3/21/94

MRID No. 429186-18

DATA EVALUATION RECORD

FILE COPY

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

2. **TEST MATERIAL:** M & B 46030 technical; Ref. No. 78GC90; 96.7% purity; a white powder.

3. **STUDY TYPE:** 71-1A. Avian Single Dose Oral LD_{50} Test.
Species Tested: House Sparrow (Passer domesticus).

4. **CITATION:** Pedersen, C.A. and B.R. Helsten. 1991. M & B 46030 Technical: 14-Day Acute Oral LD_{50} Study in House Sparrows. Study performed by Bio-Life Associates, Ltd., Neillsville, Wisconsin. Laboratory Project No. 108-002-19. Submitted by Rhone-Poulenc Ag Company, Research Triangle Park, North Carolina. EPA MRID No. 429186-18.

5. **REVIEWED BY:**

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

6. **APPROVED BY:**

Ann Stavola, Supervisory Biologist **Signature:**
Review Section 5
Ecological Effects Branch
Environmental Fate and Effects Division (7507C) **Date:** 3/10/94

James J. Goodyear, Ph.D. **Signature:**
Project Officer, EEB/EFED
USEPA **Date:** 3 24 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 1000 mg ai/kg which classifies MB 46030 as slightly toxic to house sparrows. An NOEL could not be determined.

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

9. **BACKGROUND:**

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

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5. **REVIEWED BY:**

Nicole U. Jurczyk, M.S.
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KBN Engineering and
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Signature: Nicole U Jurczyk
Date: 1/18/94

6. **APPROVED BY:**

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

Signature: Anne Lavoie
Date: 3/9/94

7. **CONCLUSIONS:** The study is scientifically sound and ~~fulfills~~ but does not fulfil ~~the~~ requirements for an avian oral LD_{50} test. Based on nominal concentrations, the LD_{50} was 1000 mg ai/kg which classifies MB 46030 as slightly toxic to house sparrows. An NOEL could not be determined. House sparrow is not a required species. AL 3/9/94

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

9. **BACKGROUND:**

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

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11. **MATERIALS AND METHODS:**

A. **Test Animals:** The birds used in the study were house sparrows (Passer domesticus) of undefined age. The birds were live-trapped by Bio-Life Associates, Ltd. personnel in Wisconsin. Approximately four months after trapping began, all birds were placed on a 21-day quarantine period. Birds selected for the experiment 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 53.3 x 45.7 x 38.1 cm.

The photoperiod was ten hours of fluorescent light per day during the acclimation period and throughout the test. The average ambient temperature was 60°F with an average relative humidity of 47%.

C. **Dosage:** Fourteen-day single dose oral LD_{50} test. Based on a preliminary study, dosage levels were 464, 681, 1000, 1470, and 2150 milligrams of active ingredient per kilogram of body weight (mg ai/kg).

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 4 2/3 hours prior to dosing. The test substance was measured and placed directly into gelatin capsules.

The dosages for the 464 and 681 mg ai/kg treatment groups were prepared one day prior to dosing. The dosages for all other birds were prepared on the day of dosing. 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 test substance active ingredient per kilogram of body weight.

All birds were fed Purina Duck Grower W/O. Food was supplied ad libitum, except for the 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 on the day prior to dosing and on test days 3, 7, and 14. Group food

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consumption values were recorded on test days 3, 7, and 14.

The 23 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 the 464, 681, and 1000 mg ai/kg treatment groups were subjected to gross pathological examinations on test day 21. The surviving birds from the 1470 and 2150 treatment groups were also examined for pathological abnormalities.

E. **Statistics:** The LD_{50} was determined using the simplified method of Litchfield and Wilcoxon. A one-way analysis of variance was used to analyze the body weight data.

12. **REPORTED RESULTS:** No clinical signs of toxicity were noted in the control birds throughout the investigation.

Clinical signs of toxicity noted in the treatment groups included piloerection, wing-beat convulsions, asthenia, and dyspnea. All birds in the control and treatment groups appeared to be nervous and were quiet immediately after dosing.

