10-1-92

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

**MEMORANDUM**

Subject: Kathon 886 Biocide Data Review

From: Doug Urban, Acting Branch Chief
Ecological Effects Branch
Environmental Fate and Effects Division (H7507 C) 10/1/92

To: John Lee, Product Manager
Reregistration Branch
Special Review and Reregistration Division (H7508 W)

The studies listed below were reviewed by EEB. These studies reflect laboratory derived toxicity values ($LC_{50}$) which are intended to provide support for risk assessments for registration. The following studies were categorized as core which can be utilized within risk assessments.

71-2 Avian Dietary $LC_{50}$ Test using Bobwhite Quail.

71-2 Avian Dietary $LC_{50}$ Test using Mallard Duck.

If you have any questions on the above, please feel free to contact Regina Hirsch (305-5366).

| DPBARCODE (Record) | D175057 |
|---|---|
| Shaughnessy Number | 128101 |

| REVIEW NO. |
|---|
| Assigned to: Hirsch |

# EEB REVIEW

Date In: 3/3/92 Date Out:

| Case #: 192535 |
|---|
| Submission #: S412458 |
| ID #: 000707-EEU |

| Reregistration Case #: |
|---|
| LIST |

Date of Submission 2/19/92

Date Received by EFED 3/3/92

RD/SRRD Requested Completion Date 6/30/92

EEB Estimated Completion Date 6/30/92

RD/SRRD Action Code/Type of Review 116

MRID #(s) 422149-01,-02

DP Type 001 Submission Related Data Package

Product Manager, No. John Lee (31)

Product Name(s) Kathon

Product Type biocide

Company Name Rohm & Haas Co.

Submission Purpose Review data and provide status data requirements

Include Use(s)

Common Chemical Name RH-287

# DATA EVALUATION RECORD

1. **CHEMICAL:** Kathon (RH-287).
Shaughnessey No. 128101.

2. **TEST MATERIAL:** RH-287 technical; 4,5-dichloro-2-n-octyl-3(2H)-isothiazolone; CAS No. 64359-81-5; Lot No. SW 5097; T.D. No. 91-014; 96.9% purity; a light tan, crystalline solid.

3. **STUDY TYPE:** Avian Dietary $LC_{50}$ Test. Species Tested: Bobwhite quail (*Colinus virginianus*).

4. **CITATION:** Pedersen, C.A. and B.R. Helsten. 1992. RH-287 Technical: 8-Day Acute Dietary $LC_{50}$ Study in Bobwhite Quail. Laboratory Study ID. BLAL No. 111-001-01. Performed by Bio-Life Associates, Ltd., Neillsville, WI. Submitted by Rohm and Haas Company, Spring House, PA. EPA MRID No. 422149-01.

5. **REVIEWED BY:**

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

**Signature:** Mark A. Mossler
**Date:** 7/7/92

Regina Duisch 9/28/92

6. **APPROVED BY:**

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

**Signature:** Michael L Whitten
**Date:** 7/7/92

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

**Signature:** Henry T. Craven
**Date:** 9/28/92

7. **CONCLUSIONS:** This study is scientifically sound and meets the guideline requirements for an avian dietary $LC_{50}$ toxicity test. Based on mean measured concentrations, the $LC_{50}$ value of RH-287 for bobwhite quail was >4,639 ppm ai. Therefore, this compound is classified as practically non-toxic to bobwhite quail. The NOEC was 1,112 ppm ai (mean measured concentration).

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



5.5 hrs

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9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** Bobwhite quail (*Colinus virginianus*) were hatched from eggs obtained from a supplier in Gravette, AR. All birds were acclimated to testing facilities for ten days and were phenotypically indistinguishable from wild birds. Thirteen mortalities among 133 chicks occurred during the first week of the quarantine period, and no mortalities occurred during the last 3 days of the quarantine period. The birds were 10 days of age at test initiation.

B. **Test System:** The birds were housed in wire pens in a thermostatically controlled room. The pens measured 45.7 x 61 x 45.7 cm. During the test, the average temperature was 39°C. The relative humidity was 60%. A 24-hour fluorescent lighting photoperiod was used throughout the study.

The test diets were prepared by mixing the test substance (67.08 g) into the diet (12,933 g Purina® Gamebird Startena) with 192.9 ml of acetone. This diet was equal to the highest test concentration. Equal amounts of the test diet and standard diet were blended to create the lower test concentrations. Prior to and following the 5-day exposure period, all birds were placed on regular feed and water *ad libitum*.

C. **Dosage:** Eight-day acute dietary $LC_{50}$ test. Dosage levels selected for the study were 312, 625, 1,250, 2,500, and 5,000 ppm. The amount of material added to the diets was adjusted for the active ingredient (ai) of the test substance. A vehicle control was prepared that contained the same amount of acetone added to the diet as did the highest treatment diet (1.5%).

