5-6-94

MRID No. 429186-13

DATA EVALUATION RECORD

1. **CHEMICAL:** MB 46030 (Fipronil).
Shaughnessey No. 129121.

2. **TEST MATERIAL:** M & B 46030 technical; Batch No. 78GC90; 97.7% purity.

3. **STUDY TYPE:** 71-1A. Avian Single Dose Oral LD_{50} Test. Species Tested: Pigeon (*Columba livia*).

4. **CITATION:** Hakin, B. and M. Rodgers. 1991. M & B 46030: Acute Oral Toxicity to the Pigeon (*Columba livia*). Project No. RNP 376/91264. Performed by Huntingdon Research Centre Ltd., Cambridgeshire, UK. Submitted by Rhone-Poulenc Agrochimie, Lyon Cedex, France. EPA MRID No. 429186-13.

5. **REVIEWED BY:**

Andrew C. Bryceland, Fishery Biologist **Signature:** [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:** [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 fulfill the guideline requirements for an oral LD_{50} test. The test species was not one of those required by the Agency. Since regurgitation was observed at the two highest dosage levels, the LD_{50} could only be reported as being greater than 500 mg/kg (nominal dosages). This would classify MB 46030 (at worst) as slightly toxic to pigeons. It was not possible to dose the birds to the recommended level of 2000 mg/kg due to emesis at dosage levels of 1000 mg/kg and greater. The NOEL could not be determined due to treatment-related reductions in body weight gain or body weight loss at all treatment levels.

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

9. **BACKGROUND:**

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

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7. **CONCLUSIONS:** The study is scientifically sound but does not fulfill the guideline requirements for an oral LD_{50} test. Since regurgitation was observed at the two highest dosage levels, the LD_{50} could only be reported as being greater than 500 mg/kg (nominal dosages). This would classify MB 46030 (at worst) as slightly toxic to pigeons. It was not possible to dose the birds to the recommended level of 2000 mg/kg due to emesis at dosage levels of 1000 mg/kg and greater. The NOEL could not be determined due to treatment-related reductions in body weight gain or body weight loss at all treatment levels.

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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 adult pigeons (*Columba livia)* obtained from a supplier in Cambridgeshire, UK. The birds were approximately one year old and were within the body weight range of 354-540 grams at the start of the study. The birds were acclimated to the laboratory for 15 days prior to testing. Water was continuously accessible. Except for an overnight fasting period immediately prior to dosing, wheat grain 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 (1.44 x 0.55 x 0.50 meters) constructed of plastic-coated wire. Lights provided ten hours of illumination per day. The average temperature was 19-20°C and the average relative humidity was 45%.

C. **Dosage:** Fourteen-day single dose oral LD_{50} test. Based on the results of a range-finding test, the five dosages selected were 125, 250, 500, 1000, and 2000 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 dispersed 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 10 ml/kg of body weight.

The birds were continuously observed for the first 2 1/2 hours after dosing. Daily inspections were made for mortality, signs of toxicity, and abnormal behavior.

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

At the termination of the study, pathological examinations were performed on the ten birds from the highest dosage group (2000 mg/kg).

E. **Statistics:** There were no mortalities during the study. Therefore, the LD_{50} was not established using statistical methods.

12. **REPORTED RESULTS:** There were no mortalities or signs of toxicity in any of the control birds.

Approximately 70 minutes after dosing, regurgitation of feed and/or dose material was noted in three birds in the 1000 mg/kg group and six birds in the 2000 mg/kg group. The regurgitation continued at varying time intervals up to approximately 140 minutes after dosing. There were no clinical signs of toxicity recorded for any of the birds after the initial regurgitation period.

Individual bodyweights measured on days 7 and 14 were statistically analyzed and the treatment-sex interaction was found to be non-significant. All treatment groups were found to have significantly lower bodyweights when compared with the control groups on day 7. At test termination, birds in the 2000 mg/kg group were significantly lighter than those in the control group (Table 1, attached).

When compared to the control group, food consumption was reduced in the four highest dosage groups during the first seven days of the study (Table 2, attached). No other treatment-related effects were observed during the study and no pathological abnormalities were observed in any of the ten birds examined at the end of the study.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The LD_{50} for the test material was determined to be greater than 2000 mg/kg. Significant bodyweight reductions were noted in all treatment groups on day 7 and in the highest treatment group on day 14. The non-emetic dose level was 500 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 concentrations of the dosing solutions were not confirmed by chemical analysis. This is recommended, but not required.

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).

The birds were not randomly assigned to groups. Instead, they were assigned to groups based on bodyweight. The groups were then randomly assigned treatment levels.

Birds in the two highest dosage level treatment groups regurgitated some or all of the administered dose.

B. **Statistical Analysis:** Since there were no mortalities during the test, the LD_{50} could not be calculated.

C. **Discussion/Results:** Six birds in the 2000 mg/kg treatment group regurgitated repeatedly soon after dosing. In addition, three of the birds dosed with 1000 mg/kg regurgitated the dose and/or the feed following dosing. This suggests that at least a portion of the dose was rejected by those birds. No regurgitation was observed in the 500 mg/kg group, and no birds died at that level; therefore, it appears that the LD_{50} was greater than 500 mg/kg.

Pathological examinations were performed only on birds from the 2000 mg/kg treatment group. In light of the problem with regurgitation of the dose in this treatment

group, it would have been prudent to examine birds that were known to have received their complete dosage.

The authors stated that the average body weights of birds in all treatment groups were significantly less than the control group on day 7. It appears that the lowered bodyweight is treatment related, and no statement was made by the authors to contradict this conclusion. The reviewer therefore concludes that a no-observed-effect-level (NOEL) was not achieved in this study.

The study is scientifically sound but does not fulfill the guideline requirements for an oral LD_{50} test. Since regurgitation was observed at the two highest dosage levels, the LD_{50} could only be reported as being greater than 500 mg/kg (nominal dosages). This would classify MB 46030 (at worst) as slightly toxic to pigeons. It was not possible to dose the birds to the recommended level of 2000 mg/kg due to emesis at dosage levels of 1000 mg/kg and greater. The NOEL could not be determined due to treatment-related reductions in body weight gain or body weight loss at all treatment levels.

D. **Adequacy of the Study:**

(1) **Classification:** Supplemental.

(2) **Rationale:** Regurgitation was observed in the two highest dosage groups. Therefore, the LD_{50} could only be reported as greater than 500 mg/kg. Additionally this test was performed using a non-standard test species, the SEP states that "testing must be done on either a waterfowl species, preferably mallard duck, or an upland game species, preferably bobwhite quail".

(3) **Repairability:** No.

15. **COMPLETION OF ONE-LINER:** Yes; January 5, 1994.

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Financial Summary

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