EEB FILES

242850
RECORD NO.

060101
SHAUGHNESSEY NO.

REVIEW NO.

EEB REVIEW

DATE: IN 4/12/89 OUT JUL 10 1989

FILE OR REG. NO 89AZ04

PETITION OR EXP. NO

DATE OF SUBMISSION: 3/8/89

DATE RECEIVED BY EFED: 4/10/89

RD REQUESTED COMPLETION DATE: 6/4/89

EEB ESTIMATED COMPLETION DATE: 6/4/89

RD ACTION CODE/ TYPE OF REVIEW: 660

TYPE PRODUCT(S): Fungicide

ACCESSION NUMBER(S): 410250-02, -03, -04, -05, -06

PRODUCT MANAGER: S. Lewis (21)

PRODUCT NAME(S): Thiabendazole

COMPANY NAME: Merck and Company

PURPOSE OF SUBMISSION: Submission of data in response to Comprehensive DCI of 3/24/88

SHAUGHNESSEY NO.	CHEMICAL AND FORMULATION	%A.I.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

JUL 10 1989

MEMORANDUM

SUBJECT: Review of thiabendazole data submitted in response to DCI.

FROM: James Akerman, Chief
Ecological Effects Branch
Environmental Fate and Effects Division (H7507C)

TO: Susan Lewis, PM 21
Fungicide-Herbicide Branch
Registration Division (H7505C)

EEB has completed review of the five toxicity studies for thiabendazole submitted in partial response to the EPA Comprehensive Data Call-In Notice of 3/24/88. Data Evaluation Records are attached.

The avian LD_{50} study (EPA Accession No. 410250-02), the avian dietary LC_{50} studies (EPA Accession Nos. 410250-03 and -04), and the coldwater fish LC_{50} study (EPA Accession No. 410250-05) fulfill the Guidelines requirements and therefore satisfy the DCI Notice. However, the warmwater fish LC_{50} study (EPA Accession No. 410250-06) was determined to be inadequate to fulfill Guidelines requirements and should be repeated as discussed in the attached DER. If EEB can be of further assistance, please contact Dave Warburton (557-1666) of my staff.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

JUL 10 1989

MEMORANDUM

SUBJECT: Review of thiabendazole data submitted in response to DCI.

FROM: James Akerman, Chief
Ecological Effects Branch
Environmental Fate and Effects Division (H7507C)

TO: Susan Lewis, PM 21
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EEB has completed review of the five toxicity studies for thiabendazole submitted in partial response to the EPA Comprehensive Data Call-In Notice of 3/24/88. Data Evaluation Records are attached.

The avian LD_{50} study (EPA Accession No. 410250-02), the avian dietary LC_{50} studies (EPA Accession Nos. 410250-03 and -04), and the coldwater fish LC_{50} study (EPA Accession No. 410250-05) fulfill the Guidelines requirements and therefore satisfy the DCI Notice. However, the warmwater fish LC_{50} study (EPA Accession No. 410250-06) was determined to be inadequate to fulfill Guidelines requirements and should be repeated as discussed in the attached DER. If EEB can be of further assistance, please contact Dave Warburton (557-1666) of my staff.

CONCURRENCES								
SYMBOL	H7507C	H7507C						
SURNAME	Warburton							
DATE	7/7/89	7/7/89						

EPA Form 1320-1 (12-70) OFFICIAL FILE COPY

Accession No. 410250-05

DATA EVALUATION RECORD

1. **CHEMICAL:** Thiabendazole
   Shaughnessey No: Not available

2. **TEST MATERIAL:** Thiabendazole; 2-(4-thiazolyl)-benzimidazole; Lot No. PRM-029; CAS Registry No. 148-79-8; 99.6% active ingredient; an off-white, odorless powder.

3. **STUDY TYPE:** Acute Toxicity Test for Freshwater Fish. Species Tested: Rainbow trout (Salmo gairdneri).

4. **CITATION:** Beglinger, J.M. and R.J. O'Boyle. 1989. Acute Aquatic Effects of Thiabendazole on the Rainbow Trout, Salmo gairdneri. Study No. EN-412-GWN001-2. Prepared by Eastman Kodak Company, Rochester, New York. Submitted by Merck and Company, Inc., Iselin, New Jersey. Accession No. 410250-05.

5. **REVIEWED BY:**

Kimberly Rhodes
Associate Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: Kimberly Rhodes
Date: May 30, 1989

6. **APPROVED BY:**

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

Signature: P. Kosalwat
Date: May 30, 1989

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

Signature: Henry T. Craven 6/14/89
Date:

7. **CONCLUSIONS:** This study appears scientifically sound and fulfills the Guideline requirements for a 96-hour static acute toxicity study for a coldwater fish species. The 96-hour LC50, based upon mean measured concentrations, of Thiabendazole to rainbow trout (Salmo gairdneri) was 0.56 mg/L. Therefore, Thiabendazole is considered highly toxic to rainbow trout. The NOEC was determined to be 0.12 mg/L after 96 hours of exposure.

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8. RECOMMENDATIONS: N/A

9. BACKGROUND:

10. DISCUSSION OF INDIVIDUAL TESTS: N/A

11. MATERIALS AND METHODS:

A. Test Animals: Juvenile rainbow trout (Salmo gairdneri) used in this test were obtained from a commercial fish supplier in California. The fish were acclimated to the diluent water for at least two weeks prior to testing.

B. Test System: The toxicity test was conducted in seamless glass 30.5-cm cuboidal Pyrex chromatography jars containing 15 L of the exposure solution. A stock solution (15 mg/L) was prepared in water and continuously supplied to a diluter. The gas-driven, siphon type diluter then proportionally delivered the test solutions to the appropriate test vessels throughout the study. The test temperature was maintained at 12 $\pm$ 1°C through the use of a refrigerated water bath. A photoperiod of 16 hours of light and 8 hours of darkness with a 20-minute transition period was provided each day.

