5/6/94

MRID No. 429186-15

DATA EVALUATION RECORD

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

2. **TEST MATERIAL:** M & B 46030 technical; Batch No. PGS 963; 95.4% purity; an off-white powder.

3. **STUDY TYPE:** 71-1A. Avian Single Dose Oral LD_{50} Test.
Species Tested: Pheasant (*Phasianus colchicus*).

4. **CITATION:** Hakin, B. and M. Rodgers. 1992. M & B 46030: Acute Oral Toxicity (LD_{50}) to the Pheasant. Study performed by Huntingdon Research Centre Ltd., Cambridgeshire, England. Laboratory Report No. RNP 389/911137. Submitted by Rhone-Poulenc Agrochimie, Lyon Cedex, France. EPA MRID No. 429186-15.

5. **REVIEWED BY:**

Andrew C. Bryceland, Fishery Biologist **Signature:**
Review Section 5
Ecological Effects Branch
Environmental Fate and Effects Division (7507C) **Date:** 3/15/94

6. **APPROVED BY:**

Ann Stavola, Supervisory Biologist **Signature:**
Review Section 5
Ecological Effects Branch
Environmental Fate and Effects Division (7507C) **Date:** 5/6/94

7. **CONCLUSIONS:** The study is scientifically sound but does not meet the guideline requirements for an avian oral LD_{50} test. The test species was not one of the Agency's required species. The oral LD_{50} was 31 mg/kg (nominal dosage), which classifies the test material as highly toxic to pheasants. The NOEL was 5 mg/kg.

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

9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

DATA EVALUATION RECORD

1. **CHEMICAL:** MB 46030 (Fipronil).
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5. **REVIEWED BY:**

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

Signature:
Date: 1/18/94

6. **APPROVED BY:**

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

Signature:
Date: 1/19/94
2/22/94

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

Signature:
Date:

7. **CONCLUSIONS:** The study is scientifically sound and meets the requirements for an avian oral LD_{50} test. The oral LD_{50} was 31 mg/kg (nominal dosage), which classifies the test material as highly toxic to pheasants. The NOEL was 5 mg/kg.

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

9. **BACKGROUND:**

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

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A. **Test Animals:** The birds used in the study were pheasants (*Phasianus colchicus*) obtained from a supplier in Kent, England. The birds were young adults over sixteen weeks of age, were phenotypically indistinguishable from the wild type, and were in the body weight range of 1015-1570 grams. The birds were acclimated to the testing facility for 15 days prior to testing. Water was continuously accessible. Except for a 20-hour fasting period immediately prior to dosing, Standard HRC layer diet in pellet form was offered *ad libitum* during acclimation and testing. No antibiotics were incorporated in the diet.

B. **Test System:** All birds were housed indoors in pens with floor spaces measuring 1.5 x 1.25 meters. The pens were constructed of galvanized steel and had concrete floors. Lights provided seven to eight hours of illumination per day. The birds were housed in two rooms. The average temperature was 15-18°C and the average relative humidity was 82-87%.

C. **Dosage:** Thirty-five-day single dose oral LD_{50} test. Based on the results of a range-finding test, the five dosages selected were 5, 10, 20, 40, and 80 milligrams of test material per kilogram of body weight (mg/kg). The dosages were not corrected for the percentage purity of the test material. Control birds were dosed with the vehicle (corn oil).

D. **Design:** Fifteen days prior to test initiation, groups of ten birds (five males and five females) were arbitrarily assigned to each treatment and control group by body weight so that all test groups would have similar initial bodyweight means. The birds were separated by sex.

The test substance was dissolved in corn oil and intubated directly into each bird using a plastic catheter and disposable syringe. A 20 milliliter (ml) sample of each dosing solution was taken immediately after preparation. The samples were stored at -20°C for possible future analysis.

Each bird was individually weighed and dosed on the basis of milligrams of test substance per kilogram of body weight. The control birds received a corresponding volume of corn oil only. The birds were dosed at a volume of 5 ml/kg of body weight.

The birds were observed daily during the study and at frequent intervals during the post-treatment period. Mortalities, signs of toxicity, and abnormal behavior were recorded at each observation.

The birds were weighed individually 15 and 7 days prior to the start of the study, at test initiation, on day 7, 14, 21, 28, and on the last day of the study (day 35). Average group food consumption values were recorded several times during the acclimation period and for days 1-7, 8-14, 15-21, 22-28, and 29-35 of the study.

