

DATA EVALUATION RECORD

1. CHEMICAL: RH-7592 Technical.
Shaughnessey Number: Not available. 129011
2. TEST MATERIAL: RH-7592 Technical; Lot No. BPP-3-1786R;
96.7% active ingredient; a white solid.
3. STUDY TYPE: Freshwater Invertebrate Acute Toxicity Test.
Species Tested: Daphnia magna.
4. CITATION: Burgess, D. 1988. Acute Flow-through Toxicity
of RH-7592 Technical to Daphnia magna. Prepared by
Analytical Bio-Chemistry Laboratories, Inc., Columbia,
Missouri. Report No. 88RC-022. Submitted by Rohm and Haas
Company, Spring House, PA. Accession No. 410735-07.
5. REVIEWED BY:

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

Signature: *Kimberly Rhodes*
Date: *June 13, 1989*
6. APPROVED BY:

Prapimpan Kosalwat, Ph.D.
Staff Toxicologist
KBN Engineering and
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Signature: *P. Kosalwat*
Date: *June 14, 1989*

Henry T. Craven
Supervisor, EEB/HED
USEPA

Signature: *Henry T. Craven*
Date: *11/27/89*
11-27-89
7. CONCLUSIONS: This study appears scientifically sound and
fulfills the Guideline requirements for an acute 48-hour
flow-through toxicity test for freshwater invertebrates.
The 48-hour EC50 of RH-7592 Technical to Daphnia magna was
2.3 mg a.i./L based on mean measured concentrations.
Therefore, RH-7592 Technical is classified as moderately
toxic to Daphnia magna. The NOEC was determined to be 0.78
mg a.i./L after 48 hours.
8. RECOMMENDATIONS: N/A

9. **BACKGROUND:**
10. **DISCUSSION OF INDIVIDUAL TESTS:** N/A
11. **MATERIALS AND METHODS:**

A. **Test Animals:** Daphnia magna used in this test were obtained from laboratory stocks cultured at the testing facility. The daphnids were cultured and tested in a temperature controlled area at $20 \pm 1^{\circ}\text{C}$. During the holding period, the daphnids were fed a suspension of algae (Selenastrum capricornutum) supplemented with a Tetramin/cereal leaves suspension. Only first-instar daphnids (<24 hours old) were selected for testing.

B. **Test System:** The test was conducted in a half-liter proportional diluter system described by Mount and Brungs (1967), utilizing a Hamilton Micro Lab 420 syringe dispenser. The diluter intermittently delivered five concentrations of RH-7592, a dilution water control and a solvent control to four replicate one-liter test chambers. The diluter provided for approximately 6.6 volume replacements per 24-hour period. A photoperiod of 16 hours of light and 8 hours of darkness with 30-minute transition periods was provided. Test temperature was maintained at $20 \pm 1^{\circ}\text{C}$ by a temperature controlled water bath.

Dilution water for the Daphnia magna test was well water characterized as having a pH of 7.6, total hardness of 242 mg/L as CaCO_3 , total alkalinity of 240 mg/L CaCO_3 .

C. **Dosage:** 48-hour flow-through acute test.

D. **Design:** Based on the results of a preliminary test, a control, solvent control, and five nominal RH-7592 concentrations of 0.18, 0.36, 0.75, 1.5, and 3.0 mg a.i./L were tested. Ten Daphnia magna were randomly assigned to each of four replicate test chambers (40 per concentration). The solvent control solution contained the maximum amount of acetone present in any test concentration (0.050 mL).

All concentrations were observed at 4, 24 and 48-hours for immobilization and other abnormal effects. Test daphnids were not fed during the 48-hour study. The water quality parameters (temperature, dissolved oxygen and pH) were measured in each concentration and control at 0 and 48 hours. The temperature was also recorded

continuously with a data logger. Analytical samples were collected from each test level and the diluter stock at 0 and 48 hours of the exposure.

- E. **Statistics:** The concentration of toxicant immobilizing 50% of the population (EC50's) and 95% confidence intervals was determined at 4-, 24- and 48-hour exposure periods by the computer program developed by Stephan et al. (1978).

12. **REPORTED RESULTS:** Mortality and behavioral observations during the acute flow-through toxicity test of RH-7592 to Daphnia magna are shown in Table 5 (attached). The mean measured concentrations of RH-7592 Technical were 0.16, 0.31, 0.78, 1.4 and 3.1 mg a.i./L. The mean measured concentrations ranged from 86% to 104% of the nominal concentrations.

The 4-hour, 24-hour and 48-hour EC50 values for RH-7592 Technical based on immobilization were >3.1, >3.1, and 2.2 mg a.i./L. The no-observed effect concentration after 48 hours was estimated to be 0.78 mg a.i./L. The abnormal effects of immobilization, erratic movement and/or daphnids on the bottom of the test vessels were observed in the 1.4 and 3.1 mg a.i./L test concentrations.