The dilution water was pumped from Lake Ontario into a large underground storage reservoir. The water was subsequently filtered, treated with 150 ppb $Na_2S_2O_3$ to reduce trace levels of residual chlorine, and tempered to 20 $\pm$ 2°C. The dilution water then passed through a column degassing unit into an open aeration basin for seasoning prior to use. The water was tempered to 12 $\pm$ 1°C by a submersible-coil refrigeration unit. The dilution water was characterized as having a total hardness of 110 mg/L as $CaCO_3$, a total alkalinity of 88 mg/L as $CaCO_3$, a pH of 8.3, and a specific conductance of 300 umhos/cm.

C. Dosage: 96-hour acute flow-through test.

D. Design: Juvenile rainbow trout, as uniform in size as possible, were randomly allocated to each vessel. Biological loading within test vessels was below 1.0 g wet weight per liter of test solution. The average wet weights of the two sets of control fish were determined at the start of the test.

A control and five nominal Thiabendazole concentrations of 0.09, 0.19, 0.38, 0.75 and 1.50 mg/L were tested in replicates of two. A total of twenty fish were exposed to each test concentration and control (ten fish\replicate). All concentrations were observed at 0, 6, 24, 48, 72, and 96 hours of exposure for mortality and signs of stress.

The water quality parameters (dissolved oxygen, pH, and temperature) were measured in the controls and all test concentrations at each 24-hour interval. Analytical determination of Thiabendazole was performed on all test concentrations and control at test initiation (0 hour) and termination (96 hours) using HPLC.

E. Statistics: The concentration of test substance lethal to 50 percent of the test population (LC50) was determined by a computerized calculation program developed by Stephan (1977) and ASTM (1987).

12. REPORTED RESULTS: A summary of the biological effects noted during the test is shown in Table 1 (attached). The mean measured concentrations of Thiabendazole ranged from 50% to 80% of the nominal concentrations.

The 96-hour LC50 for rainbow trout exposed to Thiabendazole was calculated by the probit method to be 0.55 mg/L (0.41 - 0.77 mg/L) for replicate A and 0.56 mg/L (0.39 - 0.81 mg/L) for replicate B. Based on the results of this study, the no-observed-effect concentration for rainbow trout and Thiabendazole was determined to be 0.12 mg/L, at 96 hours of exposure.

During the definitive test, the temperature in all test vessels remained at 12°C, the pH ranged from 8.1 to 8.4 and the dissolved oxygen concentration ranged from 9.1 to 10.7 mg/L. The water quality parameters measured during this study remained within acceptable ranges for the survival of the rainbow trout and are not likely to have affected the integrity of the study.

13. STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES: The results of this study indicate that Thiabendazole is highly toxic to rainbow trout (Salmo gairdneri). An isolated or intermittent exposure to a concentration of Thiabendazole less than 0.12 mg/L is unlikely to affect rainbow trout adversely.

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This study was conducted according to: Good Laboratory Practice for Nonclinical Laboratory Studies as promulgated by the Food and Drug Administration; 21 CFR Part 58; Environmental Protection Agency Good Laboratory Practice Standard 40 CFR Part 160; and Organization of Economic Cooperation and Development Principles of Good Laboratory Practice specified in Annex 2 of the OECD Guidelines for Testing of Chemicals [C(81) 30(Final)] as required by Council Directive 87/18/EEC.

14. REVIEWER'S DISCUSSION AND INTERPRETATION OF STUDY RESULTS

A. Test Procedure: The test procedures were generally in accordance with protocols recommended by the Guidelines, but deviated from the SEP as follows:

o The SEP states that use of a natural dilution water with a hardness of 40 to 48 mg/L as $CaCO_3$ can be used in lieu of reconstituted water. The dilution water used for the toxicity test had a total hardness of 110 mg/L as $CaCO_3$.

o The SEP states that temperature should be recorded every six hours in at least one test vessel during the entire study period if the temperature is controlled by a water bath. During the study, the test temperature was measured and recorded every 24 hours.

The toxicity report did not provide the following information required by the SEP:

o The age of the test fish.

o Weight and length of the fish used in the study. The SEP states that individual fish should weigh between 0.5 and 5 grams and the standard length of the longest fish should not be more than twice the length of the shortest fish.

o Complete descriptions of holding conditions. The percent of mortality 48 hours prior to test initiation and feeding schedules should have been reported.

o The flow rate of the diluter system. The SEP states that the flow rate should be five to ten volume additions per 24-hours.

B. Statistical Analysis: The concentration of test substance lethal to 50 percent of the test population (LC50) was determined by the EPA's Toxanal Computer program. These calculations are attached. The reviewer based the calculations on the combined A and B replicates of each concentration. Based on mean measured concentrations of Thiabendazole, the 96-hour LC50 value was estimated by the probit method to be 0.56 mg/L with a 95 percent confidence interval of 0.45 and 0.69 mg/L. The slope of the dose-response curve was estimated to be 4.6. The no-observed-effect concentration was determined to be 0.12 mg/L mean measured concentration, after 96 hours of exposure.

C. Discussion/Results: The study results appear to be scientifically valid. The 96-hour LC50 value, based upon mean measured concentrations, was estimated to be 0.56 mg/L. Therefore, Thiabendazole is considered highly toxic to rainbow trout (Salmo gairdneri). The NOEC was determined to be 0.12 mg/L after 96 hours of exposure.

