6-18-91

MRID No. 416273-01

# DATA EVALUATION RECORD

1. **CHEMICAL:** Profenofos.
Shaughnessey Number: 111401.

2. **TEST MATERIAL:** Profenofos Technical; 89.4% purity; Lot No. FL 851177; CAS # 41198-09-7; O-(4-bromo-2-chlorophenyl)-O-ethyl-s-propyl phosphorothioate; an amber-colored, oily liquid with a sulfur-like odor.

3. **STUDY TYPE:** Avian Single Dose Oral $LD_{50}$ Test.
Species Tested: Mallard duck (Anas platyrhynchos).

4. **CITATION:** Pedersen, C.A. 1990. Profenofos Technical: 21-Day Acute Oral $LD_{50}$ Study in Mallard Ducks. Study performed by Bio-Life Associates, Ltd., Neillsville, Wisconsin. Laboratory study #89 DD 75. Submitted by Ciba-Geigy Corporation, Greensboro, NC. EPA MRID No 416273-01.

5. **REVIEWED BY:**

Marise H. Robbins, M.S.E.S., M.A.
Associate Scientist
KBN Engineering and
Applied Sciences, Inc.

**Signature:** Michael L Whitten For Marise Robbins
**Date:** 4-10-91

6. **APPROVED BY:**

F.W. Ethridge 4/23/91

Michael L. Whitten, M.S.
Wildlife Toxicologist
KBN Engineering and
Applied Sciences, Inc.

**Signature:** Michael L Whitten
**Date:** 4-10-91

Henry T. Craven, M.S.
Supervisor, EEB/HED
USEPA

**Signature:** Henry T Craven
**Date:** 6/18/91

7. **CONCLUSIONS:** With an $LD_{50}$ of 55.0 mg a.i./kg, the test substance is considered to be moderately toxic to mallard ducks. The NOEL could not be determined. The study is scientifically sound and meets the requirements for an avian oral $LD_{50}$ test.

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 17-week-old mallard ducks (Anas platyrhynchos) obtained from Whistling Wings, Hanover, Illinois. Birds ranged in weight from 862 grams to 1455 grams at test initiation. All test birds were from the same hatch and phenotypically indistinguishable from wild birds. The birds were acclimated to laboratory conditions and observed daily for a 29-day pre-test period. Prior to initiation of the project, all birds were examined and their suitability for testing (based on general physical condition) was determined.

B. **Test System:** All birds were housed indoors in wire pens maintained over concrete. Each pen's floor space measured approximately 122 cm (4 ft) X 122 cm (4 ft). Ceiling height was approximately 122 cm (4 ft). Lighting was provided by fluorescent lights left on 10 hours per day. Maximum and minimum temperatures and the relative humidity of the animal room were recorded daily. The room temperatures during the test period ranged from 10°C (50°F) to 24°C (76°F). The relative humidity during the test period ranged between 62% and 100%.

C. **Dosage:** 21-day single dose oral $LD_{50}$ test. All dosages and the $LD_{50}$ value are reported as milligrams of active ingredient per kilogram of body weight (mg a.i./kg). Treatment levels were determined after range-finding tests. Nominal dosages were 21.5 (T-I), 31.6 (T-II), 46.4 (T-III), 68.1 (T-IV) and 100 (T-V) mg a.i./kg.

D. **Design:** Groups of ten mallards were randomly assigned to each of the five treatment groups (T-1 through T-V) and the vehicle control group. Each treatment or control group contained five males and five females. Throughout acclimation all birds were fed Purina® Duck Grower W/O. Water was supplied ad libitum during acclimation and the test. All birds were fasted for approximately 18 hours prior to dosing.
The test material was volumetrically measured and administered via gelatin capsule at 0 hour on test day 1. Each test bird received its respective dose of test

material via one capsule. Each control bird received one empty gelatin capsule only.

Each bird was individually weighed and dosed on the basis of milligrams of test substance per kilogram of body weight. The birds were individually weighed at initiation of the test and on Days 3, 7, 14 and 21. Average estimated feed consumption was determined for each dosage group and the control for Days 1-3, 4-7, 8-14 and 15-21.

All birds were observed daily to ascertain the presence (or absence) of clinical signs indicative of test material effect. Inspections were made daily for mortalities, abundance of food and water and food spillage. All birds that died during the study were subjected to gross pathological examinations. Additionally, four arbitrarily selected birds (two male and two female) sacrificed on test day 21 from each of the control and three lowest dose test groups, as well as the survivors in the 68.1 and 100 mg a.i./kg test groups were subjected to gross pathological examinations on day 21.

E. **Statistics:** At the end of the 21-day test period, the $LD_{50}$ was calculated using the Litchfield and Wilcoxon method (Table 3, attached). Body weights were analyzed statistically by one-way analysis of variance.

