5-17-89

Accession No. 407009-05

DATA EVALUATION RECORD

1. **CHEMICAL:** Ethyltrianol.
   Shaughnessey No.

2. **TEST MATERIAL:** HWG 1608 (technical grade), Bayer batch F1. No. 132, 94.7% purity, brand name: FOLICUR, a crystalline solid.

3. **STUDY TYPE:** Avian Single-Dose Oral LD50 Test.
   Species Tested: Colinus virginianus.

4. **CITATION:** Stubblefield, W.A. 1987. HWG 1608 Technical: Acute LD50 to Bobwhite Quail. Study No. 86-015-02. Prepared and Submitted by Mobay Corporation, Stilwell, KS. EPA Accession No. 407009-05.

5. **REVIEWED BY:**

   Prapimpan Kosalwat, Ph.D.
   Staff Toxicologist
   KBN Engineering and
   Applied Sciences, Inc.

   Signature: P. Kosalwat
   Date: 11/8/88

6. **APPROVED BY:**

   James R. Newman, Ph.D.
   Project Manager/
   Principal Scientist
   KBN Engineering and
   Applied Sciences, Inc.

   Signature: James R Newman
   Date: 11/11/88

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

   Signature: 6/17/89
   Date: Henry T. Craven 5/17/89

7. **CONCLUSIONS:** This study is scientifically sound and fulfills the guideline requirements for an avian single-dose oral LD50 test. With an LD50 value of 1988 mg a.i./kg, HWG 1608 is considered slightly toxic to Bobwhite quail (Colinus virginianus). The NOEL was 432 mg/kg.

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

9. BACKGROUND:

10. DISCUSSION OF INDIVIDUAL TESTS: N/A.

11. MATERIALS AND METHODS:

A. Test Animals: Adult Bobwhite quail (Colinus virginianus) from the same hatch were received at 17 weeks of age from Sand Prairie Quail Farm, Maquoketa, Iowa. The birds were placed into galvanized steel brooders (91 x 71 x 23 cm) where they were maintained at a temperature of 70 ± 4°F and a relative humidity of 40-60%, with an eight-hour light photoperiod. Pelletized wood was used as cage bedding and was changed at least weekly.

The birds were acclimated to these conditions for 21 days before test initiation. Food (Agway Gamebird Ration) and water were available ad libitum throughout the acclimation and study periods. The birds were examined daily during the acclimation period and all unsuitable birds were eliminated from inclusion in the test prior to assignment to test groups.

B. Test System: The test system was the same as the system used to acclimate the birds described above.

C. Dosage: 21-day single-dose oral LD50 test. Nominal dosages selected for the definitive study were 155, 260, 432, 720, 1200, and 2000 milligrams active ingredient (a.i.) of HWG 1608 Technical per kilogram of body weight. Dosing solutions were prepared by homogenizing appropriate amounts of HWG 1608 Technical in sufficient corn oil to give a total volume of 50 ml. Dose solutions were corrected to 100% active ingredient.

D. Design: Groups of ten quails, five males and five females, were randomly allocated to each of the six treatment groups and two control groups. All birds were fasted for approximately 20 hours prior to dose administration. Test solutions were administered by oral gavage at a rate equal to 1% of the bird's body weight.

Observations for mortality and toxic signs were made twice daily for 21 days post-dosing, except on weekends and holidays when only one observation per day was made. Body weights were recorded at test initiation and termination and on Days 8 and 15. Feed consumption for

each group was recorded daily. At the end of the study, all surviving birds were sacrificed by CO_2 asphyxiation. Necropsy examinations were conducted on all surviving birds in the control, 1200-, 2000-mg/kg groups, as well as on all birds that died during the in-life phase of the study.

E. Statistics: LD50 values were calculated using a computer program modified from Stephan (1977). Determination of differences in acute toxicity attributable to sex differences was evaluated. Body weight and feed consumption data for all treatment groups were subjected to analysis of variance (ANOVA) using SAS software. If significant differences ($p \leq 0.05$) between the treatment and control were found, the data from each treatment level would be compared to those of the control using Williams test.

12. REPORTED RESULTS: Mortality data for quail orally dosed with HWG 1608 are presented in Table 1 (attached). No significant sex-related differences were noted in toxicant response; therefore, reported LD50 calculations were based on combined sexes. Clinical signs of toxicity were noted in all dose groups in which mortalities were recorded (Table 4, attached). Two of the birds which died during the study (one in each of the dose levels examined) showed signs suggesting compound-related irritation of the GI tract. All other birds dying during the study or examined at terminal sacrifice showed no grossly observable lesions.

A significant difference in body weights was noted between controls and birds surviving to Day 8 in the 720, 1200, and 2000 mg/kg dose groups (Table 3, attached). Reduced feed consumption in those dose groups during this period support this observation. No significant differences in body weight or mean daily feed consumption were noted at test termination in any of the surviving birds, indicating recovery from the initial toxic effect.

13. STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES: The single dose acute oral LD50 of HWG 1608 to Bobwhite quail was determined to be 1988 mg a.i./kg of body weight with 95% confidence interval of 1568 to 5988 mg/kg. The no-effect-level (NOEL) was 432 mg/kg.