D. Adequacy of the Study:

(1) Classification: Core

(2) Rationale: N/A

(3) Repairability: N/A

15. COMPLETION OF ONE-LINER: Yes, 05-25-89

haughnessey No. Not available | Chemical Name Thiabendazole Chemical Class ____ | Page ____ of ____

Study/Species/Lab/ Accession	Chemical % a.i.	Results	Reviewer/ Date	Validi Stat
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:		
-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:		
-Day Dietary LC_{50}		LC50 = ppm (95% C.L.) Contr. Mort.(%)=		
pecies		Slope= # Animals/Level= Age(Days)= Sex =		
ab	____	8-Day Dose Level ppm/(%Mortality) ( ), ( ), ( ), ( ), ( )	____	____
cc.		Comments:		
48-Hour LC_{50}		LC50 = pp__ (95% C.L.) Contr. Mort.(%)= Sol. Contr. Mort.(%)=		
pecies		Slope= # Animals/Level= Temperature =		
ab	____	48-Hour Dose Level pp /(%Mortality) ( ), ( ), ( ), ( ), ( )	____	____
cc.		Comments:		
96-Hour LC_{50}		LC50 = 0.56 ppm (95% C.L. 0.45-0.69) Con. Mor.(%)= 5% Sol. Con. Mor.(%)= N/A	~~K.R.~~ 5/25/89	Core
pecies Salmo gairdneri		Slope= 4.6 # Animals/Level= 20 Temp.= 12°C		
ab Eastman Kodak Co. 99.6%		96-Hour Dose Level ppm/(%Mortality) 0.0455(0), 0.12(0), 0.275(15), 0.57(35), 1.2(100)		
cc. 410250-05		Comments: Based on mean measured concentrations.		
96-Hour LC_{50}		LC50 = pp__ (95% C.L.) Con. Mort.(%)= Sol. Con. Mort.(%)=		
pecies		Slope= # Animals/Level= Temp.=		
ab	____	96-Hour Dose Level pp /(%Mortality) ( ), ( ), ( ), ( ), ( )	____	____
cc.		Comments:		

Page 10 is not included in this copy.

Pages ___ through ___ are not included in this copy.

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.

✓ 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.

NOTE: THERE WAS CONTROL MORTALITY, BUT AT LEAST ONE
OF THE LOWER CONCENTRATIONS HAD ZERO MORTALITY.
THEREFORE, ABBOTT'S CORRECTION IS NOT APPLICABLE.

KIMBERLY RHODES THIABENDAZOLE SALMO GAIRDNERI 05-25-89

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
1.2	20	20	100	9.536742E-05
.57	20	7	35	13.1588
.275	20	3	15	.1288414
.12	20	0	0	9.536742E-05
.0455	20	0	0	9.536742E-05

THE BINOMIAL TEST SHOWS THAT .275 AND 1.2 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 .650184

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
3	.0513501	.5218211	.4291003	.6548344

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
7	.1458901	1	.1723726

SLOPE = 4.595197
95 PERCENT CONFIDENCE LIMITS = 2.840036 AND 6.350359

LC50 = .5565671
95 PERCENT CONFIDENCE LIMITS = .449298 AND .6926605

LC10 = .2945385
95 PERCENT CONFIDENCE LIMITS = .1861181 AND .3767907

****

Accession No. 410250-06

DATA EVALUATION RECORD

1. **CHEMICAL:** Thiabendazole
   Shaughnessey No: Not available

2. **TEST MATERIAL:** Thiabendazole; 2-(4-thiazolyl)-benzimidazole; Lot No. PRM-029; CAS Registry No. 148-79-8; 99.6% active ingredient; an off-white, odorless powder.

3. **STUDY TYPE:** Acute Toxicity Test for Freshwater Fish. Species Tested: Bluegill (Lepomis macrochirus)

4. **CITATION:** Beglinger, J.M. and R.J. O'Boyle. 1989. Acute Aquatic Effects of Thiabendazole on the Bluegill Sunfish (Lepomis macrochirus). Study No. EN-413-GWN001-2. Prepared by Eastman Kodak Company, Rochester, New York. Submitted by Merck and Company, Inc., Iselin, New Jersey. Accession No. 410250-06.

5. **REVIEWED BY:**

Kimberly Rhodes
Associate Scientist
KBN Engineering and
Applied Sciences, Inc.

Signature: Kimberly Rhodes
Date: May 31, 1989

6. **APPROVED BY:**

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

Signature: P. Kosalwat
Date: May 31, 1989

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

Signature: Richard m. Lee
Date: June 27, '89

7. **CONCLUSIONS:** This study appears scientifically sound but does not fulfill the Guideline requirements for a 96-hour static acute toxicity study using a warmwater fish species. The 96-hour LC50, based upon mean measured concentrations, of Thiabendazole to bluegill (Lepomis macrochirus) was greater than 13 mg/L for replicate A and greater than 12 mg/L for replicate B. Therefore, Thiabendazole is considered slightly toxic to bluegill. The NOEC was determined to be 6.8 mg/L after 96 hours of exposure.

(p.2)

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8. RECOMMENDATIONS: N/A

9. BACKGROUND:

10. DISCUSSION OF INDIVIDUAL TESTS: N/A

11. MATERIALS AND METHODS:

A. Test Animals: Juvenile bluegill (Lepomis macrochirus) used in this test were obtained from a commercial fish supplier in New Hampshire. The fish were acclimated to the diluent water for at least two weeks prior to testing.

B. Test System: The toxicity test was conducted in seamless glass 30.5-cm cuboidal Pyrex chromatography jars containing 15 L of the exposure solution. A stock solution (300 mg/L) was prepared in water and continuously supplied to a diluter. The gas-driven, siphon type diluter then proportionally delivered the test solutions to the appropriate test vessels throughout the study. The test temperature was maintained at 22 $\pm$ 1°C. A photoperiod of 16 hours of light and 8 hours of darkness with a 20-minute transition period was provided each day.

The dilution water was pumped from Lake Ontario into a large underground storage reservoir. The water was subsequently filtered, treated with 150 ppb $Na_2S_2O_3$ to reduce trace levels of residual chlorine, and tempered to 20 $\pm$ 2°C. The dilution water then passed through a column degassing unit into an open aeration basin for seasoning and additional warming prior to use. The test diluent water was drawn from this source at 22 $\pm$ 1°C. The dilution water was characterized as having a total hardness of 110 mg/L as $CaCO_3$, a total alkalinity of 88 mg/L as $CaCO_3$, a pH of 8.3, and a specific conductance of 300 umhos/cm.

