8-6-93

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MRID No. 427702-27

DATA EVALUATION RECORD

1. **CHEMICAL:** Pirate® (AC 303,630). Shaughnessey No. 129093.

2. **TEST MATERIAL:** AC 303,630 technical; CAS No. 122453-73-0; Batch No. AC-7504-59A; 94.5% purity; a tan powder.

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

4. **CITATION:** Helsten, B.R. and J.P. Sullivan. 1993. 21-Day Acute Toxicity Test with AC 303,630 Technical in the Mallard Duck (*Anas platyrhynchos*). Laboratory Project No. 105-014-04. Performed by Bio-Life Associates, Ltd., Neillsville, WI. Submitted by American Cyanamid Company, Princeton, NJ. EPA MRID No. 427702-27.

5. **REVIEWED BY:**

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

Signature: [signature]

Date: 7/23/93

6. **APPROVED BY:**

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

Signature: Michael L. Whitten

Date: 7/23/93

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

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Date: 8/6/93

7. **CONCLUSIONS:** This study is scientifically sound and meets the guideline requirements for an avian acute oral LD_{50} toxicity test. The LD_{50} value of the test material for mallard ducks was 8.3 mg/kg of body weight. Therefore, AC 303,630 technical is classified as very highly toxic to the mallard duck. The NOEL was 1 mg/kg.

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

9. **BACKGROUND:**

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

Individual body weights were measured at 8.5 hours prior to dosing on test day 1 and on test days 3, 7, 14, and 21. Average feed consumption was determined by group for days 1-3, 4-7, 8-14, and 15-21.

E. **Statistics:** Analysis of variance was used to analyze the body weight data. The LD_{50} was determined using the simplified version of Litchfield and Wilcoxon.

12. **REPORTED RESULTS:** No mortality occurred in the control or two lowest (1 and 2 mg/kg) treatment groups. Mortality at the 4, 8, 16, 32, 64, and 128 mg/kg treatment levels was 10, 80, 70, 90, 100, and 100%, respectively. All deaths were recorded within the first three days of the test. The LD_{50} was determined to be 10.3 mg/kg (95% confidence interval of 7.0-15.1 mg/kg), which classifies AC 303,630 technical as highly toxic to mallard ducks.

No signs of toxicity were apparent in the vehicle control or 1 mg/kg groups. Clinical signs of toxicity at higher treatment levels consisted of dyspnea, loose green and loose chalky excreta, convulsions, wing beat convulsions, opisthotonos (head stretched over back), lethargy, neck stretching, and quietness. Complete remission of clinical signs of toxicity was achieved in survivors of all treatment groups by test day 4.

Gross changes were noted in 41 of the 45 birds found dead during the test. The majority of the gross changes were in birds that had died during the night and were found the next morning. These changes, except for firm pectoral muscles, were probably due to postmortem autolysis and were therefore not believed to be treatment-related. Gross necropsy of the 22 surviving birds revealed no abnormal findings.

There were no significant reductions in body weight for any of the weighing periods (Table 7, attached). However, statistical analysis was not conducted for groups containing two or less survivors. Food consumption was reduced in the 4, 8, 16, and 32 mg/kg groups for days 1 through 3. With this exception, all other control and treatment values were similar (Table 7).

The no-observed-effect level (NOEL) was determined to be 1 mg/kg, based on the lack of mortality or signs of toxicity at this level.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** No conclusions other than those stated previously were made by the study authors.

A Quality Assurance statement indicating that the study was conducted in accordance with Good Laboratory Practices (GLP) was included in the report. A separate GLP compliance statement was also included in the report. The compliance statement indicated that the feed component analysis and water contaminant analysis were not performed under GLPs.

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

A. Test Procedure: The test procedures were in accordance with Subdivision E and SEP guidelines.

B. Statistical Analysis: The reviewer used EPA's Toxanal program to determine the LD_{50} and obtained a slightly lower value than the authors. Based on nominal dosage levels, the LD_{50} and 95% confidence interval were 8.3 mg/kg and 5.7-12.0 mg/kg, respectively. The slope of the probit curve was 2.9 (see attached printout).

C. Discussion/Results: The LD_{50} calculated using probit analysis was 8.3 mg/kg, and 8.7 mg/kg using the moving average method. Both of these values are only slightly lower than the authors' value of 10.3 mg/kg. The value of 8.3 mg/kg is accepted as the LD_{50}, since it is the most conservative of the three values. Since the accepted LD_{50} is less than 10 mg/kg, AC 303,630 is classified as very highly toxic to the mallard duck.

Based on signs of toxicity, and review of the body weight and feed consumption data, the reviewer agrees that the NOEL was 1 mg/kg.

The authors stated that abnormal observations (except for firm pectoral muscles) noted at necropsy of adults found dead were probably due to postmortem autolysis. However, empty gastro-intestinal tracts were noted in three mortalities, and these were not due to postmortem autolysis.

This study is scientifically sound and meets the guideline requirements for an avian acute oral LD_{50} toxicity test.

D. Adequacy of the Study:

(1) Classification: Core.

(2) Rationale: N/A.

(3) Repairability: N/A.

15. **COMPLETION OF ONE-LINER:** Yes, 7-16-93.

Page 6 is not included in this copy.

Pages _____ through _____ are not included.

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_____ Identity of product impurities.

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MOSSLER AC 303630 ANAS PLATYRHYNCHOS 7-16-93

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
128	10	10	100	9.765625E-02
64	10	10	100	9.765625E-02
32	10	9	90	1.074219
16	10	7	70	17.1875
8	10	8	80	5.46875
4	10	1	10	1.074219
2	10	0	0	9.765625E-02
1	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 4 AND 32 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 6.006627

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
7	.1144044	8.708597	5.31422	13.33803

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
5	.1534691	1	.4013415

SLOPE = 2.876929
95 PERCENT CONFIDENCE LIMITS = 1.749888 AND 4.00397

LC50 = 8.296721
95 PERCENT CONFIDENCE LIMITS = 5.705681 AND 12.04611

LC10 = 3.002366
95 PERCENT CONFIDENCE LIMITS = 1.366326 AND 4.55674

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