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Shaughnessy No.: ------
Date Out of EFGWB: OCT 12 1989

TO: Lewis
Product Manager 21
Registration Division (TS-767)

FROM:

Paul Mastradone, Section Chief
Environmental Chemistry Review Section #1
Environmental Fate and Groundwater Branch

THRU:

Henry Jacoby, Acting Chief
Environmental Fate and Groundwater Branch
Environmental Fate and Effects Division (H7507C)

Attached please find the EFGWB review of:

Reg./File # : 707-EUP-RER

Chemical Name: Fenethanil

Product Type : Fungicide

Product Name : RH 7592 2F Fungicide

Company Name : Rohm and Haas Co.

Purpose : Review EUP to test on stone fruit

Date Received: 4-28-89 Action Code: 711

EFGWB # 90546 Total Reviewing Time (decimal days):

Deferrals to:
_____Ecological Effects Branch, EFED
_____Science Integration & Policy Staff, EFED
_____Non-Dietary Exposure Branch, HED
_____Dietary Exposure Branch
_____Toxicology Branch, HED

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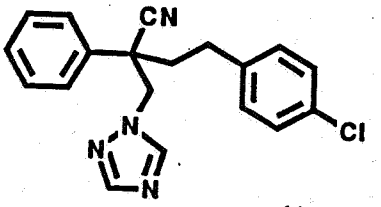
1.0 CHEMICAL:

Common name: Fenethanil, RH-7592

Chemical name: alpha-[2-(4-chlorophenyl)ethyl]-alpha-phenyl-1,2,4-1H-triazole-1-propanenitrile

Trade Name:

Chemical Structure:



2.0 TEST MATERIAL: ^{14}C-triazole- and ^{14}C-phenyl-RH-7592

3.0 STUDY/ACTION TYPE: Review data in support of EUP for use on stone fruits

4.0 STUDY IDENTIFICATION:

4.1 O'Dowd, M. L. 1988. RH-7592: Hydrolysis Study. Technical Report No. 34S-88-05. Rohm and Haas Company. MRID No. 410312-46.

4.2 Schieber, C. 1988. Soil Metabolism of RH-7592. Technical Report No. 345-88-13. Rohm and Haas Co. MRID 410312-47. (Note: This study contains the report of the aerobic and anaerobic soil metabolism studies.)

4.3 Schieber, C. 1988. Adsorption and Desorption of RH-7592. Technical Report No. 34S-88-06. Rohm and Haas Company. MRID No. 41312-49.

4.4 Schieber, C. 1988. Aged Leaching Study of RH-7592. Technical Report No. 34S-88-09. Rohm and Haas Company. MRID No. 410312-48

4.5 O'Dowd, M. L. 1988. Laboratory Studies of Pesticide Accumulation in Fish; RH-7592 Metabolism in Bluegill Sunfish. ABC Laboratories for Rohm and Haas. MRID No. 410735-09.

5.0 REVIEWED BY:

Clinton Fletcher
Chemist, Review Section 1
EFGWB/EFED

Signature: Clinton Fletcher
Date: 9-20-89

6.0 APPROVED BY:

Paul Mastradone
Section Chief, Review Section 1
EFGWB/EFED

Signature: Paul J. Mastradone
Date: OCT 12 1989

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7.0 CONCLUSIONS:

7.1 EFGWB concludes that the data requirements necessary to support the proposed EUP have been satisfied.

The reviewed studies include:

1. 161-1 Hydrolysis. FGWB concludes that the study is acceptable and satisfies the data requirement for the hydrolysis study.

   Based on the results of the study, EFGWB concludes that RH-7592 will be stable to hydrolysis at pH levels found in the environment.

2. 162-1 Aerobic Soil Metabolism. EFGWB concludes that the study satisfies the data requirements for the aerobic metabolism study.