C. Dosage: 96-hour acute flow-through test.

D. Design: Juvenile bluegill, as uniform in size as possible, were randomly allocated to each vessel. Biological loading within test vessels was below 1.0 g wet weight per liter of test solution. The average wet weights of the two sets of control fish were determined at the start of the test.

A control and five nominal Thiabendazole concentrations of 1.9, 3.8, 7.5, 15 and 30 mg/L were tested in replicates of two. A total of twenty fish were exposed to each of the five test concentrations and control (ten fish/replicate). All concentrations were observed at 0, 6, 24, 48, 72, and 96 hours of exposure for mortality and signs of stress.

The water quality parameters (dissolved oxygen, pH, and temperature) were measured in the controls and all test concentrations at each 24-hour interval. Analytical determination of Thiabendazole was performed on all test concentrations and control at test initiation (0 hour) and termination (96 hours) using HPLC.

E. Statistics: The concentration of test substance lethal to 50 percent of the test population (LC50) was determined by a computerized calculation program developed by Stephan (1977) and ASTM (1987).

12. REPORTED RESULTS: Thiabendazole did not cause mortality at any of the exposure concentrations tested (Table 1, attached). The mean measured concentrations of Thiabendazole ranged from 40% to 47% of the nominal concentrations.

The concentration of Thiabendazole in the exposure solutions considerably dropped during the 96-hour exposure (Table 2, attached). The concentration discrepancy detected between the analyzed values at times 0 and 96 hours during this bluegill sunfish study could be related to the undissolved Thiabendazole observed to be falling out of solution (in increasing amounts) in the diluter test article train glassware and in the 15- and 30-mg/L doses throughout the study. This agglomeration of undissolved material probably facilitated the steadily increasing precipitation of the test article from the aqueous phase of the exposure solutions. This precipitation continued to occur up to the time of collection of analytical samples at test end. The authors felt that the measured values represented the maximum solubilization of the test article that could be attained for the nominal concentrations during a 96-hour exposure. The recorded observations for the two highest doses clearly indicated that the aqueous solubility of Thiabendazole was exceeded in these exposure solutions while no mortality occurred in either replicate dose series.

The 96-hour LC50 for bluegill exposed to Thiabendazole was calculated to be > 13 mg/L mean measured concentration for replicate dose series A and > 12 mg/L mean measured concentration for replicate dose series B. Abnormal orientations and a dark color were noted in the highest exposure concentration. However, all fish in the highest dose reverted to a normal condition at 96 hours of exposure. Based on the results of this study, the no-observed-effect concentration for bluegill and Thiabendazole was determined to be 6.8 mg/L, at 96-hours of exposure.

During the definitive test, the temperature in all test vessels remained at 22°C, the pH ranged from 8.2 to 8.5 and the dissolved oxygen concentration ranged from 7.9 to 8.8 mg/L. The water quality parameters measured during this study remained within acceptable ranges for the survival of the bluegill and were not likely to have caused any adverse effects.

13. STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES: The results of this study indicated that an isolated or intermittent exposure to a concentration of the test Thiabendazole less than 6.8 mg/L was unlikely to affect bluegill sunfish adversely.

This study was conducted according to: Good Laboratory Practice for Nonclinical Laboratory Studies as promulgated by the Food and Drug Administration; 21 CFR Part 58; Environmental Protection Agency Good Laboratory Practice Standard 40 CFR Part 160; and Organization of Economic Cooperation and Development Principles of Good Laboratory Practice specified in Annex 2 of the OECD Guidelines for Testing of Chemicals [C(81) 30(Final)] as required by Council Directive 87/18/EEC.

14. REVIEWER'S DISCUSSION AND INTERPRETATION OF STUDY RESULTS

A. Test Procedure: The test procedures were generally in accordance with protocols recommended by the Guidelines, but deviated from the SEP as follows:

o The dosage levels tested were less than 100 ppm but not high enough to produce a more precise LC50 value.

o The SEP states that use of a natural dilution water with a hardness of 40 to 48 mg/L as $CaCO_3$ can be used in lieu of reconstituted water. The dilution water used for the toxicity test had a total hardness of 110 mg/L as $CaCO_3$.

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o The SEP states that temperature should be recorded every six hours in at least one test vessel during the entire study period if the temperature is controlled by a water bath. During the study, the test temperature was measured and recorded every 24 hours.

The toxicity report did not provide the following information required by the SEP:

o The age of the test fish.

o Weight and length of the fish used in the study. The SEP states that individual fish should weigh between 0.5 and 5 grams and the standard length of the longest fish should not be more than twice the length of the shortest fish.

o Complete descriptions of the holding conditions. The percent of mortality 48 hours prior to test initiation and feeding schedules should also have been reported.

o The flow rate of the diluter system. The SEP states that the flow rate should be five to ten volume additions per 24-hours.

B. Statistical Analysis: Since there was no mortality in any test solution statistical analysis was not needed.

C. Discussion/Results: The study appears to be scientifically valid but it does not fulfill the requirements for a freshwater fish test. A more precise LC50 value could not be determined since all concentrations tested were too low to produce any mortality. The two highest test concentrations did not clearly indicate that the aqueous solubility limit was exceeded as the authors claimed (i.e., the highest measured concentration was almost two times as that of the second highest concentration). Higher concentrations should have been included in the test to show that the test material reached its solubility limit. From Table 2 (attached), the 96-hour measured concentrations ranged from 28% to 38% of the 0-hour measured concentrations. Therefore, the diluter system might not have been functioning properly to maintain uniform test concentrations. Before conducting another definitive test, the authors should conduct several range-finding tests using different types of solvent to determine if the solubility of the test material will improve in the test solutions.

