

6/10/87

25

Shaughnessy No.: 128857
Date out of EAB: MAY 22 1987

To: Lois Rossi
Product Manager 21
Registration Division (TS 767C)

From: Emil Regelman, Supervisory Chemist
Review Section #3
Exposure Assessment Branch
Hazard Evaluation Division (TS 769C)

R

Soil photo
not acceptable

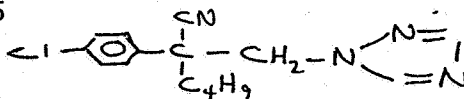
Attached, please find the EAB review of...

Reg./File # 701-ERE, -ERN, -ERR
Chemical Name: Myclobutanil
Type Product: fungicide
Product Name: Rally
Company Name: Rohm and Haas
Purpose: submission of environmental fate data in support of registration
Action Code: 110 EAB # (s): 70448, 70449, 70450
Date Received: 3/25/87 TAIS Code: _____
Date Completed: MAY 22 1987 Total Reviewing Time: 0.5 Day
Monitoring Study Requested: _____
Monitoring Study Volunteered: _____

Deferrals to: _____ Ecological Effects Branch
_____ Residue Chemistry Branch
_____ Toxicology Branch

1. CHEMICAL:

chemical name: alpha-butyl-alpha-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile
common name: myclobutanil
trade name: Rallytm, RH-3866
structure:
CAS #
Shaughnessy #: 128857



2. TEST MATERIAL: described in specific study
3. STUDY/ACTION TYPE: data submission in support of registration
4. STUDY IDENTIFICATION:

Nelson, S.S. Laboratory Soil Photolysis Study of RH-3866. Rohm and Haas Company, Philadelphia, PA. Technical Report No. 310-85-08 dated April 26, 1985, received 11/5/86. Acc. # 7F3475, 7H5524

5. REVIEWED BY:

Typed Name: E. Brinson Conerly
Title: Chemist, Review Section 3
Organization: EAB/HED/OPP

E. Brinson Conerly 5/20/87

6. APPROVED BY:

Typed Name: Emil Regelman
Title: Supervisory Chemist, Review Section 3
Organization: EAB/HED/OPP

Emil Regelman
MAY 22 1987

7. CONCLUSIONS:

This study is not acceptable to fulfill the requirements for photolysis on soil, because the light source used had essentially no visible wavelengths, and therefore did not simulate sunlight. The applicant has demonstrated stability of the compound at 34° C in the dark and under "black-light" irradiation, but this study does not translate into usual environmental conditions. Commercial sources of sun-simulating light are available.

We reiterate our previous review of December 1986 (EBC -- copy attached) which acknowledges the existence of the referenced studies and gives their status:

hydrolysis -- satisfied

photodegradation in water -- a study is on file, but was not acceptable since it was done with pond water instead of deionized or distilled water containing an appropriate buffer

photodegradation in soil -- reviewed in this document

aerobic and anaerobic soil metabolism -- a study is on file which requires information on degradates to be acceptable

leaching -- not fully satisfied, requires data on "aged" compound

adsorption/desorption -- satisfied

field dissipation -- not satisfied -- information needed from study on file regarding identification of degradates and specificity of analytical method

fish bioaccumulation -- requires additional information on k_{ow} of

principal degradates.

To our knowledge, the requested additional information and studies have not been submitted.

8. RECOMMENDATIONS:

The applicant should furnish a similar study, done either in sunlight or using a light source which closely simulates sunlight.

9. BACKGROUND:

The applicant has submitted three volumes of material: the A, B, E, F, and G sections of the tolerance petition in one volume, the above described photolysis study in the second volume, and summary and discussion of RH-3866 environmental fate. Previous reviews have been written regarding other submissions which the applicant mentions as being on file.

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

A. STUDY IDENTIFICATION

Nelson, S.S. Laboratory Soil Photolysis Study of RH-3866. Rohm and Haas Company, Philadelphia, PA. Technical Report No. 310-85-08 dated April 26, 1985, received 11/5/86. Acc. # 7F3475, 7H5524

B. MATERIALS AND METHODS

test chemical - Solubility in water is 142 ppm.

¹⁴C RH-3866 was labelled as follows:

in the 3,5 position of the triazole ring -- 10.98 mCi/gm, 100% radiopure

working solution -- 0.71 ml solution to 10.0 ml with methanol

uniformly in the phenyl ring -- 10.28 mCi/gm, 98.0% radiopure

working solution -- 0.94 ml solution to 10.0 ml with methanol.

