5-17-89

Accession No. 407009-08

DATA EVALUATION RECORD

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

2. **TEST MATERIAL:** HWG 1608 (technical grade), Batch No. 86R0082I, CAS Registry No. 107534-96-3, 96.28% purity, Common name: FOLICUR, a crystalline solid.

3. **STUDY TYPE:** Avian Dietary LC50 Test.
   Species Tested: Colinus virginianus.

4. **CITATION:** Toll, P.A. 1988. HWG 1608 (FOLICUR): Subacute Dietary LC50 to Bobwhite Quail. Study No. 87-175-02. Prepared and Submitted by Mobay Corporation, Stilwell, KS. EPA Accession No. 407009-08.

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

7. **CONCLUSIONS:** This study is scientifically sound and fulfills the guideline requirements for an avian dietary LC50 test. With an LC50 value of greater than 5000 ppm a.i., HWG 1608 is considered practically non-toxic to Bobwhite quail (Colinus virginianus). The NOEL was less than 325 ppm a.i. A more precise NOEL could not be determined due to the test material-related effect found at all test levels.

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

9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. Test Animals: Bobwhite quail (Colinus virginianus) eggs were obtained from Sandprairie Quail Farm, Maquoketa, Iowa. At hatch, the chicks were placed into galvanized steel brooders (91 x 71 x 23 cm) maintained at a heater temperature of approximately 100°F with a temperature gradient to ambient temperature (approximately 72°F), with relative humidity of 45-70%. Room lighting was maintained under a 16/8-hour light/dark cycle. Brooder bedding (pelletized wood) was changed once during the course of the study.

Food (Teklad JQ-15 Bobwhite Quail Starter) and water (Kansas City Municipal water) were available ad libitum prior to and throughout the 12-day laboratory acclimation period. Less than 5% mortality was noted during the three days prior to test initiation and all unsuitable birds were eliminated from inclusion in the test prior to assignment to test groups.

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

C. Dosage: 12-day Dietary LC50 test. Based on results of range-finding studies, nominal concentrations selected for the definitive study were 312, 625, 1250, 2500, and 5000 ppm a.i. Appropriate amounts of technical grade HWG 1608, corn oil, and acetone were combined in an Erlenmeyer flask, then added to the feed while mixing in a Hobart mixer. Compensation was made for the HWG 1608 purity in calculating diet concentrations. Samples from all prepared diets were taken for HWG 1608 (a.i.) concentration analysis prior to study initiation.

D. Design: At thirteen days of age, ten birds of unknown sex weighing 23 to 32 g were randomly allocated to each of the five treatment groups and two control groups. Treatment groups were housed in separate brooders throughout the exposure period. Birds were given feed with appropriate concentrations of HWG 1608 for five days, then given control feed for a seven-day observation period.

Observations for mortality and toxic signs were made twice daily except on weekends when only one observation per day was made. Body weights were recorded at test initiation and termination and on Day 5. 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 2500- and 5000-ppm levels, as well as on all birds that died during the course of the study.

E. Statistics: Bartlett's test of equal variance was performed on the body weight and feed consumption data for each end-point to determine if the dose groups have equal variances ($p \leq 0.001$). If the variances were equal, subsequent analysis was conducted using parametric techniques (ANOVA, Dunnett's test, Williams'test); otherwise, non-parametric techniques (Kruskal-Wallis test, Dunn's Summed Rank test) were used. All statistical analyses were conducted using software supplied by SAS Institute Inc.

12. REPORTED RESULTS: Mean measured concentrations of HWG 1608 measured in the 312-, 1250-, and 5000-ppm test diets ranged from 94 to 104% of the nominal concentrations. Chemical analyses also showed that diet preparations containing HWG 1608 were homogeneous and stable throughout the five-day exposure period for the 312-, 1250-, and 5000-ppm dietary levels.

Compound-related mortalities occurred at HWG 1608 dietary levels of $\geq$ 2500 ppm (Table 2, attached). The only clinically observable sign of toxicity was wing drop, also noted on the 2500-ppm dietary group. However, the author considered this wing drop to be incidental since it was associated with birds with symptoms of cage-mate aggression (lacerations on the feet). One bird died at 325 ppm and was also not considered compound-related. This bird had lacerations on the feet and showed signs of loss of equilibrium due to cage-mate aggression.