The 96-hour LC50 value, based upon mean measured concentrations, was estimated to be greater than 13 mg/L for replicate A and greater than 12 mg/L for replicate B. Therefore, Thiabendazole is considered slightly toxic to bluegill (Lepomis macrochirus) in this test. The NOEC was determined to be 6.8 mg/L after 96 hours of exposure.

D. Adequacy of the Study:

(1) **Classification:** Supplemental

(2) **Rationale:** See comments in 14A and 14C.

(3) **Repairability:** No

15. **COMPLETION OF ONE-LINER:** Yes, 05-26-89

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Shaughnessey No. Not available Chemical Name Thiabendazole Chemical Class ____ Page ____ of ____

Study/Species/Lab/ Accession	Chemical % a.i.	Results	Reviewer/ Date	Validity Stat
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}		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.(%)=		
Species		Slope= # Animals/Level= Sol. Contr. Mort.(%)=		
Lab ____		48-Hour Dose Level pp /(%Mortality) Temperature = ( ), ( ), ( ), ( ), ( )	____	—
Acc.		Comments:		
96-Hour LC_{50}		LC50 = pp__ (95% C.L.) Con. Mor.(%)=		
Species		Slope= # Animals/Level= Sol. Con. Mor.(%)=		
Lab ____		96-Hour Dose Level pp /(%Mortality) Temp.= ( ), ( ), ( ), ( ), ( )	____	—
Acc.		Comments:		
96-Hour LC_{50}	Replicate A LC50 = >13 Replicate B LC50 = >12	ppm (95% C.L. N/A) Con. Mort.(%)= 0		
Species Lepomis macrochirus		Slope= N/A # Animals/Level= 20 Sol. Con. Mort.(%)= N/A	K.R 5/30/89	Suppl
Lab Eastman Kodak Company	99.6 %	Temp.= 22 ± 1°C		
Acc. 410250-06	Replicate A	96-Hour Dose Level pp /(%Mortality) 0.78 (0), 1.8 (0), 3.5 (0), 6.8 (0), 13 (0)		
	B	0.76 (0), 1.8 (0), 3.5 (0), 6.8 (0), 12 (0)		
		Comments: Based on mean measured concentrations.		

Page ___ is not included in this copy.

Pages 19 through 20 are not included in this copy.

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.

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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.

Accession No. 410250-02

DATA EVALUATION RECORD

1. **CHEMICAL:** Thiabendazole.
Shaughnessey Number: not available.

2. **TEST MATERIAL:** Thiabendazole Technical, Product No. 47982, Lot No. PRM 029, 99.6% purity, a white powder.

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

4. **CITATION:** Grimes, J. and M. Jaber. 1988. Technical Thiabendazole: An Acute Oral Toxicity Study With the Bobwhite. Conducted by Wildlife International, Ltd., Easton, Maryland. Project No. 105-138. Submitted by Merck and Company, New Jersey. EPA Accession No. 410250-02.

5. **REVIEWED BY:**

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

Signature: P. Kosalwat
Date: May 31, 1989

6. **APPROVED BY:**

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

Signature: James R Newman
Date: 5/31/89

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

Signature: Henry T. Craven
Date: 6/14/89

7. **CONCLUSIONS:** This study is scientifically sound and fulfills the guideline requirements for an avian LD50 test. With a 14-day LD50 value of greater than 2250 mg a.i./kg, Thiabendazole technical is considered practically non-toxic to bobwhite quail (Colinus virginianus) when administered as a single oral dose. The NOEL was determined to be 486 mg a.i./kg, based on signs of toxicity observed at dosage levels of 810 mg/kg and higher.

8. **RECOMMENDATIONS:** N/A

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9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** Bobwhite quail (Colinus virginianus) obtained from Fritts' Quail Farm, Phillipsburg, New Jersey, were approximately 25 weeks old and appeared to be in good health at study initiation. The birds ranged in weight from 180 grams to 238 grams. All birds were pen-reared and phenotypically indistinguishable from wild birds. The birds were acclimated to the caging and facilities for 12 weeks prior to the initiation of the study. During acclimation, all birds were observed daily. Birds exhibiting abnormal behavior or physical injury were not used.

All test birds were fed a game bird ration and water from the town of Easton ad libitum throughout the acclimation and testing periods. During the study period, they received no form of antibiotic medication. The birds were fasted for a minimum of 15 hours prior to dosing.

B. **Test System:** Test birds were housed indoors by dosage group in batteries of commercial pens. Each pen had floor space that measured approximately 78 x 51 cm. The floors were sloped so that the ceiling height ranged from approximately 20 to 25 cm. External walls, ceilings and floors were constructed of galvanized wire while side walls were constructed of galvanized sheeting. Birds were maintained at ambient room temperature which had an average temperature of 22 $\pm$ 2°C with an average relative humidity of 65%. The photoperiod was eight hours of light per day during acclimation and throughout the study. The birds received approximately twelve footcandles of illumination.

The test material was dispersed in corn oil. The concentration of the test material in the diluent was adjusted to provide a constant volume to body weight dosage for all treatment birds. All dosages were adjusted to 100% active ingredient.

C. **Dosage:** Fourteen-day single-dose oral LD50 test. Based upon known toxicity data, the nominal dosages selected for the study were 292, 486, 810, 1350, and 2250 mg a.i. of Thiabendazole technical per kg body weight.

D. **Design:** Groups of ten bobwhite, five males and five females, were assigned to each of the five treatment groups and the control group by random draw. At initiation of the test, a single dose of the test material in diluent was orally intubated directly into the crop or proventriculus of each bird using a stainless steel catheter. Each bird was individually weighed and dosed on the basis of milligrams of test substance per kilogram of body weight. The control birds received a corresponding volume of diluent only. All treatment and control birds received a constant dosage volume of 6 milliliters per kilogram of body weight.