Statistical analysis of the body weights at each weighing interval revealed no statistically significant differences (Table 6, attached). All food consumption values in the treatment groups were considered to be near control levels.

None of the control birds died, but deaths were recorded at each of the dosage levels tested. The deaths were distributed as follows: two birds in the 464 mg ai/kg group, four birds in the 681 mg ai/kg group, five birds in the 1000 mg ai/kg group, six birds in the 1470 mg ai/kg group, and six birds in the 2150 mg ai/kg group. All 23 deaths occurred on test day 1. Total remission of all clinical signs was achieved in survivors by the end of test day 1.

Gross pathological examinations revealed abnormal findings in 11 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 464 mg ai/kg treatment group included a gizzard that was twice the normal size and hemorrhagic tissue in the abdominal cavity. Pathological findings in the 681 mg ai/kg birds included friable livers, empty gizzards, and black contents in the gizzards. The findings in the 1000 mg ai/kg birds were an empty gizzard and pooled blood around the heart and lungs.

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Yellow mucus was noted in the gizzard of a 1470 mg ai/kg bird and one bird from the same group had hemorrhagic tissue in the abdominal cavity. Black contents were found in gizzards of 2150 mg ai/kg birds and some birds in this group also had discolored intestines (either red or black). The only abnormal finding in surviving birds arbitrarily selected for necropsy was an enlarged liver in one 1470 mg ai/kg bird.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The acute oral LD_{50} for the test material was determined to be 1120 mg ai/kg with 95% confidence limits of 742 to 1691 mg ai/kg. A no-observed-effect-level (NOEL) was not achieved in this study.

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 age of the birds was not estimated. The age, or in the case of live-trapped birds, the estimated age of the birds should be included in the report.

The birds were fasted for only 4 2/3 hours prior to dosing. Guidelines suggest a longer period of fasting, but the nutritional requirements of this species are not specifically addressed in the guidelines.

Due to time constraints, the birds were weighed on the day prior to the start of the test, instead of on the first day of the test.

The house sparrow is not a species recommended by guidelines, but parallel studies using the recommended species have been submitted for review (MRID Nos. 429186-16 and 429186-17).

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} (1000 mg ai/kg) was lower than the reported LD_{50} (1120 mg ai/kg). The author did not report the slope of the dose-response line. The slope calculated by the reviewer using the Toxanal program was 1.6.

C. **Discussion/Results:** Although the house sparrow is not a recommended species, the authors did make it clear that the species was chosen because the birds "possess ground-feeding habits and would be likely to be exposed to the test material in the natural environment."

The study is scientifically sound but does not meet the requirements of an avian single dose oral LD_{50} study. Based on nominal concentrations, the LD_{50} was 1000 mg ai/kg which classifies the test material as slightly toxic to house sparrows. An NOEL was not achieved in this study. House sparrow is not a required species.

D. **Adequacy of the Study:**

(1) **Classification:** Supplemental.

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

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

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

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

Fipanil Insecticide

Page 8 is not included in this copy.

Pages _____ through _____ 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.

✓ Information about a pending registration action.

_____ FIFRA registration data.

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_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

Nicole Jurczyk FIPRONIL PASSER DOMESTICUS 01-06-94

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
2150	10	6	60.00001	37.69531
1470	10	6	60.00001	37.69531
1000	10	5	50	62.30469
681	10	4	40	37.69531
464	10	2	20	5.46875

THE BINOMIAL TEST SHOWS THAT 0 AND +INFINITY 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 999.9999

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
4	1.252151	1104.676	0	+INFINITY

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
3	.9553035	1	.8977158

SLOPE = 1.578066

95 PERCENT CONFIDENCE LIMITS = 3.567016E-02 AND 3.120461

LC50 = 1172.986

95 PERCENT CONFIDENCE LIMITS = 467.5911 AND 1389753

LC10 = 183.8697

95 PERCENT CONFIDENCE LIMITS = 1.365321E-30 AND 464.0717

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