   Based on the results of the study, EFGWB concludes that RH-7592 will degrade in soil under aerobic conditions with a half-life of 285 and 367 days in Lawrenceville silty clay loam and Pasquotank sandy loam soils, respectively.

   Mineralization to CO_2 and soil binding appear to be the major routes of dissipation of RH-7592 in soil under aerobic conditions maintained in the laboratory. In addition to $^{14}CO_2$, concentrations of metabolites RH-9129, RH-9130, RH-6467 increased in soil during the study period. See attached Figure 2 for structures of metabolites and proposed metabolic degradation pathway.

3. 162-2 Anaerobic Soil Metabolism. EFGWB concludes that the study satisfies the data requirements for the anaerobic metabolism study.

   Based on the results of the study, EFGWB concludes that RH-7592 will degrade in soil under anaerobic conditions with a half-life of 451 and 655 days in the Lawrenceville silty clay loam and the Pasquotank sandy loam soils, respectively.

   Soil binding appear to be the major route of dissipation of RH-7592 in soil maintained under anaerobic conditions in the laboratory. Metabolites RH-9129, RH-9130/RH-6467 were also present and appeared to increase in concentration duing the incubation period.

4. 163-1 Mobility/Leaching-Batch Equilibrium. EFGWB concludes that this study satisfies the data requirement for batch equilibrium study.

   Based on the results of the study, EFGWB concludes that RH-7592 will be only slightly mobile to immobile in soils. Adsorption appears to be associated with percent organic matter present. RH-7592 will be slightly mobile in soils

containing a low percent of organic material (≤ 1%) and relatively immobile in soils with higher levels of organic material

5. 163-1 Mobility/Leaching-Aged Residues. EFGWB concludes that the study is acceptable and satisfies the data requirement for mobility/leaching-aged residue study.

   Based on the results of the study, EFGWB concludes that RH-7592 residues have only a slight potential to leach in the soil environment.

6. 165-4 Fish Accumulation. EFGWB concludes that this study partially satisfies the data requirement for a fish accumulation study. It is adequate to support the application for the EUP. However, for registration the registrant should identify more conclusively the residues associated with the polar unknown metabolite 3.

   The results of this study indicated that bluegill sunfish had maximum bioaccumulation factors of 170X, 50X and 330X in whole fish, fillet and viscera tissues, respectively, during 28 days exposure and that 95-98% of these residues were eliminated during the 14 day depuration period. Identified radioactive residues in the fish tissue were primarily parent RH-7592 with RH-9129 (lactone A) and the ketone RH-6467. Also, unidentified polar metabolites were observed. See attached Figure 2a for proposed metabolic pathway of RH-7592 in fish.

   Based on the results of the study, EFGWB concludes that RH-7592 will not bioaccumulate in fish and any residues that are taken up will be depurated when fish are no longer exposed to RH-7592 residues.

7. 165-1 Confined Rotational Crop. The proposed use is on stone fruits, an orchard crop use not usually rotated. Therefore, no data are necessary to support this EUP.

8.0 <u>RECOMMENDATIONS:</u>

8.1 Inform the registrant that the following data requirements have been satisfied for the experimental use of RH-7592 on stone fruit:

161-1	Hydrolysis
162-1	Aerobic soil metabolism
162-2	Anaerobic soil metabolism
163-1	Mobility/batch equilibrium
	Mobility/aged column leaching

8.2 Inform the registrant that the following data requirement has been partially satisfied:

165-4 Fish accumulation

The study is sufficient to support the experimental use permit for use of RH-7592 for use on stone fruit. However, in order to fully satisfy the data requirement, the registrant must more completely characterize the residue associated with the polar unknown identified as metabolite 3 in the study.

8.3 The registrant should be informed that, for future studies submitted to support registration, storage stability data must be submitted for samples stored prior to analysis. Such storage stability period should include a period of time approximating the storage period for the samples.

8.4 The registrant should provide the IUPAC designations for all identified metabolites listed in these and future studies, if available.