D. **Design:** Ten chicks per test level and in each of five controls were arbitrarily assigned to pens. Observations were made daily to ascertain the presence or absence of clinical signs indicative of test material effect. Inspections were made daily for mortalities, abundance of food and water, and food spillage.

The three birds that died and four arbitrarily selected birds sacrificed from the control and each treatment



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group at the termination of the project were subjected to a complete gross pathological examination.

Body weights by group were measured at 0-hour on day 1, day 5, and day 8 of the test. Average feed consumption was determined daily by group for days 0-5 (the exposure period) and through days 6-8 (the observation period).

Immediately after diet preparation, three 20 g samples of each test diet were sent to the sponsor's laboratory for verification of test concentration and homogeneity. Additionally, samples were taken from the test concentrations and controls and left in the testing room during the exposure period. These samples, as well as samples of frozen diet, were sent to the laboratory for verification of test substance stability.

E. **Statistics:** No statistical methods or results were reported.

12. **REPORTED RESULTS:** No mortality or abnormal behavior was observed in the control groups or the four lowest concentration treatment groups during the study. Three mortalities were noted in the 5,000 ppm ai group (one each on days 3, 4, and 5). The $LC_{50}$ was determined to be in excess of 5,000 ppm ai.

Lethargy and anorexia was observed in the 5,000 ppm ai test group. Complete remission of clinical signs was achieved in survivors by test day 6. Gross necropsies revealed no abnormal findings.

The concentration of RH-287 in the feed was presented in the report (Appendix C, Table 1, attached). Measured concentrations at test initiation ranged from 81 to 93% of nominal concentrations.

There was a reduction in body weight gain and food consumption during the exposure period at the two highest treatment concentrations (Tables 2 and 3, attached), when compared to the vehicle controls. The no-observed-effect concentration (NOEC) was determined to be 1,250 ppm ai.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** No conclusions other than those stated above or tabularized were presented by the authors.

Quality Assurance and Good Laboratory Practice (GLP) compliance statements were included in the report,

indicating that the study was conducted in accordance with GLPs as set forth in 40 CFR Part 160.

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

**A. Test Procedure:** The test procedures were in accordance with Subdivision E, ASTM, and SEP guidelines with the following exceptions:

The pen dimensions (45.7 x 61 cm = 2,788 $cm^2$) were smaller than recommended (35 x 100 cm = 3,500 $cm^2$).

Birds were weighed by group. The guidelines recommend that the birds be weighed individually.

The average room temperature (39°C) was greater than recommended (35°C).

**B. Statistical Analysis:** Since a dose response was not evident by the end of the testing period, an $LC_{50}$ value and 95% confidence limits could not be obtained. A discussion of the $LC_{50}$ is presented below.

**C. Discussion/Results:** The results from the dietary analyses demonstrated that the diets were slightly less in concentration than the desired nominal concentrations. The highest test concentration that the chicks were exposed to was 4,639 ppm ai. The guidelines state that an LC value must be established unless it can be shown that the $LC_{50}$ is greater than 5,000 ppm. Using measured concentrations, the study does not meet this requirement. However, an additional 361 ppm probably would not change the results of this test. Therefore, this result does not invalidate the study and the $LC_{50}$ is greater than 4,639 ppm ai.

This study is scientifically sound and meets the guideline requirements for an avian dietary $LC_{50}$ toxicity test. Based on mean measured concentrations, the $LC_{50}$ value of RH-287 for bobwhite quail was >4,639 ppm ai. Therefore, this compound is classified as practically non-toxic to bobwhite quail. The NOEC was 1,112 ppm ai, (mean measured concentration) based on reduced bodyweight gain and feed consumption observed at the two highest test concentrations.

**D. Adequacy of the Study:**

**(1) Classification:** Core.

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

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

15. **COMPLETION OF ONE-LINER:** Yes, 6-26-92.

KATHON 287 T

Page _____ is not included in this copy.

Pages 8 through 10 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.

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.

Shaughnessey # 128101 Chemical Name Kathon (KH-287) Chemical Class _____ Page 1 of 1

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Study/Species/Lab/ MRID # | Chemical % a.i. | Results | Reviewer/ Date | Validation Status

14-Day Single Oral $LD_{50}$

$LD_{50}$ = _____ mg/kg ( 95% C.L. ) Control Mortality (%) =

Species

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

Sex =

Lab

14-Day Dose Level mg/kg/(% Mortality)

( ), ( ), ( ), ( ), ( )

MRID #

Comments:

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8-Day Dietary $LC_{50}$

96.9

$LC_{50}$ = >4639 ppm a.i.* ( 95% C.L. n/a ) Control Mortality (%) = 0

Species

Colinus virginianus

Slope = n/a # Animals/Level = 10/lvl 50/control Age (Days) = 10

Sex = n/a

Lab

Bio-Life Associates Ltd.