¹⁴C 2,4-D was uniformly labelled in the aromatic ring, 26.42 mCi/gm, 91.7% radiopure

working solution -- 0.93 mg in 10.0 ml methanol

analytical methods

LSC -- direct counting of liquid samples, or combustion followed by counting autoradiography

TLC

ethyl acetate/2-propanol/H₂O 70:20:10

chloroform/methanol 90:10

photolysis apparatus -- alternating fluorescent blacklights and fluorescent sunlamps, said by the author to emit a range of 290 - 760 nm.

test soil -- Lawrenceville silt-loam soil (see attached table of properties) air-dried, sieved to <2.00 mm. 15 gm aliquots were used for the tests.

test samples -- Aliquots spiked with 1.5 ml of working solutions of RH-3866 or 0.75 ml working solution 2,4-D. Incubation flasks were continuously purged with filtered air (water and CO₂ removed). Volatile organic compounds in the effluent were trapped on Chromosorb, and CO₂ was trapped in 30% ethanolamine/methyl cellosolve.

sampling protocol -- Soil was sampled at day 3, 7, 16, and 30.

Trapping solutions And Chromosorb were changed at the same intervals.

soil extraction -- The entire 15 gm aliquot was extracted with 25 ml acetonitrile/1 M acetic acid 70:30 with mixing for 2 minutes. The mixture was centrifuged, the supernatant decanted, and the soil pellet reextracted as described. The combined supernatants were diluted with 50 ml H₂O and extracted with 3 x 50 ml chloroform. The combined chloroform extracts were concentrated under reduced pressure and analyzed by TLC (for the RH-3866 samples were done in both systems, for 2,4-D only in the first system above).
temperature of incubation -- said to be 34 °C

C. REPORTED RESULTS

There was little or no degradation either in the irradiated samples or dark controls, while reference 2,4-D did degrade when irradiated. The projected half-lives for the differently labelled compound agreed well.

D. STUDY AUTHOR'S CONCLUSIONS/QUALITY ASSURANCE MEASURES

- 1) Photodegradation performed under "black light" and at 34 °C showed little or no degradation.
- 2) The projected half life of 142 days for photolysis is much greater than the soil metabolic half-life of 66 days. Therefore, photolysis will not be a major degradative pathway.
- 3) Day 0 controls were consistently higher than in later samples, possibly due to solvent evaporation of working solution during the storage period.
- 4) The rationale for using more extreme conditions than Guidelines prescribe was to "force" photoproducts to occur.
- 5) The compound does not absorb in the visible range, and additional light in the visible range would not affect the outcome.

E. REVIEWER'S DISCUSSION AND INTERPRETATION OF STUDY RESULTS

- 1) The study is clearly non-Guidelines, but does demonstrate stability under the experimental conditions.
- 2) By our treatment of the submitted data, only the phenyl-labelled Day 0 sample is an "outlier" in relation to the later samples. Reporting the results as percent of recovered does not appear to alter the interpretation of the data, although the general practice is should be to report % of applied.
- 3) Although the applicant makes a case for the limited spectrum of the irradiating light, we cannot accept this study as fully satisfying this data requirement. If type and degree of photolability were completely predictable on the basis of theoretical considerations such as molecular structure and spectral characteristics, another study would indeed seem to be unnecessary. However, the only way to determine the actual behavior is to simulate "real-life" conditions as nearly as feasible.

11. COMPLETION OF ONE-LINER: n.a.

12. CBI APPENDIX: included

Page 5 is not included in this copy.

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.
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5/28/85

NOTE - Review and upgrading of study

This study has been reexamined (See A. Vaughan's review of 5.30.85), and found to be acceptable to support registration.

After rereview of this study and discussion with various Branch members, it has been decided to make this study Core. The rationale is that:

1. A good dose-response was achieved even though an actual observed no-effect level was not obtained;
2. Because of the good dose-response it appears highly likely that a no-effect level is below 316 mg/kg and, therefore, performing another study would provide minimal information;
3. The test material does not appear highly toxic (LD_{50} = 498 mg/kg) and, therefore, determining a no-effect level is not critical; and
4. The two dietary LC_{50} studies add further support to the conclusion that the material is not highly toxic (LC_{50} 's: > 5000 ppm for both studies) and, therefore, determining a no-effect level is not critical.

Norman J. Cook
5-28-85

DATA EVALUATION RECORD

1. CHEMICAL: α -butyl- α -(4-chlorophenyl)-1H - 1,2,4-triazole-1-propanenitrile

Shaughnessy Number 128857

2. Test Material: RH-53, 866 technical. Lot L5PL 83/0017E, 84.5% a.i.

3. Study Identification: Fletcher, D.W. 1984. Avian Acute Single Oral Dose LD₅₀ study with RH-53,866 Technical in Bobwhite quail, Bio-Life Associates. Ltd. Report # 84RC-14. EPA EUP Nos. 707-EUP-RNL and 707-EUP-RNU, Acc. No. 072894