12. **REPORTED RESULTS:** The $LD_{50}$ of the test material was 56.0 mg a.i./kg with 95% confidence limits of 40.3 to 77.8 mg a.i./kg (Table 3, attached). Two deaths were recorded in the 21.5 mg a.i./kg group, one in the 31.6 mg a.i./kg group, three in the 46.4 mg a.i./kg group, six in the 68.1 mg a.i./kg group and nine in the 100 mg a.i./kg group. The first deaths occurred within approximately 4 3/4 hours post-dosing. Signs of toxicity noted in the test groups included lethargy, chalky diarrhea, bloody droppings, anorexia, inability to stand, and tachypnea. Total remission of all clinical signs except anorexia was achieved by the end of test day 5.

No mortalities occurred in the control group. No abnormal behavioral reactions or systemic signs of toxicity were noted in the control group.

Gross pathological examinations of the twenty-one birds that died during the study and of twenty-one selected survivors at termination revealed no abnormal pathological findings.

Average body weight and estimated food consumption data are presented in Table 5 (attached). The individual body weight data collected during the investigation are presented in the report.

Statistical analysis of the body weights revealed no significant differences at any of the weighing intervals.

Food consumption in the control group ranged from 60 to 92 grams/bird/day throughout the investigation. Anorexia was noted in the 21.5 mg a.i./kg group during the first three test days, in the 31.6 mg a.i./kg, 46.4 mg a.i./kg and 68.1 mg a.i./kg test groups during the first seven test days, and in the 100 mg a.i./kg test group during the first fourteen test days. All other food consumption values in the test groups were comparable to or greater than the Control group's values.

A no-observed-effect-level was not achieved in this study.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The 21-day oral $LD_{50}$ was 56.0 mg a.i./kg with 95% confidence limits of 40.3 to 77.8 mg a.i./kg. A no-observed-effect level was not achieved in this study.

The report stated that the study was conducted in conformance with Good Laboratory Practice regulations. Quality assurance audits were conducted and the final report was signed by the Study Director and Quality Assurance Officer of Bio-Life Associates, Ltd.

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

A. **Test Procedure:** The test procedures were in accordance with Subdivision E - Hazard Evaluation: Wildlife and Aquatic Organisms, and SEP guidelines except for the following deviations:

The lowest temperature (10°C) and the maximum humidity (100%) were outside the normal range of values for these parameters.

The report did not mention the diet during the study, nor whether the food was available ad libitum after dosing.

The report did not indicate when the signs of toxicity were first noted, nor in which specific groups they were observed.

B. **Statistical Analysis:** The reviewer calculated the $LD_{50}$ using EPA's Toxanal computer program (attached). The $LD_{50}$ calculated using the Probit Method (55.0 mg a.i./kg with 95% confidence limits of 41.4 to 79.1) is practically the same as reported by the author.

C. **Discussion/Results:** The report did not indicate when the signs of toxicity were first noted, nor in which specific groups they were observed. Based on the observed mortality in all treatment groups on day 1, it is assumed that the behavioral signs of toxicity occurred in all treatment groups, and were present on day 1. For purposes of risk assessment, therefore, behavioral signs of toxicity occurred from day 1 until day 5. The registrant should ensure that, in future reports, data regarding behavioral signs of toxicity are sufficiently reported.

The results show that a single dose of the test material resulted in notable signs of toxicity and decreased food consumption in all test groups. The NOEL, therefore, could not be determined.

With an $LD_{50}$ of 55.0 mg a.i./kg, the test substance is considered to be moderately toxic to mallard ducks.

The study is scientifically sound and meets the requirements for an avian oral $LD_{50}$ test.

D. **Adequacy of the Study:**

**(1) Classification: Core.**

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

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

15. **COMPLETION OF ONE-LINER:** Yes; April 9, 1991.

TABLE 3

$LD_{50}$ CALCULATIONS

PROFENOFOS TECHNICAL

| Group | Nominal Concentration (mg a.i./kg) | Observed Response | Expected Response | Residual | Contribution to Chi Square |
|---|---|---|---|---|---|
| T-I | 21.5 | 20.0 | 9.6 | +10.4 | 0.1320 |
| T-II | 31.6 | 10.0 | 21.8 | -11.8 | 0.0840 |
| T-III | 46.4 | 30.0 | 39.5 | -9.5 | 0.0380 |
| T-IV | 68.1 | 60.0 | 60.0 | 0.0 | 0.0000 |
| T-V | 100 | 90.0 | 78.0 | +12.0 | 0.0920 |
| | | | | Total | 0.3460 |
| | | | | | x10 |
| | | | | | 3.460 |

Total Number of Animals = 50
Number of Groups = 5

Total contributions to Chi square = 3.460

Chi square (P=0.05) for 3 degrees of freedom is 7.82

The data are not significantly heterogeneous.