Body weight gain was affected at all levels tested at the end of the five-day exposure period (Table 4, attached). Growth rates of all treatment groups returned to control levels during the seven-day observation period, indicating recovery. Feed consumption was only decreased at levels $\geq$ 2500 ppm during the treatment period (Table 5, attached). The 2500-ppm level also had decreased feed consumption after

they were returned to HWG 1608-free feed. However, the 5000-ppm dietary group returned to control levels during this time.

Results from postmortem examinations of those animals found dead during the course of the study are presented in Table 6 (attached). "No specific compound-related lesions were noted during necropsy."

13. STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES: The subacute dietary LC50 of HWG 1608 to Bobwhite quail was determined to be >5000 ppm a.i. The no-observed-effect level (NOEL) was <325 ppm, based on depressed weight gain.

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 The range of concentrations tested did not include a no-observed-effect level (NOEL).

o The brooder was reported as being "maintained at a heater temperature of approximately 100°F (38°C) with a temperature gradient to ambient temperature (approximately 72°F or 22°C)." The SEP recommends the brooder temperature of approximately 35°C.

o Control diet contained 1% of corn oil by weight, while the maximum corn oil available to treatment birds (i.e., 2500-ppm test level) was 1.5%. The SEP states that "control diets must contain the maximum amount of vehicle available to treatment birds."

B. Statistical Analysis: The statistical analysis performed by the author was appropriate and the results appeared to be valid. The LC50, calculated by the reviewer using EPA's TOXANAL computer program, was 11,100 ppm a.i. (attached).

C. Discussion/Results: The chemical analysis of the diet used in the test showed malathion concentration of 0.11 ppm. However, this low level of the pesticide probably did not affect the test birds. With an LC50 value of greater than 5000 ppm a.i., HWG 1608 is considered practically non-toxic to Bobwhite quail, when administered through a diet for five days. The NOEL was <325 ppm mean measured concentration. A more precise NOEL could not be determined due to test material-related effect found at all test levels.

D. Adequacy of the Study:

(1) Classification: Core.

(2) Rationale: Although the test procedures deviated from the guidelines, the reviewer does not believe they significantly affected the validity of the test results.

(3) Repairability: N/A.

15. COMPLETION OF ONE-LINER: Yes, November 1, 1988.

Page_____ is not included in this copy.

Pages 6 through 9 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.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

X FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

KOSALWAT HWG 1608 COLINUS VIRGINIANUS 10-28-88

****

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
5202	10	3	30	17.1875
2500	10	4	40	37.69531
1250	10	0	0	9.765625E-02
606	10	0	0	9.765625E-02
325	10	1	10	1.074219

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 5201.996

THE MOVING AVERAGE METHOD CANNOT BE USED WITH THIS DATA SET BECAUSE NO SPAN WHICH PRODUCES MOVING AVERAGE ANGLES THAT BRACKET 45 DEGREES ALSO USES TWO PERCENT DEAD BETWEEN 0 AND 100 PERCENT.

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
5	.8949879	1	.139792

SLOPE = 1.188036

95 PERCENT CONFIDENCE LIMITS = 6.410885E-02 AND 2.311962

LC50 = 11100.22

95 PERCENT CONFIDENCE LIMITS = 3754.008 AND 5.134116E+17

LC10 = 946.9785

95 PERCENT CONFIDENCE LIMITS = 3.688044E-03 AND 2284.339

****

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

(HWG 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 = mg/kg. (95% C.L) Contr. Mort.(%)=		
Species	____	Slope= # Animals/Level= Age(Days)= Sex =	_____	____
Lab		14-Day Dose Level mg/kg/(% Mortality) ( ), ( ), ( ), ( ), ( )		
Acc.		Comments:		
8-Day Dietary LC_{50} 2		LC50 = >5000 ppm* (95% C.L. —) Contr. Mort.(%)= 0		
Species Colinus virginianus		Slope= — # Animals/Level= 10 Age(Days)= 13 Sex = not determined	PK/11-1-88	Core
Lab Mobay Corporation 96.28		8-Day Dose Level ppm*/(%Mortality) 325(10), 606(0), 1250(0), 2500(40), 5202(30)		
Acc. 407009-08		Comments: * based on 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:		
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:		

//