Water chemistry parameters measured at 0 and 48 hours were considered adequate for testing. The dissolved oxygen concentration ranged from 8.6 to 8.9 mg/L (representing 99 and 102% saturation at 20°C), and pH ranged from 8.1 to 8.3.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:**
No conclusions were made by the author.

Quality Assurance and Good Laboratory Practice Regulation Statements were included in the report.

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 ASTM (1980 and 1988) standard protocols state that "the concentration of toxicant in the test chambers should be measured as often as practical during the test. At a minimum, the concentration of toxicant must be measured in (a) each chamber concurrently at least once during the test,

preferably near the beginning of the test; (b) except for the control treatment, each test chamber (especially for those toxicant concentrations closest to the LC_{50} or EC_{50}) at least one additional time during the test, on a schedule designed to give reasonable confidence in the concentration of toxicant in the test chambers, . . . and (c) at least one appropriate chamber whenever a malfunction is detected in any part of the metering system. In this study the concentrations of toxicants were measured as composites and only the "AB" composite replicates (control AB, 1AB, 2AB, etc.) were measured at the beginning of the test and the "CD" composite replicates (control CD, 1CD, 2CD, etc.) were measured at the end of the test. At no time were the concentrations in all of the individual chambers measured concurrently.

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 242 mg/L as $CaCO_3$.

o The SEP states that each designated treatment group should be exposed to a concentration of toxicant that is at least 60% of the next highest concentration. Each designated treatment group for this test was only 50% of the next highest concentration.

- B. **Statistical Analysis:** The reviewer used EPA's Toxanal computer program to calculate the EC_{50} values. These calculations are attached. The probit method provides a 48-hour EC_{50} value of 2.3 mg a.i./L with a 95 percent confidence interval of 2.0 to 2.7 mg a.i./L which is the similar to that reported by the author (i.e., 2.2 mg a.i./L with a 95% confidence interval of 2.0 to 2.6 mg/L). The slope of the dose-response curve was 5.3.
- C. **Discussion/Results:** Although the study results appear to be scientifically valid, the 48-hour EC_{50} value is based upon the mean of composite concentration measurements. Due to the fact that using composite concentration measurements and means of these measurements is improper (since measurements were not made in accordance with established standards), the EC_{50} thus calculated is speculative. Using averages of

averages as data in statistical analyses has the potential of masking significant problems that may have occurred during the test study. The reviewer used EPA's Toxanal computer program to calculate EC₅₀ values using 1) the composite measured concentration values of the "AB" replicates only and 2) the composite measured concentration values of the "CD" replicates only. The EC₅₀ values and the 95 percent confidence intervals thus calculated were 2.2 mg/L (1.8-2.8 mg/L) and 2.4 mg/L (1.9-3.1 mg/L) respectively. Although this method of analysis is also based on averages, (composite measured concentrations), in light of the similarity of the calculated EC₅₀ values and the cumulative immobilization data, which shows no significant differences between individual replicate samples, the study author's value, EC₅₀ of 2.3 mg/L, will be accepted. Therefore, RH-7295 Technical is classified as moderately toxic to Daphnia magna. The no-observed effect concentration (NOEC) was determined to be 0.78 mg a.i./L mean measured concentration.

D. Adequacy of the Study:

(1) **Classification:** Core.

(2) **Rationale:** Although the test procedures and analyses deviated from accepted standards, the reviewer does not believe they significantly affected the toxicity results.

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

15. **COMPLETION OF ONE-LINER FOR STUDY:** Yes, 06-06-89.

Shaugnessy No. Not availableChemical Name BH-7592
Technical

Chemical Class _____ Page _____ of _____

Study/Species/Lab/
Accession _____ Chemical
_____ & a.l.

Results

Reviewer/
Date _____ Valid
Stat _____14-Day Single Dose Oral LD₅₀LD₅₀ = _____ mg/kg (95% C.L.) Contr. Mort. (X) = _____

Species _____

Slope = _____ # Animals/Level = _____ Age (Days) = _____
Sex = _____

Lab _____

14-Day Dose Level mg/kg/(X Mortality)
() , () , () , () , () , () , ()

Acc. _____

Comments: _____

14-Day Single Dose Oral LD₅₀LD₅₀ = _____ mg/kg. (95% C.L.) Contr. Mort. (X) = _____

Species _____

Slope = _____ # Animals/Level = _____ Age (Days) = _____
Sex = _____

Lab _____

14-Day Dose Level mg/kg/(X Mortality)
() , () , () , () , () , () , ()

Acc. _____

Comments: _____

8-Day Dietary LC₅₀LC₅₀ = _____ ppm (95% C.L.) Contr. Mort. (X) = _____

Species _____

Slope = _____ # Animals/Level = _____ Age (Days) = _____
Sex = _____

Lab _____

8-Day Dose Level ppm/(X Mortality)
() , () , () , () , () , () , ()