Following test initiation until test termination (Day 14), all birds were observed at least twice daily. A record was maintained of all mortality, signs of toxicity, or abnormal behavior. Individual body weights were measured at initiation of the test and by group on Days 3, 7, and 14 of the test. Average estimated feed consumption was determined for each dosage group and the control for Days 0-3, 4-7, and 8-14. The feed consumption was presented as an estimate due to the unavoidable wastage by the birds. Samples of the stock solutions for each dosage level were analyzed for Thiabendazole technical.

E. **Statistics:** An estimation of the LD50 value was made by a visual inspection of the data since the mortality pattern in this study was not conducive to calculating the LD50.

12. **REPORTED RESULTS:** Mean measured concentrations of Thiabendazole technical in the stock solutions ranged from 96 to 104% of the nominal concentrations, indicating that the test substance was mixed properly in the diluent.

There were no mortalities in any treated or control groups. All control birds were normal in appearance and behavior throughout the test period. At 292 mg/kg and 486 mg/kg, there were no overt signs of toxicity and all birds were normal in appearance and behavior. At 810 mg/kg, signs of toxicity were noted in one male approximately one hour and fifteen minutes after dosing. Although no clinical signs were noted during Day 1, one male and one female were noted

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with a ruffled appearance on Day 2. The male continued to display a ruffled appearance on Day 3. All birds appeared normal by the morning of Day 4.

At 1350 mg/kg, signs of toxicity were noted in one female approximately thirty minutes after dosing. All birds appeared normal from the morning of Day 1. At 2250 mg/kg, signs of toxicity were noted in one female approximately one hour and thirty minutes after dosing. A male was noted displaying signs of toxicity approximately four hours and forty-five minutes after dosing. All birds appeared normal from the morning of Day 1.

Typical signs of toxicity of intoxication with Thiabendazole technical included reduced reaction to external stimuli, lethargy, ruffled appearance, wing droop, loss of coordination and lower limb weakness.

When compared to the controls, there was a loss in body weight among males at 1350 mg/kg and among males and females at 2250 mg/kg from Day 0 to Day 3 (Table 3, attached). Feed consumption was highly variable among the treatment groups and a dose-response relationship could not be detected.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The bobwhite acute oral LD50 value for Thiabendazole technical was determined to be greater than 2250 mg a.i./kg, the highest dosage tested. The no-observed-effect level (NOEL) was 486 mg a.i./kg, based on overt signs of toxicity at 810 mg/kg.

The study was conducted so as to conform with Good Laboratory Practices as published by the U.S. Environmental Protection Agency, Office of Pesticide Programs in 40 CFR Part 160. The study was examined and the final report signed by the Quality Assurance Unit of Wildlife International Ltd.

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

A. **Test Procedure:** The test procedures are in accordance with the SEP guidelines, except for the following deviations:

o Gross necropsy was not performed at test termination.

o Individual body weights were measured only at test initiation. The SEP recommends that individual body weights be measured and reported at the beginning and the end of the study.

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B. **Statistical Analysis:** Since no mortalities occurred during the test, statistical analysis was not used to calculate the LD50 value.

C. **Discussion/Results:** The LD50 value of Thiabendazole technical for bobwhite quail, when administered as an oral single dose, was greater than 2250 mg a.i./kg. Therefore, Thiabendazole technical is considered practically non-toxic to bobwhite quail. The NOEL was determined to be 486 mg a.i./kg, based on signs of toxicity observed at dosage level of 810 mg/kg.

D. **Adequacy of the Study:**

(1) Classification: Core.

(2) Rationale: N/A.

(3) Repairability: N/A.

15. **COMPLETION OF ONE-LINER:** Yes, May 24, 1989.

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Page 26 is not included in this copy.

Pages ___ through ___ are not included in this copy.

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.

✓ FIFRA registration data.

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

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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.

No. _____ Chemical Name Thiabendazole Technical Chemical Class ____ Page 1 of 1

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 = >2250 mg/kg * (95% C.L. N/A) Contr. Mort.(%)= 0		
Species Colinus Virginianus	99.6	Slope= N/A # Animals/Level= 10 Age(Days)= 175 Sex = M/F	PK 5-24-89	Core
Lab Wildlife International Ltd.		14-Day Dose Level mg/kg/(% Mortality) (1:1) 292(0), 486(0), 810(0), 1350(0), 2250(0)		
Acc. 410250-02		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:		

Accession No. 410250-03

DATA EVALUATION RECORD

1. **CHEMICAL:** Thiabendazole.
   Shaughnessey Number: Not available

2. **TEST MATERIAL:** Technical Thiabendazole, 99.6% active ingredient, a white powder.

3. **STUDY TYPE:** Avian Dietary LC50 Test.
   Species Tested: Bobwhite quail (Colinus virginanius).

4. **CITATION:** Grimes, J., and M. Jaber. 1989. Technical Thiabendazole: A Dietary LC50 Study with the Bobwhite. Submitted by Merck and Company, Rahway, NJ. Study performed by Wildlife International Ltd., Easton, Maryland. Laboratory Study No. 105-136. EPA Accession No. 410250-03.

5. **REVIEWED BY:**

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

   Signature: Michael L. Whitten
   Date: 5-26-89

6. **APPROVED BY:**

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

   Signature: James R Newman
   Date: 6/31/89

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

   Signature: Henry T. Craven
   Date: 6/14/89

7. **CONCLUSIONS:** With an LC50 value greater than 5620 ppm a.i, technical thiabendazole is considered practically non-toxic to bobwhite chicks. The no-observed-effect concentration was 3160 ppm based on a reduction in body weight gain and food consumption at 5620 ppm. The study is scientifically sound and meets the requirements for an avian dietary LC50 test.

8. **RECOMMENDATIONS:** N/A

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9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** The birds used in the study were 10-day old Bobwhite quail (Colinus virginanius), obtained from Sand Prairie Quail Farm, Maquoketa, Iowa. All birds were acclimated to the facilities for 9 days prior to initiation of the study. Birds exhibiting abnormal behavior or physical injury during acclimation were not used in the test.