$LD_{16}$ = 26.8 mg a.i./kg  Slope Function = 2.10

$LD_{50}$ = 56.0 mg a.i./kg  N' = 40

$LD_{84}$ = 118 mg a.i./kg  $F(LD_{50})$ = 1.39

95% confidence limits of $LD_{50}$

$LD_{50}$ = 56.0 mg a.i./kg (40.3 to 77.8)

TABLE 4

DAILY MORTALITY

PROFENOFOS TECHNICAL

| Group | Dose Level (mg a.i./kg) | RECORDED TIME OF DEATH TEST DAY | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 |
| Control | 0 | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- |
| T-I | 21.5 | 10 3:10 p.m. 10 7:45 a.m. | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- |
| T-II | 31.6 | -- | 10 10:15 a.m. | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- |
| T-III | 46.4 | 30 7:45 a.m. | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- |
| T-IV | 68.1 | 50 7:45 a.m. | 10 9:10 a.m. | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- |
| T-V | 100 | 30 3:10 p.m. 60 7:45 a.m. | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- | -- |

-- = no mortalities occurred

The $LD_{50}$ was determined to be 56.0 mg/kg of body weight with 95% confidence limits of 40.3 to 77.8 mg a.i./kg of body weight.

TABLE 5

AVERAGE BODY WEIGHT AND ESTIMATED FOOD CONSUMPTION

PROFENOFOS TECHNICAL

| Group | Dose Level (mg a.i./kg) | Average Body Weight (g) 0 Hour | Test Day 3 | Test Day 7 | Test Day 14 | Test Day 21 | Estimated Food Consumption Per Bird Per Day (g) Test Days 1-3 | 4-7 | 8-14 | 15-21 |
|---|---|---|---|---|---|---|---|---|---|---|
| Control | 0 | 1136(±171) | 1118(±147) | 1083(±159) | 1085(±154) | 1125(±160) | 73 | 60 | 77 | 92 |
| T-I | 21.5 | 1143(±113) | 1137(±138) | 1169(±118) | 1153(±112) | 1196(±123) | 40 | 92 | 82 | 80 |
| T-II | 31.6 | 1123(±144) | 1010(±123) | 1032(±141) | 1086(±142) | 1094(±150) | 40 | 38 | 89 | 85 |
| T-III | 46.4 | 1164(±158) | 1068(±122) | 1081(±121) | 1105(±117) | 1125(±115) | 10 | 53 | 72 | 98 |
| T-IV | 68.1 | 1209(±106) | 1062(±91) | 1127(±44) | 1140(±64) | 1182(±80) | 14 | 12 | 89 | 137 |
| T-V | 100 | 1154(±130) | A | A | A | A | 2 | 17 | 46 | 62 |

A = There was only one survivor in this group at the end of this interval.

No statistically significant differences in body weights were noted.

MARISE ROBBINS PROFENOFOS MALLARD DUCK 04-03-91

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| CONC. | NUMBER EXPOSED | NUMBER DEAD | PERCENT DEAD | BINOMIAL PROB. (PERCENT) |
|---|---|---|---|---|
| 100 | 10 | 9 | 90 | 1.074219 |
| 68.1 | 10 | 6 | 60.00001 | 37.69531 |
| 46.4 | 10 | 3 | 30 | 17.1875 |
| 31.6 | 10 | 1 | 10 | 1.074219 |
| 21.5 | 10 | 2 | 20 | 5.46875 |

THE BINOMIAL TEST SHOWS THAT 0 AND 100 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 60.01775

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

| SPAN | G | LC50 | 95 PERCENT CONFIDENCE LIMITS | |
|---|---|---|---|---|
| 3 | .2694202 | 58.76315 | 45.93648 | 77.67195 |

RESULTS CALCULATED USING THE **PROBIT METHOD**

| ITERATIONS | G | H | GOODNESS OF FIT PROBABILITY |
|---|---|---|---|
| 3 | .288556 | 1 | .3292188 |

SLOPE = **3.382748**
95 PERCENT CONFIDENCE LIMITS = 1.565624 AND 5.199873

LC50 = **54.95025**
95 PERCENT CONFIDENCE LIMITS = **41.39789 AND 79.13364**

LC10 = 23.14916
95 PERCENT CONFIDENCE LIMITS = 8.80105 AND 32.76345

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10

Shaughnessey # 111401 Chemical Name Profenofos Chemical Class _____ Page 1 of 1

| Study/Species/Lab/ MRID # | Chemical % a.i. | Results | Reviewer/ Date | Validation Status |
|---|---|---|---|---|
| 14-Day Single Oral $LD_{50}$ | 89.4% | $LD_{50}$ = 55.0 mg/kg (95% C.L.: 41.4 - 79.1) Control Mortality (%) = 0 | | |
| Species Anas platyrhynchos | | Slope = 3.38 # Animals/Level = 10 Age (Days) = ≈17 weeks ≈119 days | | |
| Lab Bio Life Associates | | Sex = 5♂ 5♀ | M. Whitten CORE 4-9-91 | |
| MRID # 416273-01 | | 14-Day Dose Level mg/kg/(% Mortality): 21.5 (20), 31.6 (10), 46.4 (30), 68.1 (60), 100 (90) | | |
| | | Comments: Behavioral signs of toxicity at all treatment dosages. | | |
| 8-Day Dietary $LC_{50}$ | | $LC_{50}$ = ppm (95% C.L. ) Control Mortality (%) = | | |
| Species | | Slope = # Animals/Level = Age (Days) = | | |
| Lab | | Sex = | | |
| MRID # | | 8-Day Dose Level ppm /(% Mortality): ( ), ( ), ( ), ( ), ( ) | | |
| | | Comments: | | |