5-25-93

MRID No. 423597-01

DATA EVALUATION RECORD

1. **CHEMICAL:** Endothall.
Shaughnessey No. 038901.

2. **TEST MATERIAL:** Endothall technical; 7-oxabicyclo[2.2.1] heptane-2,3-dicarboxylic acid; CAS No. 145-73-3; Lot No. G05A; Batch No. 259; purity of 83.02%; an off-white, crystalline solid with a slight distinctive odor.

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

4. **CITATION:** Pedersen, C.A. and B.R. Helsten. 1992. Endothall Technical: 21-Day Acute Oral LD_{50} Study in Mallard Ducks. Conducted by Bio-Life Associates, Ltd., Neillsville, WI. Project ID BLAL No. 106-004-04. Submitted by Atochem North America, Inc., Philadelphia, PA. EPA MRID No. 423597-01.

5. **REVIEWED BY:**

Dennis J. McLane, Wildlife Biologist **Signature:** Dennis J McLane 5-24-93
Section 1, Ecological Effects Branch **Date:**
Environmental Fate and Effects Branch

6. **APPROVED BY:**

Les Touart, Chief, Section 1 **Signature:** L T
Ecological Effects Branch
Environmental Fate and Effects Branch **Date:** 5/25/93

7. **CONCLUSIONS:** This study is scientifically sound and does not fulfills the requirements for an avian single dose oral LD_{50} test using mallard ducks (*Anas platyrhynchos*). The LD_{50} can not be determined because vomiting may have effected the dose. The NOEL could not be determined based on toxicity signs at all levels tested.

8. **RECOMMENDATIONS:** Provide another study using the LD_{50} protocol to determine an NOEL based on any sign of toxicity.

9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** The birds used in the study were mallard

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5. **REVIEWED BY:**

Charles G. Nace Jr.
Associate Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: Charles G Nace Jr.
Date: 10/07/92

6. **APPROVED BY:**

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

Signature:
Date: 10/7/92

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

Signature:
Date:

7. **CONCLUSIONS:** This study is scientifically sound and fulfills the requirements for an avian single dose oral LD_{50} test using mallard ducks (*Anas platyrhynchos*). The LD_{50} was 105 mg/kg, which classifies Endothall technical as moderately toxic to mallard ducks. The NOEL could not be determined based on toxicity signs at all levels tested.

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

9. **BACKGROUND:**

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ducks (*Anas platyrhynchos*) obtained from Whistling Wings, Hanover, IL, at 16 weeks of age. All birds were phenotypically indistinguishable from wild birds and from the same hatch. The test birds were acclimated to the caging and facilities for 15 days prior to initiation of the study. All the ducks appeared to be in good health at study initiation.

B. **Test System:** All birds were housed indoors in 4-foot cubical wire cages with concrete floors. Each cage held five males and five females. A photoperiod of 10-hours light and 14-hours dark was provided. The average temperature was 73°F (23°C) and the average relative humidity was 89%.

C. **Dosage:** Twenty-one-day single dose oral LD_{50} test. Based on a range finding study, five nominal concentrations [30, 48, 78, 120, and 200 mg per kg of body weight (mg/kg)] and one control group were used for the definitive test.

The test substance was gravimetrically measured and administered via gelatin capsules. Each treatment bird received a dose via two capsules and control birds received two empty capsules.

D. **Design:** Ten birds (five males and five females) were randomly assigned to each of the five treatment groups and the control group. All birds were fasted for approximately 21 hours prior to dosing.

Observations were made daily for mortalities, signs of toxicity, or abnormal behavior. The birds were individually weighed on Days 1, 3, 7, 14, and 21. Food consumption was measured for the following intervals: Days 1 to 3, 4 to 7, 8 to 14, and 15 to 21 of the test. Fresh food was provided to each pen on Days 1, 3, 7, and 14. Water was provided *ad libitum* via an automatic watering system.

Gross pathological examinations were performed on all birds that died and on four arbitrarily selected birds (two male and two female) from each of the three lowest treatment levels and control. Two males and one female from the second highest test group were also necropsied.

E. **Statistics:** The median lethal dose (LD_{50}) and associated 95% confidence intervals (C.I.) were

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calculated using a simplified method of Litchfield and Wilcoxon. Statistical evaluations of the body weight data were conducted by using one-way analysis of variance.