9.0 BACKGROUND:

The registrant has submitted an application for a experimental use permit for testing the fungicide RH-7592 on stone fruits.

10.0 DISCUSSION OF INDIVIDUAL STUDIES:

See attached Data Evaluation Records (DERs)

11.0 COMPLETION OF ONE-LINER:

Data have been included in the One-liner.

12.0 CBI APPENDIX: N/A

Fenbuconazole

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___ The product confidential statement of formula.

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DATA EVALUATION RECORD

STUDY IDENTIFICATION:

O'Dowd, M. L. 1988. RH-7592: Hydrolysis Study. Technical Report No. 34S-88-05. Rohm and Haas Company. MRID No. 410312-46.

TYPE OF STUDY: 161-1 Hydrolysis

REVIEWED BY:

Clinton Fletcher, Chemist
Review Section 1, EFGWB, EFED

Signature: Clinton Fletcher
Date: 10-3-89

APPROVED BY:

Paul J. Mastradone, Section Chief
Review Section 1, EFGWB, EFED

Signature: Paul J. Mastradone
Date: OCT 12 1989

CONCLUSIONS:

EFGWB concludes that the study is acceptable and satisfies the data requirement for the hydrolysis study. RH-7592 was stable to hydrolysis at pH 5, 7, and 9 during the 30 day incubation period.

Based on the results of the study, EFGWB concludes that RH-7592 will be stable to hydrolysis at pH levels found in the environment.

MATERIALS AND METHODS:

Sterile solutions of 0.1 ppm of ^{14}C-triazole-RH-7592 (specific activity 20.95 miCi/g or 46,509 dpm/ug, chemical purity 99.1%) in 0.1 M buffer solutions at pH 5 (acetate), 7 (phosphate) and 9 (borate). Individual sample tubes were maintained at 25 $\pm$ 1° C for 30 days in the dark. Samples were taken at days 0, 1, 2, 4, 8, 15, 22, and 30 after initiation of the study. Aqueous solutions were extracted with ethyl acetate and analyzed by thin-layer chromatography (TLC) with comparison with known standards. The separated radioactivity was located with autoradiography and quantitated by liquid scintillation counting (LSC) of the scraped plates. (Note: HPLC did not give reproducible chromatography separation due to interfering buffer salts.)

All buffers and glassware were autoclave sterilized.

REPORTED RESULTS:

The author reported that ^{14}C-RH 7592 was almost quantitatively extracted with ethyl acetate (extraction efficiency was 99.3%). Recovery ranged from 94.2% to 103.3% (average 99.4%). Table 2

During the course of the study, parent ^{14}C-RH-7592 accounted for 97.6% to 100% of the extracted radioactivity. Table 5.

Based on the results of the study, the author concluded that RH-7592 is stable to hydrolysis in aqueous solutions at pH 5, 7, and 9.

DISCUSSION:

EFGWB concludes that the study is acceptable and satisfies the data requirement for the hydrolysis study.

Based on the results of the study, EFGWB concludes that RH-7592 will be stable to hydrolysis at pH levels found in the environment.

Fenbuconazole

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DATA EVALUATION RECORD

STUDY IDENTIFICATION:

Schieber, C. 1988. Soil Metabolism of RH-7592. Technical Report No. 345-88-13. Rohm and Haas Co. MRID 410312-47.

TYPE OF STUDY: 162-1 Aerobic Soil Metabolism
162-2 Anaerobic Soil Metabolism

REVIEWED BY:

Clinton Fletcher, Chemist
Review Section 1, EFGWB, EFED

Signature: Clinton Fletcher
Date: 9-20-89

APPROVED BY:

Paul J. Mastradone, Section Chief
Review Section 1, EFGWB, EFED

Signature: Paul J. Mastradone
Date: OCT 2 [illegible]

CONCLUSIONS:

EFGWB concludes that the study satisfies the data requirements for both the aerobic and anaerobic soil metabolism studies.