4. STUDY TYPE: Avian Single Dose LD₅₀

5. REVIEWED BY: Robert W. Pilsucki
Microbiologist
Ecological Effects Branch/HED *Robert W. Pilsucki* 1/2/85

6. APPROVED BY: *for* Raymond Matheny *Ray Matheny*
Head, Review Section 1

7. REPORTED CONCLUSIONS: The acute oral LD₅₀ was 510 (95% C.L. = 408 and 638) mg/kg.

8. REVIEWER S CONCLUSIONS:

This study is scientifically sound and with an LD₅₀ of 510 mg/kg RH3866 is slightly toxic to bobwhite quail. This study does not fulfill the requirement for an LD₅₀ to an upland gamebird because a no-effect level was not achieved because a no-effect level was not achieved and toxic symptoms were manifest at all dose levels.

This study has been reexamined. (See A. Vaughan's review of 5.30.85.) and found to be acceptable to support registration. H/CWK 5.17.85

Sum
✓

9. Materials/Methods

Species: Bobwhite quail (Colinus virginianus)

Age of birds: 33-36 weeks old

Source of Rearing History:

Thompson Game Farm
Route 2
Franksville, Wisconsin

The rearing history of the birds was not explicitly stated but is available from the breeders on request of Rohm and Haas.

Selection of test birds:

Birds were identified using numbered metal wing tags and randomly assigned to test groups using a random number generator. The sex composition of the groups were equalized.

Housing conditions:

Temperature: 40-84 F (4.4-28.9 C)
Humidity: 35-84%
Lighting: 8 hr light/16 hr dark

Food consumption and weight:

See attached tables.

Fasting:

Eighteen hours prior to dosing.

Diluent and concurrent vehicle control:

The diluent used was corn oil. The amount of diluent was adjusted to yield a constant volume of test material plus diluent of 2.50 ml. Vehicle controls were run concurrently (2.50 ml of corn oil only) and showed no mortalities.

Number of birds/dose level: 10

Observation period: 21 days

Dose Levels - mortalities

Acute LD50		Bobwhite Quail	
Dose mg/kg	Number Dosed	Number Dead	Percent Mortality
1470	10	10	100
1000	10	10	100
681	10	8	80
464	10	4	40
316	10	1	10

Toxic symptoms:

Lethargy and anorexia were observed in all birds receiving the test material. These symptoms lasted until death in the two highest test doses, seven days at 681 mg/kg, three days at 464 mg/kg, and two days at the lowest dose.

Necropsies

All birds except for one in the 1000 mg/kg groups and one in the 681 mg/kg group showed distention of the crop containing either test material or air, and food. Five birds (two from the 464 mg/kg group and one each from the 681, 1000 and 1470 mg/kg groups) showed positive findings in liver and intestinal tissues. Three of the surviving birds showed positive finding in liver and intestinal tissues.

Statistical Analysis

The LD₅₀ and 95% confidence limits were determined using the Litchfield-Wilcoxon method.

11. Discussion: There was no Discussion section in this study.

12. Reviewer s Evaluation:

Test procedures: The test procedures generally follow EPA s guidelines for an avian single-dose oral LD₅₀.

Statistical Analysis: EEB verification of the results using the the probit method gave an LD₅₀ of 497.85 (95% C.L. = 407.5 and 598.16) mg/kg. Therefore, the statistical analysis is adequate.

Discussion:

The results of this study generally coincide with those obtained by EEB and showed that RH3866 is slightly toxic to bobwhite quail under these conditions. However, mortality occurred at all dose levels and birds showed positive pathological findings at all levels. Therefore, another single-dose oral LD₅₀ is needed to define the no effect level.

13. Conclusion:

Category: ~~Supplemental~~ *Cere* *W/CWK* *5-17-85*

Rationale: This study generally follows EPA's guidelines for an avian single-dose LD₅₀. However, due to the fact that a no-effect level was not achieved and toxic symptoms were manifest by the lowest dose level, the study cannot be considered core.

N/A W/CWK
5-17-85

Repairability: ~~Submission of another study where dose-response data are shown along with a no-effect level.~~

N/A W/CWK
5-17-85

After review of this study and discussion with various Branch members, it has been decided to make this study *CERE*. The rationale is that:

2. A good dose-response was achieved even though an actual observed no-effect level was not obtained;
2. Because of the good dose-response it appears highly likely that a no-effect level is below 316 mg/kg and, therefore, performing another study would provide minimal information;
3. The test material does not appear highly toxic (LD₅₀ = 498 mg/kg) and, therefore, determining a no-effect level is not critical; and
4. The two dietary LC₅₀ studies add further support to the conclusion that the material is not highly toxic (LC₅₀'s: > 5000 ppm for both studies) and, therefore, determining a no-effect level is not critical.

W/CWK
5-17-85

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