Pathological examinations were performed on all birds that died during the study and all surviving birds in the highest treatment level group (80 mg/kg).

E. **Statistics:** The LD_{50} and 95% confidence interval were determined by probit analysis with MLP. Analysis of variance was carried out for individual body weight data.

12. **REPORTED RESULTS:** All control birds remained in good health throughout the study.

Clinical signs in test birds included subdued behavior, unsteadiness, inability to stand, and death. The 5 mg/kg dosed birds were in good health and showed no clinical signs except one bird that was subdued on days 12 to 14 of the study. This clinical sign was believed to be unrelated to treatment.

All birds in the 10 mg/kg group were subdued on day 10 and one bird continued to be subdued on days 12 through 21 (Appendix 2, attached).

At the 20 mg/kg treatment level there were three mortalities and subdued behavior between days 7 and 30.

There were seven mortalities at the 40 mg/kg treatment level. Six of the deaths occurred between days 3 and 10, and the seventh occurred on day 18. Subdued behavior and varying degrees of unsteadiness were observed from day 3 to 30.

At 80 mg/kg, the highest dose level tested, nine birds died by day 15. Subdued behavior and varying degrees of unsteadiness were observed from day 3 to 35 in this group.

Individual body weights measured on days 7, 14, 21, 28, and 35 were statistically analyzed. The 80 mg/kg body weights

were not analyzed due to high mortality in this group. A complete record of individual body weights was included in the report. The only statistically significant weight differences were in the 20 and 40 mg/kg groups on day 7. The birds in these two groups were significantly lighter than the controls (Table 2, attached).

A clear reduction in food consumption during days 1 to 7 was observed in male birds treated at 20, 40, and 80 mg/kg of the test material. A clear reduction in food consumption was observed during days 1 to 21 in female birds treated with 40 mg/kg and 80 mg/kg (Table 3, attached).

There were no abnormal pathological findings in any of the birds that were examined.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The LD_{50} for the test material was calculated to be 31 mg/kg with 95% confidence limits of 22 to 44 mg/kg. The no-observed-effect-level (NOEL) was 10 mg/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 test species is not a species recommended by SEP guidelines, but parallel studies (MRID Nos. 429186-16 and 429186-17) were performed using recommended species (mallard ducks and bobwhite quail).

B. **Statistical Analysis:** The reviewer used EPA's Toxanal computer program to calculate the LD_{50} value (attached printout). The LD_{50} (31 mg/kg) and confidence interval were the same as reported by the authors. The slope of the probit dose response curve was 3.7.

C. **Discussion/Results:** Pathological examinations were performed only on birds from the 80 mg/kg treatment group. A cross-section of test groups may have provided more definitive evidence that there were also no abnormalities at lower dose levels.

The reviewer does not agree that the NOEL was 10 mg/kg. The highest level at which no treatment-related effects

occurred was 5 mg/kg. The authors state that all birds in the 10 mg/kg group were subdued on day 10 and that one bird remained subdued for nine days (Appendix 2). An NOEL of 5 mg/kg will therefore be reported.

This study is scientifically sound but does not fulfill the guideline requirements for an oral LD_{50} test. With an LD_{50} of 31 mg/kg (nominal dosage), the test material is classified as highly toxic to pheasants. The NOEL was 5 mg/kg.

D. **Adequacy of the Study:**

(1) **Classification:** Supplemental.

(2) **Rationale:** Test species not one of those required by the Agency.

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

15. **COMPLETION OF ONE-LINER:** Yes; January 6, 1994.

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Figure Deleted

Page _____ is not included in this copy.

Pages 7 through 13 are not included in this copy.

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Nicole Ushakoff FIPRONIL PHASIANUS COLCHICUS 01-07-94

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CONC.	NUMBER EXPC3ED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
80	10	9	90	1.074219
40	10	7	70	17.1875
20	10	3	30	17.1875
10	10	0	0	9.765625E-02
5	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 10 AND 80 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 28.28427

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
3	.167754	30.42928	21.76614	43.81271

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
4	.2265628	1	.8352036

SLOPE = 3.702101
95 PERCENT CONFIDENCE LIMITS = 1.939952 AND 5.464249

LC50 = 30.90433
95 PERCENT CONFIDENCE LIMITS = 22.04331 AND 44.31796

LC10 = 14.0272
95 PERCENT CONFIDENCE LIMITS = 6.309082 AND 20.08238

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