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

Ten, 20, 50, and 100% mortality was observed in the 48, 78, 120, and 200 mg/kg groups, respectively (Table 2, attached). At least one bird from all of the treatment groups exhibited emesis within twenty minutes to two hours after dosing. All birds in all the treatment groups had vomit on their heads and backs within two hours of dosing. Birds at the three highest concentrations exhibited polydipsia and chalky, white excreta. At the 200 mg/kg level, the birds appeared lethargic. All deaths occurred within 24 hours after dosing. Total remission of all signs of toxicity (except for reduced feeding) was achieved by the end of Day 2.

Reduced feed consumption was noted at the 78 mg/kg level for Days 4 to 7 and at the 120 mg/kg level for Days 1 to 7 (Table 6, attached). All other groups were comparable to the control values. There were no significant differences in mean body weights at any of the treatment levels (Table 5, attached).

Gross pathological examinations of the 18 birds that died revealed abnormal findings in 17 birds. These included: legs stretched behind the body, gaseous intestines, blood-filled abdominal cavity, subcutaneous hemorrhaging, hemorrhaging intestines and testes, and clotted blood below the lungs. Examinations of the 19 arbitrary birds revealed no abnormal findings.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** "The acute oral LD_{50} of Endothall Technical was determined to be 111 mg/kg of body weight with 95% confidence limits of 87 to 141 mg/kg of body weight. The no-observed-effect level was estimated as less than 30 mg/kg, due to emesis in the lowest dose tested."

Good Laboratory Practice and Quality Assurance Inspection statements were included in the report indicating compliance with EPA Good Laboratory Practice Standards, 40 CFR Part 160.

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

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

B. **Statistical Analysis:** No valid LD_{50} can be determined because the ducks vomited after dosing.

C. **Discussion/Results:** The reported LD_{50} may not be accurate due to vomit being found on all of the treatment birds. It is possible that some of the dose was rejected, resulting in actual lower testing concentrations. Therefore the actual exposure is unknown.

There appeared to be a reduction in feed consumption at all dosage levels for Days 1-3 and 4-7.

The no-observed-effect level (NOEL) could not be determined due to toxicity signs at all levels tested. Because of the emesis appears likely at lethal levels, NOEL, based on signs of toxicity, should be established as a toxicological end point.

D. **Adequacy of the Study:**

(1) **Classification:** Supplemental

(2) **Rationale:** The actual exposure or dose is unknown.

(3) **Repairability:** No

15. **COMPLETION OF ONE-LINER:** Yes, 10/05/92.

Page_____ is not included in this copy.

Pages 6 through 8 are not included.

The material not included contains the following type of information:

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____ Description of quality control procedures.

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CHUCK NACE ENDOTHALL TECHNICIAL MALLARD DUCK 10/05/92

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB.(PERCENT)
200	10	10	100	9.765625E-02
120	10	5	50	62.30469
78	10	2	20	5.46875
48	10	1	10	1.074219
30	10	0	0	9.765625E-02

THE BINOMIAL TEST SHOWS THAT 48 AND 200 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 120

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
3	.1677542	105.472	84.16841	136.6167

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
5	.2315949	1	.4687944

SLOPE = 5.179672
95 PERCENT CONFIDENCE LIMITS = 2.68699 AND 7.672353

LC50 = 104.955
95 PERCENT CONFIDENCE LIMITS = 83.17731 AND 135.9903

LC10 = 59.67795
95 PERCENT CONFIDENCE LIMITS = 33.94184 AND 76.66535

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Shaughnessey # 038901 Chemical Name Endothall Chemical Class Page 1 of 1

Study/Species/Lab/ MRID #	Chemical % a.i.	Results	Reviewer/ Date	Validation Status
21-Day Single Oral LD_{50}	83.02%	LD_{50} = 105 mg/kg* (84 - 137) 95% C.L. (Moving average) Control Mortality (%) = 0		
Species: *Anas platyrhynchos*		Slope = NA # Animals/Level = 10 Age (Days) = approx. 140 Sex = 5 Male/5 Female		
Lab: Bio-life Associates, Ltd.		21-Day Dose Level mg/kg* /(% Mortality) 30 (0), 48 (10), 78 (20), 120 (50), 200 (100)	Charles A Maxey 10/05/92	Core.
MRID # 423597-01		Comments: * nominal concentration		
8-Day Dietary LC_{50}		LC_{50} = pp ( ) 95% C.L. Control Mortality (%) =		
Species		Slope = # Animals/Level = Age (Days) = Sex =		
Lab		8-Day Dose Level pp /(% Mortality) ( ), ( ), ( ), ( ), ( )		
MRID #		Comments:		

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