Based on the results of the two studies, EFGWB concludes that RH-7592 will degrade in soil under aerobic conditions with a half-life of 285 and 367 days in Lawrenceville silty clay loam and Pasquotank sandy loam soils, respectively. Under anaerobic soil conditions RH-7592 will degrade with a half-life of 451 and 655 days in the Lawrenceville and the Pasquotank soils.

Mineralization to CO_2 and soil binding appear to be the major routes of dissipation of RH-7592 in soil maintained under aerobic conditions in the laboratory. Soil binding appears to be the major route of dissipation in soil maintained under anaerobic soil conditions in the laboratory.

MATERIALS AND METHODS:

1. Aerobic

Two soils, Lawrence silty clay loam and Pasquotank sandy loam (See Table II for characteristics) sieved through 2 mm mesh screen were fortified with either ^{14}C-triazole-RH-7592 or ^{14}C-phenyl-UL-RH-7592 to approximately 1 ppm by mixing soil with ^{14}C-RH 7592-spiked cellulose. A treated soil sample was taken of each soil and frozen for later analysis. A control sample was prepared by adding unspiked cellulose to soil sample. To facilitate isolation and identification of metabolites, a soil sample was treated with ^{14}C-RH-7592 to 30 ppm level. To measure microbial effects, a soil sample was autoclave sterilized and fortified to 1 ppm with ^{14}C-RH-7592.

Fortified soil samples were placed in biometer flasks with a side arm containing NaOH to trap volatilized $^{14}CO_2$. Samples were maintained in the dark at a constant temperature of 25 ± 1° C. Soil moisture was monitored by either a moisture balance apparatus or by oven drying a soil sample.

A subsample of soil was taken at days 7, 14, 21, 28, 44, 61, 90, 120, 181, 240 and 363 days after treatment and frozen 1 to 3 days before analysis. The NaOH trap was replaced on days 5, 7, 14, 21, 28, 44, 61, 90, 120, 140, 153, 181, 216, 240, 282 and 363 (but not replaced).

2. Anaerobic

A soil sample was fortified and maintained under aerobic conditions as described above and aged for 30 days prior to initiating anaerobic conditions. After the 30 day aerobic aging (day 0 of anaerobic conditions) a soil sample was taken, the flask containing the soil was repeatedly evacuated with nitrogen gas then covered with oxygen-purged water (boiled) and then gassed with nitrogen. Soil and water samples were taken at days 17, 30 and 60 days after initiating anaerobic conditions. At sampling, the soil and water were swirled to mix than sampled. The slurry was filtered and soil air-dried.

3. Analytical

Total radioactivity in the NaOH trap was quantitated by liquid scintillation (LSC) counting of an aliquot of the trapping solution. The trapping solution was analyzed for residual radioactivity by LSC after barium chloride precipitation of the $^{14}CO_2$.

Total radioactivity in the soil samples was quantitated by LSC counting of $^{14}CO_2$ from combustion of soil samples. Total radioactivity in the various extraction phases was also quantitated by LSC of aliquots of the extracted fraction.

Soil samples were extracted with 70:30 acetonitrile/1.0 M acetic acid three times, aliquots combined, extracted with ethyl acetate and reduced in volume. Extracted radioactivity was re-dissolved in methanol then analyzed by normal phase thin-layer chromatography (TLC). Separated radioactive material was visualized on the TLC plate with autoradiography. The plates were then scraped of the radioactive areas and total radioactivity was measured by LSC.

^{14}C-Triazole residues were extracted from the aqueous phase of the extractions using affinity resin chromatography. After elution from the resin column the residues were derivatized with pentafluorobenzyl bromide and cleaned-up with column chromatography. The 1-pentafluorobenzyl-1,2,4-triazole was separated using TLC with co-chromatography of derivatized reference standard.