B. **Test System:** All birds were housed indoors in 90 cm x 72 cm x 23 cm high wire pens. Fluorescent lights provided 16 hours of light per day. The temperature in the brooding compartments was 38°C ± 3°C. Average ambient room temperature was 26°C ± 2°C with an average relative humidity of 53%.

C. **Dosage:** Acute dietary LC50 test. The diets were prepared by mixing the test substance into the food with corn oil. The concentration of corn oil in the treated and control diets was 2%. Diets were prepared on the day of study initiation. Based upon "known toxicity data" nominal dietary concentrations selected for the study were 562, 1000, 1780, 3160, and 5620 parts per million (ppm). All test concentrations were adjusted to 100% active ingredient based upon the reported purity of the test substance. All dietary concentrations and the LC50 are thus reported as parts per million of active ingredient in the diet.

D. **Design:** Groups of ten birds were randomly assigned to each of five treatment groups and four control groups. The birds were too immature to differentiate by sex. The birds were fed a game bird ration formulated to Wildlife International Ltd.'s specifications. Food and water were supplied ad libitum. Each group was fed the appropriate test or control diet for five days. Following the five day exposure period all groups were given untreated food for three days. All birds were observed at least twice each day during the test for mortalities and abnormal behavior. Birds were weighed by group at test initiation, on day 5, and at termination of the test on day 8. Group food consumption was determined at the end of the five-day

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exposure period and at the end of the three-day recovery period. Samples of each of the test diets were taken for analysis of homogeneity, stability, and verification of test concentrations.

E. **Statistics:** The LD50 was not calculated, since only one bird died during the study. No statistical analyses of body weight or food consumption were reported.

12. **REPORTED RESULTS:** The mean measured concentration of technical thiabendazole in the diets was 99% (562 ppm), 91% (1000 ppm), 97% (1780 ppm), 100% (3160 ppm), and 106% (5620 ppm) of nominal values. Homogeneity and stability were verified as within acceptable limits (Tables 1-3, attached).

One mortality occurred during the study. This bird, from the 3160 ppm group, was found dead on the morning of day 3. On day 2 the bird had displayed wing droop, a ruffled appearance, lethargy, and lesions in the area around the cloacal vent.

Lesions in the cloacal area were also noted on another bird in the 3160 ppm group during days 2 and 3. The lesions on these two birds were caused by pecking of pen mates. Lesions from toe-pecking, "a cannibalistic form of aggression" were also noted in two birds in the control group, one in the 1780 ppm group, and one in the 5620 ppm group.

All other birds in all treatment and control groups were normal in appearance and behavior throughout the study.

When compared to controls, there was a reduction in body weight gain in the 5620 ppm group during days 0-5. A corresponding effect on food consumption was noted for the same period (Tables 6-7, attached).

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The bobwhite dietary LC50 of technical thiabendazole was determined to be greater than 5620 ppm a.i., the highest concentration tested. The no-observed-effect concentration was 3160 ppm based on a reduction in body weight gain and food consumption at 5620 ppm.

The study was designed and conducted in conformance with Good Laboratory Practice regulations. The data were inspected and the final report signed by the Quality Assurance Officer of Wildlife International Ltd.

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

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

Body weights were measured by group. Individual body weights should have been measured.

The SEP recommends that gross necropsies be performed. This was not done.

B. **Statistical Analysis:** Since only one bird died during the study, the LD50 can not be calculated and is assumed to be greater than 5620 ppm, the highest concentration tested.

C. **Discussion/Results:** Although no statistical analyses were performed, body weight gain and food consumption were reduced at 5620 ppm during days 1-5. Altered growth or development of birds caused by exposure to this concentration in the wild could result in reduced survival rates.

The bobwhite dietary LC50 of technical thiabendazole was determined to be greater than 5620 ppm a.i., the highest concentration tested. This value classifies technical thiabendazole as practically non-toxic to bobwhite chicks. The no-observed-effect concentration was 3160 ppm based on a reduction in body weight gain and food consumption at 5620 ppm.

With only minor deviations the study followed recommended guidelines. The study is scientifically sound and meets the requirements for an avian dietary LC50 test.

D. **Adequacy of the Study:**

(1) **Classification:** Core

(2) **Rationale:** N/A

(3) **Repairability:** N/A

15. **COMPLETION OF ONE-LINER:** Yes; May 25, 1989.

Page ___ is not included in this copy.

Pages 32 through 34 are not included in this copy.

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.

✓ FIFRA registration data.

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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.

Shaughnessey No. NOT AVAILABLE Chemical Name Thiabendazole Chemical Class ____ Page 1 of 1

Study/Species/Lab/ Accession	Chemical % a.i.	Results	Reviewer/ Date	Valid Sty
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}		LC50 > 5620ppm (95% C.L. N/A) Contr. Mort.(%)= 0		
Species Bobwhite (Colinus virginianus)		Slope= N/A # Animals/Level= 10 Age(Days)= 10 Sex = UNKNOWN	M.L.WHITTEN	
Lab Wildlife International, Ltd.	99.6 *	8-Day Dose Level ppm/(%Mortality) 562 (0), 1000 (0), 1780 (0), 3160 (0), 5620 (0)	5-25-89	CORE
Acc. 410250-03		Comments: *TEST CONCENTRATION ADJUSTED TO 100% a.i.		
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:		

Accession No. 410250-04

DATA EVALUATION RECORD

1. **CHEMICAL:** Thiabendazole.
   Shaughnessey Number: Not available.

2. **TEST MATERIAL:** Technical Thiabendazole, 99.6% active ingredient, a white powder.

3. **STUDY TYPE:** Avian Dietary LC50 Test.
   Species Tested: Mallard duck (Anas platyrhynchos).

4. **CITATION:** Grimes, J., and M. Jaber. 1989. Technical Thiabendazole: A Dietary LC50 Study with the Mallard. Submitted by Merck and Company, Rahway, NJ. Study performed by Wildlife International Ltd., Easton, Maryland. Laboratory Study No. 105-137. EPA Accession No. 410250-04.

