DP Barcode : D192329
PC Code No : 128725
EEB Out : JUN 8 1994

To: Robert Forrest
Product Manager 14
Registration Division (H7505C)

From: Anthony F. Maciorowski, Chief
Ecological Effects Branch/EFED (H7507C)

Attached, please find the EEB review of...

Reg./File # : 058035-I
Chemical Name : Methyl anthralinate
Type Product : repellent
Product Name : Rejex
Company Name : PMC Specilaties
Purpose : Review new chemical which has passed screen.

Action Code: 146 Date Due: 9/30/93
Reviewer: Regina Hirsch

EEB Guideline/MRID Summary Table: The review in this package contains an evaluation of the following:

| GDLN NO | MRID NO | CAT | GDLN NO | MRID NO | CAT | GDLN NO | MRID NO | CAT |
|---|---|---|---|---|---|---|---|---|
| 71-1(A) | | | 72-2(A) | | | 72-7(A) | | |
| 71-1(B) | | | 72-2(B) | | | 72-7(B) | | |
| 71-2(A) | | | 72-3(A) | | | 122-1(A) | | |
| 71-2(B) | | | 72-3(B) | | | 122-1(B) | | |
| 71-3 | | | 72-3(C) | | | 122-2 | | |
| 71-4(A) | | | 72-3(D) | | | 123-1(A) | | |
| 71-4(B) | | | 72-3(E) | | | 123-1(B) | | |
| 71-5(A) | | | 72-3(F) | | | 123-2 | | |
| 71-5(B) | | | 72-4(A) | | | 124-1 | | |
| 72-1(A) | | | 72-4(B) | | | 124-2 | | |
| 72-1(B) | | | 72-5 | | | 141-1 | | |
| 72-1(C) | | | 72-6 | | | 141-2 | | |
| 72-1(D) | | | | | | 141-5 | | |

Y=Acceptable (Study satisfied Guideline)/Concur
P=Partial (Study partially fulfilled Guideline but additional information is needed
S=Supplemental (Study provided useful information but Guideline was not satisfied)
N=Unacceptable (Study was rejected)/Nonconcur

# DATA EVALUATION RECORD

1. **CHEMICAL:** Methyl Anthranilate.
Shaughnessey Number: 128725.

2. **TEST MATERIAL:** Methyl Anthranilate; 99.9% purity; a clear liquid.

3. **STUDY TYPE:** 71-1A. Avian Single Dose Oral $LD_{50}$ Test.
Species Tested: Mallard (*Anas platyrhynchos*).

4. **CITATION:** Campbell, S.M. and M. Jaber. 1992. Methyl Anthranilate (MA): An Acute Oral Toxicity Study with the Mallard. Study performed by Wildlife International Ltd., Easton, Maryland. Laboratory Study No. 343-102. Submitted by ERM Program Management Company, McLean, Virginia. EPA MRID No. 426088-07.

5. **REVIEWED BY:**

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

**Signature:** Michael L. Whitten
**Date:** 9/1/93

6. **APPROVED BY:**

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

**Signature:** Mark A. Mossler
**Date:** 9/1/93

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

**Signature:** T. Wilson 5/19/94
**Date:**

7. **CONCLUSIONS:** This study is scientifically sound, but does not meet the requirements for an avian oral $LD_{50}$ test. Because several birds were seen regurgitating, it must be assumed that the dosages were rejected. Therefore, the $LD_{50}$ could not be determined. The NOEL was not established, due to signs of toxicity at the lowest dosage tested.

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

9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** Mallards (*Anas platyrhynchos*) were obtained from Whistling Wings, Hanover, Illinois. All birds were from the same hatch, pen-reared, and phenotypically indistinguishable from wild birds. The birds were acclimated to the facilities for 16 days prior to initiation of the test, and were 17 weeks of age at test initiation.