After organic solvent extraction, soil samples were refluxed with 70:30 acetonitrile/1.0 M acetic acid then extracted with 0.5 N NaOH to remove the bound humic and fulvic acid fractions. The aqueous fractions were partitioned with ethyl acetate and n-butanol then extracted radioactivity was analyzed by TLC. The aqueous fraction was extracted with resin chromatography to extract any triazole residues.

The preparative soil sample was extracted and analyzed as described above. Metabolites Nos. 1 (RH-9129), 2 (RH-9130), and 3 (RH-6467), were identified using co-chromatography (TLC and HPLC) of known chemical reference standards and structures were verified by GC/MS.

REPORTED RESULTS:

The author reports that recovery ranged from 88.3% to 116% of the applied radioactivity. The reported low recovery for day 28 was attributed to erroneous combustion data. Tables VII-X

The author noted that soil moisture was not maintained at 75% of 1/3 bar in the Pasquotank soil because of the difficulty in handling the soil at that moisture level. Although the soil moisture level was maintained at a relatively constant level during the study. During the study the soil moisture levels were 15.0%0 (day 0) to 11.5% (day 363) for the Lawrenceville soil and 19.7% (day 0) to 16.1% (day 363) for the Pasquotank soil. Table IV

1. Aerobic Metabolism Study

After 363 days incubation, $^{14}CO_2$ accounted for 35-37% and 21% of the applied ^{14}C-phenyl-RH-7592 in the Lawrenceville and Pasquotank soils, respectively. $^{14}CO_2$ accounted for 1.2%-1.5% of the applied ^{12}C-triazole-RH-7592 in both soils. Table V

Extractable ^{14}C in the Lawrenceville soil treated with either ^{14}C-triazole- or ^{14}C-phenyl-RH 7592 declined with increasing incubation time. 96.5%-97.4% at day 0 to 72.4%-75.2% at day 363. Correspondingly, bound residues increased with incubation from 2.3%-3.5% at day 0 to 24.8%-27.6% at day 365. Similar results were reported for the Pasquotank soil. Tables XI-XVIII.

Parent compound accounted for average of 47.8% and 59.0% of the extractable residues from application of ^{14}C-triazole-RH 7592 in the Lawrenceville and Pasquotank soils, respectively, after 363 days incubation. Parent compound accounted for 32.9% and 50.3% of the applied ^{14}C-phenyl-RH-7592 in the Lawrenceville and Pasquotank soils, respectively. Metabolites RH-9129, RH-9130 and RH-6467 increased with time during the incubation period, accounting for 2.5%-9.6% of the applied radioactivity in both soils treated with both radiolabels. Triazole accounted for 11.2%-13.6% and for 6.5%-6.6% of applied ^{14}C-triazole-RH-7592 in the Lawrenceville and Pasquotank soils, respectively. Tables XIX-XXVI (See Figure 2 for structures of metabolites and proposed metabolic degradation pathway.)

Based on the results of the study the author calculated the half-lives of RH-7592 to be 258 and 367 days in the Lawrenceville and Pasquotank soils, respectively.

No degradation was observed in the sterile soils.

2. Anaerobic Metabolism Study

The author reported a material balance ranging from 81.0% to 119% and 75.7%-95.9% of the applied radioactivity in both the Lawrenceville and Pasquotank soils treated with ^{14}C-triazole- and ^{14}C-phenyl-RH-7592, respectively. For the most part, the higher values occurred at the beginning of the study and the lower values after 30 and 60 days incubation. Tables XXXI-XXXII.

Of the applied radioactivity, 90.9%-93.8% was extracted at day 0 and that extractable declined to 76.8%-78.3% by day 363 of anaerobic soil conditions. Also, 6.2%-9.7% of the applied radioactivity was bound to the soil at day 0 and increased to 23.6% by day 60 under anaerobic soil conditions. Tables XXXIII-XXXVI.