5. **REVIEWED BY:**

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

   Signature: Michael L. Whitten
   Date: 5-26-89

6. **APPROVED BY:**

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

   Signature: James R Newman
   Date: 5/31/89

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

   Signature: Henry T. Craven
   Date: 6/1/89

7. **CONCLUSIONS:** With an LC50 value greater than 5620 ppm a.i., technical thiabendazole is considered practically non-toxic to mallard ducklings. The no-observed-effect concentration was 1780 ppm based on a reduction in body weight gain and food consumption at 3160 ppm. The study is scientifically sound and meets the requirements for an avian dietary LC50 test.

8. **RECOMMENDATIONS:** N/A

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9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** The birds used in the study were 10-day old mallards (Anas platyrhynchos) obtained from Whistling Wings, Hanover, Illinois. All birds were acclimated to the facilities for 9 days prior to initiation of the study. Birds exhibiting abnormal behavior or physical injury during acclimation were not used in the test.

B. **Test System:** All birds were housed indoors in 90 cm x 72 cm x 24 cm high wire pens. Fluorescent lights provided 16 hours of light per day. The temperature in the brooding compartments was 29°C ± 2°C. Average ambient room temperature was 24°C ± 2°C with an average relative humidity of 64%.

C. **Dosage:** Acute dietary LC50 test. The diets were prepared by mixing the test substance into the food with corn oil. The concentration of corn oil in the treated and control diets was 2%. Diets were prepared on the day of study initiation. Based upon "known toxicity data" nominal dietary concentrations selected for the study were 562, 1000, 1780, 3160, and 5620 parts per million (ppm). All test concentrations were adjusted to 100% active ingredient based upon the reported purity of the test substance. All dietary concentrations and the LC50 are thus reported as parts per million of active ingredient in the diet.

D. **Design:** Groups of ten birds were randomly assigned to each of five treatment groups and five control groups. The birds were too immature to differentiate by sex. The birds were fed a game bird ration formulated to Wildlife International Ltd.'s specifications. Food and water were supplied ad libitum. Each group was fed the appropriate test or control diet for five days. Following the five day exposure period all groups were given untreated food for three days. All birds were observed at least twice each day during the test for mortalities and abnormal behavior. Birds were weighed by group at test initiation, on day 5, and at termination of the test on day 8. Group food consumption was determined at the end of the five-day

37

exposure period and at the end of the three-day recovery period. Samples of each of the test diets were taken for analysis of homogeneity, stability, and verification of test concentrations.

E. **Statistics:** The LD50 was not calculated, since no birds died during the study. No statistical analyses of body weight or food consumption were reported.

12. **REPORTED RESULTS:** The mean measured concentration of technical thiabendazole in the diets was 99% (562 ppm), 91% (1000 ppm), 97% (1780 ppm), 100% (3160 ppm), and 106% (5620 ppm) of nominal values. Homogeneity and stability were verified as within acceptable limits (Tables 1-3, attached).

There were no mortalities in any group during the study.

There were no overt signs of toxicity at any of the concentrations tested. All birds in all treatment and control groups were normal in appearance and behavior throughout the study.

When compared to controls, there was a reduction in body weight gain in the 3160 ppm and 5620 ppm groups during days 0-5. A corresponding reduction in food consumption was noted for the same period at these two concentrations (Tables 6-7, attached).

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** The mallard dietary LC50 of technical thiabendazole was determined to be greater than 5620 ppm a.i., the highest concentration tested. The no-observed-effect concentration was 1780 ppm based on a reduction in body weight gain and food consumption at 3160 ppm.

The study was designed and conducted in conformance with Good Laboratory Practice regulations. The data were inspected and the final report signed by the Quality Assurance Officer of Wildlife International Ltd.

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

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

Body weights were measured by group. Individual body weights should have been measured.

The average temperature in the brooding compartments was 29°C ± 2°C. The recommended temperature is 35°C.

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B. **Statistical Analysis:** Since no birds died during the study, the LD50 can not be calculated and is assumed to be greater than 5620 ppm, the highest concentration tested.

C. **Discussion/Results:** Although no statistical analyses were performed, body weight gain and food consumption were reduced at 3160 ppm and 5620 ppm during days 1-5. Altered growth or development of birds caused by exposure to these concentrations in the wild could result in reduced survival rates.

The bobwhite dietary LC50 of technical thiabendazole was determined to be greater than 5620 ppm a.i., the highest concentration tested. This value classifies technical thiabendazole as practically non-toxic to mallard ducklings. The no-observed-effect concentration was 1780 ppm based on a reduction in body weight gain and food consumption at 3160 ppm.

With only minor deviations the study followed recommended guidelines. The study is scientifically sound and meets the requirements for an avian dietary LC50 test.

D. **Adequacy of the Study:**

(1) Classification: Core

(2) Rationale: N/A

(3) Repairability: N/A

15. **COMPLETION OF ONE-LINER:** Yes; May 25, 1989.

Page ___ is not included in this copy.

Pages 40 through 42 are not included in this copy.

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.

✓ FIFRA registration data.

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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.

Shaughnessey No. NOT AVAILABLE Chemical Name Thiabendazole Chemical Class ____ Page 1 of 1

Study/Species/Lab/ Accession	Chemical % a.i.	Results	Reviewer/ Date	Valid Sts
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}		LC50 = >5620ppm (95% C.L. N/A) Contr. Mort.(%)= 0	5-25-89	
Species Mallard (Anas platyrhynchos)	99.6%*	Slope= N/A # Animals/Level= 10 Age(Days)= 10 Sex = UNKNOWN	ML WHITTEN	
Lab Wildlife International, Ltd.		8-Day Dose Level ppm/(%Mortality) 562(0),1000(0),1780(0),3160(0),5620(0)	CORE	
Acc. 410250-04		Comments: * TEST CONCENTRATION ADJUSTED TO 100% a.i.		
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:		

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