B. **Test System:** Birds were housed indoors in pens constructed of wire grid. Pen dimensions were 75 cm x 90 cm x 45 cm high. The photoperiod was 8 hours of light per day. The average temperature was 21.2°C ± 1.2°C. The average relative humidity was 66 ± 10%.

C. **Dosage:** Fourteen-day single dose oral $LD_{50}$ test. Nominal dosages selected for the study were 292, 486, 810, 1350, and 2250 milligrams of methyl anthranilate per kilogram of body weight (mg/kg). The dosages were not corrected for purity of the test substance.

D. **Design:** Groups of ten birds (five males and five females) were indiscriminately assigned to each of five treatment groups and one control group. Each dosage group was assigned two pens. One pen contained five males and the other contained five females. All birds were fed Wildlife International Ltd.'s game bird ration. Food and water were supplied *ad libitum* during acclimation and during the test, except during the 15-hour period prior to dosing, when the birds were fasted.

The test substance was administered by gelatin capsule. Each bird was individually weighed and dosed on the basis of milligrams of test substance per kilogram of body weight. The control birds received empty gelatin capsules.

All birds were observed at least twice daily for mortalities, signs of toxicity, and abnormal behavior. Body weights were measured individually one day prior to test initiation and by group on days 3, 7, and 14. Group food consumption was determined for days 0-3, 4-7, and 8-14.

E. **Statistics:** Due to the absence of mortality in all treatment groups, the $LD_{50}$ was not calculated. An estimation of the $LD_{50}$ was made by a visual inspection of the mortality data.

12. **REPORTED RESULTS:** There were no mortalities in the control group. All birds in the control group were normal in appearance and behavior throughout the study.

There were no mortalities at any of the dosages tested.

Regurgitation was noted in all treatment groups shortly after dosing with methyl anthranilate. One bird was seen regurgitating in the 292-mg/kg group, six birds in the 486-mg/kg group, eight at 810 mg/kg, two at 1350 mg/kg, and six at 2250 mg/kg.

Behavioral signs of toxicity were noted in all five treatment groups, and consisted of reduced reaction to external stimuli, lethargy, and loss of coordination. One or more of these symptoms were observed in 1, 3, and 2 birds in the 292, 486, and 810 mg/kg groups, respectively. All birds in these three groups had recovered by the first morning after dosing. Signs of toxicity were observed in all birds in the two highest dosage groups. After two days, all birds in these two groups appeared normal.

"Body weight and feed consumption measurements were highly variable and confounded evaluation of those results. Regurgitation may have been a contributing factor to the variability observed."

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The $LD_{50}$ was greater than 292 mg/kg, the highest dosage at which no significant regurgitation occurred. The $LD_{50}$, irrespective of regurgitation, was greater than 2250 mg/kg. The no observed effect level was less than 292 mg/kg, based on signs of toxicity and regurgitation at 292 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 with the following exceptions:

Body weights were measured by group, rather than individually, on days 3, 7, and 14.

The birds were not randomly assigned to pens. Instead, they were assigned by "indiscriminate draw."

B. **Statistical Analysis:** Due to the absence of mortality in all treatment groups, the $LD_{50}$ could not be calculated.

C. **Discussion/Results:** The report stated that the birds were assigned to groups by indiscriminate draw. Strictly speaking, "indiscriminate draw" is not the same as "random" assignments. However, this method of assignment probably did not affect the results of the test.

Regurgitation was observed in all dosage groups. The elapsed time from dosing to regurgitation ranged from 0 to 30 minutes. This suggests that at least a portion of the dose was rejected by those birds. Therefore, the $LD_{50}$ cannot be determined. Since only one bird was seen regurgitating in the 292 mg/kg group, and no birds died at that level, it appears that the $LD_{50}$ was greater than 292 mg/kg. As the authors indicated, body weight and feed consumption measurements were highly variable (Table 2, attached). The variability was probably due to regurgitation of the test material.