8-Day Dose Level ppm a.i.* /(% Mortality)

252 ( 0 ), 529 ( 0 ), 1,112 ( 0 ), 2,295 ( 0 ), ~~5000~~ 4639 ( 30 )

MRID #

422149-01

Comments: * Based on mean measured concentrations

Note: 1,112 ppm a.i.*

M. Master 6/26/92

Core

# DATA EVALUATION RECORD

1. **CHEMICAL:** Kathon (RH-287).
Shaughnessey No. 128101.

2. **TEST MATERIAL:** RH-287 technical; 4,5-dichloro-2-n-octyl-3(2H)-isothiazolone; CAS No. 64359-81-5; Lot No. SW 5097; T.D. No. 91-014; 96.9% purity; a light tan, crystalline solid.

3. **STUDY TYPE:** Avian Dietary $LC_{50}$ Test. Species Tested: Mallard duck (*Anas platyrhynchos*).

4. **CITATION:** Pedersen, C.A. and B.R. Helsten. 1992. RH-287 Technical: 9-Day Acute Dietary $LC_{50}$ Study in Mallard Ducklings. Laboratory Study ID. BLAL No. 111-002-02. Performed by Bio-Life Associates, Ltd., Neillsville, WI. Submitted by Rohm and Haas Company, Spring House, PA. EPA MRID No. 422149-02.

5. **REVIEWED BY:**

Mark A. Mossler, M.S.
Associate Scientist
KBN Engineering and
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**Signature:** Mark A. Mossler
**Date:** 7/7/92

Regina Hesch 9/28/92

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**Signature:** Michael L. Whitten
**Date:** 7/7/92

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

**Signature:** Henry T. Craven 9/28/92
**Date:**

7. **CONCLUSIONS:** This study is scientifically sound and meets the guideline requirements for an avian dietary $LC_{50}$ toxicity test. Based on mean measured concentrations, the $LC_{50}$ value of RH-287 for mallard ducklings was >4,639 ppm ai. Therefore, this compound is classified as practically non-toxic to the mallard duck. The NOEC was 529 ppm ai (mean measured concentration).

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



5 hrs

12

9. **BACKGROUND:**

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

11. **MATERIALS AND METHODS:**

A. **Test Animals:** Mallard ducklings (*Anas platyrhynchos*) were obtained from a supplier in Hanover, IL. All birds were acclimated to the caging and facilities for eight days and were phenotypically indistinguishable from wild birds. Two mortalities among 120 ducklings occurred during the first two days of the quarantine period, and none occurred during the final six days. The birds were 10 days of age at test initiation.

B. **Test System:** The birds were housed in wire pens in a thermostatically controlled room. The pens measured 61 x 61 x 45.7 cm. During the test, the average temperature was 28°C. The relative humidity was 83%. A 24-hour fluorescent lighting photoperiod was used throughout the study.

The test diets were prepared by mixing the test substance (67.08 g) into the diet (12,933 g Purina® Gamebird Startena) with 192.9 ml of acetone. This diet was equal to the highest test concentration. Equal amounts of the test diet and standard diet were blended to create the lower test concentrations. Prior to and following the 5-day exposure period, all birds were placed on regular feed and water *ad libitum*.

C. **Dosage:** Nine-day acute dietary $LC_{50}$ test. Dosage levels selected for the study were 312, 625, 1,250, 2,500, and 5,000 ppm. The amount of material added to the diets was adjusted for the active ingredient (ai) of the test substance. A vehicle control was prepared that contained the same amount of acetone added to the diet as did the highest treatment diet (1.5%).

D. **Design:** Ten ducklings per test level and in each of five controls were arbitrarily assigned to pens. Observations were made daily to ascertain the presence or absence of clinical signs indicative of test material effect. Inspections were made daily for mortalities, abundance of food and water, and food spillage.

The three birds that died and four arbitrarily selected birds sacrificed from the control and each treatment

group at the termination of the project were subjected to a complete gross pathological examination.

Body weights by group were measured at 0-hour on day 1, day 5, and day 9 of the test. Average feed consumption was determined daily by group for days 0-5 (the exposure period) and through days 6-9 (the observation period).

Immediately after diet preparation, three 20 g samples of each test diet were sent to the sponsor's laboratory for verification of test concentration and homogeneity. Additionally, samples were taken from the test concentrations and controls and left in the testing room during the exposure period. These samples, as well as samples of frozen diet, were sent to the laboratory for verification of test substance stability.

E. **Statistics:** No statistical methods or results were reported.

12. **REPORTED RESULTS:** No mortality or abnormal behavior was observed in the control groups or the 312 and 625 ppm ai treatment groups during the study. One mortality occurred in each of the 1,250 and 2,500 ppm ai groups on day 5. One mortality was noted in the 5,000 ppm ai group at the beginning of day 7, and the study was extended to 9 days because of this observation. No other mortalities occurred. The $LC_{50}$ was determined to be in excess of 5,000 ppm ai.