Acc. _____

Comments: _____

8-Day Dietary LC₅₀LC₅₀ = _____ ppm (95% C.L.) Contr. Mort. (X) = _____

Species _____

Slope = _____ # Animals/Level = _____ Age (Days) = _____
Sex = _____

Lab _____

8-Day Dose Level ppm/(X Mortality)
() , () , () , () , () , () , ()

Acc. _____

Comments: _____

48-Hour EC₅₀EC₅₀ = 2.3 ppm (95% C.L.) *probit method
2.0 - 2.7) Contr. Mort. (X) = 0Species Daphnia magna

Slope = 5.3 # Animals/Level = 40 Sol. Contr. Mort. (X) = 0

Lab Analytical Bio-Chemistry
Laboratories48-Hour Dose Level ppm/(X Mortality)
0.16(0) , 0.31(0) , 0.78(0) , 1.4(15) , 3.1(75)
Temperature = 20 ± 1°C 24.2 06/06/89 Cone

Acc. 410735-07

Comments: Based on mean measured concentrations

96-Hour LC₅₀LC₅₀ = _____ PP (95% C.L.) Contr. Mort. (X) = _____
Sol. Contr. Mort. (X) = _____

Species _____

Slope = _____ # Animals/Level = _____ Temp. = _____

Lab _____

96-Hour Dose Level pp / (X Mortality)
() , () , () , () , () , () , ()

Acc. _____

Comments: _____

96-Hour LC₅₀LC₅₀ = _____ PP (95% C.L.) Contr. Mort. (X) = _____
Sol. Contr. Mort. (X) = _____

Species _____

Slope = _____ # Animals/Level = _____ Temp. = _____

Lab _____

96-Hour Dose Level pp / (X Mortality)
() , () , () , () , () , () , ()

Acc. _____

Comments: _____

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RIN 3477-95

EEB FENBUCONAZOLE REVIEW

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Pages _____ through _____ 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.
- ☒ 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.

KIMBERLY RHODES RH7592 DAPHNIA MAGNA 06-06-89

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
3.1	40	30	75	9.536742E-05
1.4	40	6	15	41.19014
.78	40	0	0	9.536742E-05
.31	40	0	0	9.536742E-05
.16	40	0	0	9.536742E-05

BECAUSE THE NUMBER OF ORGANISMS USED WAS SO LARGE, THE 95 PERCENT CONFIDENCE INTERVALS CALCULATED FROM THE BINOMIAL PROBABILITY ARE UNRELIABLE. USE THE INTERVALS CALCULATED BY THE OTHER TESTS.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 2.248594

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS
1	.1191013	2.248594	1.957075 2.637442

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
6	9.173153E-02	1	.9372214

SLOPE = 5.270943
95 PERCENT CONFIDENCE LIMITS = 3.674521 AND 6.867365

LC50 = *2.281818
95 PERCENT CONFIDENCE LIMITS = 1.989415 AND 2.666334

LC10 = 1.310199
95 PERCENT CONFIDENCE LIMITS = 1.013041 AND 1.543324

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EC₅₀ BASED ON CONCENTRATION MEASUREMENTS OF "AB" COMPOSITES

Harry A. Winnik RH-7592 10-25-89

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
3.2	20	16	80	0
1.5	20	4	20	0
.85	20	0	0	0
.32	20	0	0	0
.18	20	0	0	0

THE BINOMIAL TEST SHOWS THAT 1.5 AND 3.2 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 2.19089

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS		
2	9.753802E-02		2.19089	1.820831	2.831941

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
6	.1681605	1	.9541112

SLOPE = 5.354023

95 PERCENT CONFIDENCE LIMITS = 3.276463 AND 7.831582

LC50 = 2.217628

95 PERCENT CONFIDENCE LIMITS = 1.839777 AND 2.754645

LC10 = 1.309862

95 PERCENT CONFIDENCE LIMITS = .8869671 AND 1.611188

EC₅₀ BASED ON CONCENTRATION MEASUREMENTS OF "CD" COMPOSITES

Harry A. Winnik RH-7592 10-25-89

CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
3	20	14	70	0
1.3	20	2	10	0
.72	20	0	0	0
.3	20	0	0	0
.15	20	0	0	0

THE BINOMIAL TEST SHOWS THAT 1.3 AND 3 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 2.314135

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
1	.235757	2.314135	1.886661	3.130153

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
6	.2048037	1	.9914988

SLOPE = 5.171898
95 PERCENT CONFIDENCE LIMITS = 2.831344 AND 7.512452

LC50 = 2.360507
95 PERCENT CONFIDENCE LIMITS = 1.917261 AND 3.064244

LC10 = 1.341058
95 PERCENT CONFIDENCE LIMITS = .840843 AND 1.685337