The study appears to be scientifically sound. However, because the $LD_{50}$ could not be determined, the study does not meet the requirements for an oral $LD_{50}$ test.

The NOEL was not established, due to signs of toxicity at the lowest dosage tested.

D. **Adequacy of the Study:**

(1) **Classification:** Supplemental.

(2) **Rationale:** Regurgitation was observed in all dosage groups. Therefore, the $LD_{50}$ could not be determined.

(3) **Repairability:** No.

15. **COMPLETION OF ONE-LINER:** Yes; August 16, 1993.

TABLE 2

AVERAGE BODY WEIGHT AND ESTIMATED FEED CONSUMPTION OF MALLARDS DOSED WITH METHYL ANTHRANILATE (MA)

| Dosage | | Average Body Weight in Grams | | | | | | | | Estimated Feed Consumption Grams/Bird/Day | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| mg/kg | Sex | Day -1 | Change | Day 3 | Change | Day 7 | Change | Day 14 | Total Change | Days 0-3 | Days 4-7 | Days 8-14 |
| Control | M | 1193 | 7 | 1200 | -16 | 1184 | -52 | 1132 | -61 | 136 | 102 | 85 |
| | F | 1045 | -4 | 1041 | 11 | 1052 | -47 | 1005 | -40 | 109 | 105 | 80 |
| 292 | M | 1183 | -63 | 1120 | 34 | 1154 | -117 | 1037 | -146 | 155 | 144 | 71 |
| | F | 1022 | -18 | 1004 | -1 | 1003 | -44 | 959 | -63 | 119 | 128 | 71 |
| 486 | M | 1185 | -38 | 1147 | -42 | 1105 | -52 | 1053 | -132 | 82 | 81 | 70 |
| | F | 1021 | -4 | 1017 | 11 | 1028 | -82 | 946 | -75 | 126 | 122 | 69 |
| 810 | M | 1270 | -28 | 1242 | -20 | 1222 | -68 | 1154 | -116 | 109 | 95 | 67 |
| | F | 1005 | -29 | 976 | 26 | 1002 | -68 | 934 | -71 | 110 | 116 | 74 |
| 1350 | M | 1184 | -72 | 1112 | 31 | 1143 | -126 | 1017 | -167 | 101 | 125 | 58 |
| | F | 1037 | -1 | 1036 | 1 | 1037 | -22 | 1015 | -22 | 109 | 127 | 84 |
| 2250 | M | 1150 | 13 | 1163 | -41 | 1122 | -88 | 1034 | -116 | 170 | 151 | 62 |
| | F | 1058 | 19 | 1077 | 9 | 1086 | -102 | 984 | -74 | 182 | 206 | 62 |

Ecological Effects Branch One-Liner Data Entry Form

Chemical Methyl anthranilate Shaughnessy No. 128725 Pesticide Use repellent

| AVIAN ORAL TOX SPECIES (AGE) | % AI | $LD_{50}$ (95%CL) | SLOPE | NOEL | STUDY/REVIEW DATES | MRID/ CATEGORY | LAB | RC |
|---|---|---|---|---|---|---|---|---|
| 1. Anas platyrhynchos | 99.99% | Not determined * | N/A | Not established | 1992/1993 | Supplemental | WLI | MCW |
| 2. | | | | | | | | |
| 3. | | | | | | | | |
| 4. | | | | | | | | |
| 5. | | | | | | | | |

| AVIAN DIETARY SPECIES (AGE) | % AI | $LC_{50}$ (95%CL) | SLOPE | NOEL | STUDY/REVIEW DATES | MRID/ CATEGORY | LAB | RC |
|---|---|---|---|---|---|---|---|---|
| 1. | | | | | | | | |
| 2. | | | | | | | | |
| 3. | | | | | | | | |
| 4. | | | | | | | | |
| 5. | | | | | | | | |

COMMENTS: *Regurgitation seen at all dosage levels.