Smallness of size and asthenia were observed in one bird in each of the 1,250 and 2,500 ppm ai test groups on day 4. The affected bird in the 1,250 ppm ai group also had a twisted beak and this bird was found dead on day 5. Lethargy was observed in the 5,000 ppm ai test group. Complete remission of clinical signs was achieved in survivors by test day 6.

The concentration of RH-287 in the feed was presented in the report (Appendix C, Table 1, attached). Measured concentrations at test initiation ranged from 81 to 93% of nominal concentrations.

Besides the twisted beak, gross necropsies revealed no abnormal findings. The twisted beak was not believed to be related to treatment.

There was a reduction in body weight gain and food consumption during the exposure period at the two highest treatment concentrations (Tables 2 and 3, attached), when



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compared to the vehicle controls. The no-observed-effect concentration (NOEC) was determined to be 625 ppm ai.

13. **STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES:** No conclusions other than those stated above or tabularized were presented by the authors.

Quality Assurance and Good Laboratory Practice (GLP) compliance statements were included in the report, indicating that the study was conducted in accordance with GLPs as set forth in 40 CFR Part 160.

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

A. **Test Procedure:** The test procedures were in accordance with Subdivision E, ASTM, and SEP guidelines with the following exceptions:

The pen dimensions (61 x 61 cm = 3,721 $cm^2$) were smaller than recommended (70 x 100 cm = 7,000 $cm^2$).

Ten-day old ducklings were used. Five-day old birds are preferred.

Birds were weighed by group. The guidelines recommend that the birds be weighed individually.

The average humidity in the test room (83%) was greater than recommended (80%).

The average room temperature (28°C) was less than recommended (35°C).

B. **Statistical Analysis:** Since a dose response was not evident by the end of the testing period, an $LC_{50}$ value and 95% confidence limits could not be obtained. A discussion of the $LC_{50}$ is presented below.

C. **Discussion/Results:** The results from the dietary analyses demonstrated that the diets were slightly less in concentration than the desired nominal concentrations. The highest test concentration that the ducklings were exposed to was 4,639 ppm ai. The guidelines state that an $LC_{50}$ value must be established unless it can be shown that the $LC_{50}$ is greater than 5,000 ppm. Using measured concentrations, the study does not meet this requirement. However, an additional 361 ppm probably would not change the results of this



15

test. Therefore, this result does not invalidate the study and the $LC_{50}$ is greater than 4,639 ppm ai.

This study is scientifically sound and meets the guideline requirements for an avian dietary $LC_{50}$ toxicity test. Based on mean measured concentrations, the $LC_{50}$ value of RH-287 for mallard ducklings was >4,639 ppm ai. Therefore, this compound is classified as practically non-toxic to the mallard duck. The NOEC was 529 ppm ai, (mean measured concentration) based on mortality and sublethal effects observed at the three highest test concentrations.

D. Adequacy of the Study:

(1) **Classification:** Core.

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

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

15. COMPLETION OF ONE-LINER: Yes, 6-25-92.

KATHON 287 T

Page _____ is not included in this copy.

Pages 17 through 19 are not included in this copy.

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Shaughnessey # 128101 Chemical Name Kathon (RH-287) Chemical Class _____ Page 1 of 1

| Study/Species/Lab/ MRID # | Chemical % a.i. | Results | Reviewer/ Date | Validation Status |
|---|---|---|---|---|
| 14-Day Single Oral $LD_{50}$ | _____ | $LD_{50}$ = mg/kg (95% C.L.) Control Mortality (%) = | | |
| Species | | Slope = # Animals/Level = Age (Days) = Sex = | | |
| Lab | | | _____ | _____ |
| MRID # | | 14-Day Dose Level mg/kg/(% Mortality) ( ), ( ), ( ), ( ), ( ) Comments: | | |

| | | | | |
|---|---|---|---|---|
| 8-Day Dietary $LC_{50}$ | 96.9 | $LC_{50}$ = >4639 ppm ai* (95% C.L. N/A) Control Mortality (%) = 0 | | |
| Species | | Slope = N/A # Animals/Level = 10/rep + 30/control Age (Days) = 10 Sex = N/A | | |
| Lab | Fio-Life Associates Ltd. | 9 8-Day Dose Level ppm ai* /(% Mortality) 252 ( 0 ), 529 ( 0 ), 1112 ( 10 ), 2287 ( 10 ), 4639 ( 10 ) | Middleton 6/25/92 | Core |
| MRID # | 42214902 | Comments: * - based on mean measured concentrations. NOEC = 529 ppm ai* | | |