liver, blood clot around the heart, and various gastro-intestinal abnormalities. The 46.4 mg/kg treatment level birds were reported as having large crops filled with feed, water and air, friable livers, and void intestines. The only abnormal finding in birds arbitrarily selected for necropsy was an enlarged liver in one 4.64 treatment level bird.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The acute oral LD_{50} for the test material was determined to be 11.3 mg/kg with 95% confidence limits of 9.2 to 13.9 mg/kg. The no-observed-effect-level (NOEL) could not be determined. Mortality in the study was markedly delayed. This is abnormal for an insecticide, but might be considered normal for a rodenticide, such as an anticoagulent. Based on the results of the study, the test material would be classified as practically non-toxic.

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 had been in egg production before their shipment to the testing facility. The SEP recommends birds be used that are not in a reproductive state.

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 results were similar to the author's results.

C. **Discussion/Results:** The study is scientifically sound and meets the requirements of an avian acute oral LD_{50} study. Based on nominal concentrations, the LD_{50} was 11.3 mg/kg for bobwhite quail. This classifies the test material as highly toxic to bobwhite quail. The NOEL could not be determined due to a reduction in food consumption at all treatment levels.

D. **Adequacy of the Study:**

(1) **Classification:** Core.

(2) **Rationale:** N/A.

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

15. **COMPLETION OF ONE-LINER:** Yes; January 4, 1994.

nicole jurczyk FIPRONIL COLINUS VIRGINIANUS 01-04-94

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
46.4	10	10	100	9.765625E-02
21.5	10	10	100	9.765625E-02
10	10	3	30	17.1875
4.64	10	0	0	9.765625E-02
1	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 4.64 AND 21.5 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 11.90934

WHEN THERE ARE LESS THAN TWO CONCENTRATIONS AT WHICH THE PERCENT DEAD IS BETWEEN 0 AND 100, NEITHER THE MOVING AVERAGE NOR THE PROBIT METHOD CAN GIVE ANY STATISTICALLY SOUND RESULTS.

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FIPRONIL REVIEW

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