The study had been audited periodically at all phases by the quality assurance unit in compliance with the Good Laboratory Practice regulations. The final report was reviewed and signed by the quality assurance unit of Mobay Corporation.

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

A. Test Procedure: The test procedures and the report were in accordance with the SEP guidelines, except for the following deviations:

o Information on range-finding studies was not included in the report.

o Vehicle control groups were not tested, concurrently. Since corn oil had been used as a "vehicle" to administer the test material in this study, the test should have included vehicle control birds receiving the maximum amount of corn oil available to any treatment group.

o Data on the amount of test material given to each bird were not included in the report. Therefore, the dosages given to each bird could not be verified.

B. Statistical Analysis: The statistical analysis performed by the author was appropriate and the results appeared to be valid. The reviewer recalculated the LD50 using EPA's TOXANAL computer program and obtained a similar result (i.e., 1988 mg/kg with 95% C.I. of 1568-5983 mg/kg).

C. Discussion/Results: With an LD50 value of 1988 mg a.i./kg body weight, HWG 1608 Technical is considered slightly toxic to Bobwhite quail, when administered as oral single dose. The NOEL was considered to be 432 mg a.i./kg, based on significant decreases in body weight observed on Day 8 at 720 mg/kg and higher doses.

D. Adequacy of the Study:

(1) Classification: Core.

(2) Rationale: N/A.

(3) Repairability: N/A.

15. COMPLETION OF ONE-LINER: Yes, October 31, 1988.

Page_____ is not included in this copy.

Pages 5 through 7 are not included.

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.

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____ Sales or other commercial/financial information.

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KOSALWAT HWG 1608 TECHNICAL COLINUS VIRGINIANUS 10-28-88

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)-
2000	10	5	50	62.30469
1200	10	1	10	1.074219
720	10	0	0.	9.765625E-02
432	10	0	0	9.765625E-02
260	10	0	0	9.765625E-02
155	10	0	0	9.765625E-02

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 2000

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
1	1.077681	1999.998	1533.878	+INFINITY

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
7	.6923058	1	.999699

SLOPE = 6.134034
95 PERCENT CONFIDENCE LIMITS = 1.030216 AND 11.23785

LC50 = 1987.594
95 PERCENT CONFIDENCE LIMITS = 1568.348 AND 5983.374

LC10 = 1233.918
95 PERCENT CONFIDENCE LIMITS = 270.5863 AND 1564.306

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8

No. _____ Chemical Name Ethyltrianol Chemical Class _____ Page 1 of 1

(CHWG 1608 Technical)

Study/Species/Lab/ Accession	Chemical % a.i.	Results	Reviewer/ Date	Validati Status
14-Day Single Dose Oral LD_{50}		LD50 = mg/kg (95% C.L.) Contr. Mort.(%)=		
Species	_____	Slope= # Animals/Level= Age(Days)= Sex =	_____	_____
Lab		14-Day Dose Level mg/kg/(% Mortality) ( ), ( ), ( ), ( ), ( )		
Acc.		Comments:		
14-Day Single Dose Oral LD_{50}		LD50 = 1988* mg/kg. (95% C.L. 1568-5983) Contr. Mort.(%)= 0		
21 Species Colinus virginianus	94.7	Slope= 6.13 # Animals/Level= 10 Age(Days)= 119 Sex = M/F	PK/10-31-88	Core
Lab Mobay Corporation		14-Day Dose Level mg*/kg/(% Mortality) (1:1) 155(0), 260(0), 432(0), 720(0), 1200(10), 2000(50)		
Acc. 407009-05		Comments: * active ingredient		
8-Day Dietary LC_{50}		LC50 = ppm (95% C.L.) Contr. Mort.(%)=		
Species		Slope= # Animals/Level= Age(Days)= Sex =		
Lab	_____	8-Day Dose Level ppm/(%Mortality) ( ), ( ), ( ), ( ), ( )	_____	_____
Acc.		Comments:		
8-Day Dietary LC_{50}		LC50 = ppm (95% C.L.) Contr. Mort.(%)=		
Species		Slope= # Animals/Level= Age(Days)= Sex =		
Lab	_____	8-Day Dose Level ppm/(%Mortality) ( ), ( ), ( ), ( ), ( )	_____	_____
Acc.		Comments:		
48-Hour LC_{50}		LC50 = pp__ (95% C.L.) Contr. Mort.(%)= Sol. Contr. Mort.(%)=		
Species		Slope= # Animals/Level= Temperature =		
Lab	_____	48-Hour Dose Level pp /(%Mortality) ( ), ( ), ( ), ( ), ( )	_____	_____
Acc.		Comments:		
96-Hour LC_{50}		LC50 = pp__ (95% C.L.) Con. Mor.(%)= Sol. Con. Mor.(%)=		
Species		Slope= # Animals/Level= Temp.=		
Lab	_____	96-Hour Dose Level pp /(%Mortality) ( ), ( ), ( ), ( ), ( )	_____	_____
Acc.		Comments:		
96-Hour LC_{50}		LC50 = pp__ (95% C.L.) Con. Mort.(%)= Sol. Con. Mort.(%)=		
Species		Slope= # Animals/Level= Temp.=		
Lab	_____	96-Hour Dose Level pp /(%Mortality) ( ), ( ), ( ), ( ), ( )	_____	_____
Acc.		Comments:		