Parent-RH-7592 accounted for the majority of the radioactive residues under anaerobic soil conditions. Parent RH- 7592 accounted for an average of 80.9% of the applied radioactivity at day 0 of anaerobic conditions (day 30 of aerobic conditions) and averaged 73.2% of the applied radioactivity after 60 days incubation under anaerobic soil conditions. During the study metabolites RH-9129 and combined RH-9130/RH-6467 accounted for 0.6% (at day 0) to 7.33% (at day 60) of applied radioactivity, respectively. Table XL

Based on the results of the study, the author calculated the half-life of RH-7592 to be 451 and 655 days in the Lawrenceville and the Pasquotank soils, respectively, maintained under anaerobic conditions.

DISCUSSION:

EFGWB concludes that the study satisfies the data requirements for the aerobic and anaerobic soil metabolism studies.

Based on the results of the two studies, EFGWB concludes that RH-7592 will degrade in soil under aerobic and anaerobic conditions with a half-life of 285 and 367 days in Lawrenceville silty clay loam and Pasquotank sandy loam soils, respectively, under aerobic soil conditions and a half-life of 451 and 655 days in the Lawrenceville and the Pasquotank soils, respectively, under anaerobic condition.

In the aerobic study, metabolites RH-9129, RH-9130 and RH-6467 increased with time during the 363 day incubation period and accounted for 2.5%-9.6% of the applied radioactivity in both soils treated with both radiolabels.

In the anaerobic study, metabolites RH-9129 and combined RH-9130/RH-6467 accounted for 0.6% (at day 0) to 7.33% (at day 60) of applied radioactivity, respectively.

Mineralization to CO_2 and soil binding appear to be the major routes of dissipation of RH-7592 in soil maintained under aerobic conditions maintained in the laboratory. Soil binding appears to be the major route of dissipation in soil maintained under anaerobic conditions in the laboratory.

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DATA EVALUATION RECORD

STUDY IDENTIFICATION:

Schieber, C. 1988. Adsorption and Desorption of RH-7592. Technical Report No. 34S-88-06. Rohm and Haas Company. MRID No. 41312-49.

TYPE OF STUDY: 163-1 Mobility/Leaching

REVIEWED BY:

Clinton Fletcher, Chemist
Review Section 1, EFGWB, EFED

Signature: Clinton Fletcher
Date: 9-20-89

APPROVED BY:

Paul J. Mastradone, Section Chief
Review Section 1, EFGWB, EFED

Signature: Paul J Mastradone
Date: OCT 12 1989

CONCLUSIONS:

EFGWB concludes that this study satisfies the data requirement for 163-1 adsorption/desorption study.

Based on the results of the study, EFGWB concludes that RH-7592 will be only slightly mobile to immobile in soils. Adsorption appears to be associated with percent organic matter present. RH-7592 was slightly mobile in soils containing a low percent of organic material ($\leq$ 1%) and relatively immobile in soils with higher levels or organic material

MATERIALS AND METHODS:

1. Adsorption

^{14}C-triazole-RH-7592 (specific activity 20.29 miCi/g (46,509 dpm/ug, chemical purity 98%) in 0.01 N calcium chloride stock solutions ranging from 0.039 to 0.334 ppm concentration was added to air-dried (and sieved through 2 mm mesh screen) clay, sand, sandy loam and silty clay loam in duplicate tubes, wrapped in foil and shaken for 24 hours to reach equilibrium in enclosed chamber maintained at 25 $\pm$ 1° C. See Table II for soil characteristics.

Samples were centrifuged and aliquots of the supernatant were taken. Radioactivity in the supernatant solution was quantitated by liquid scintillation counting (LSC).

2. Desorption

Following adsorption study, soil was re-suspended in 0.01 N calcium chloride and shaken for 72 hours then centrifuged. An aliquot of the supernatant was taken and the radioactivity was quantitated by LSC.

Total radioactivity in the soil was determined by combustion and quantitated by LSc of the released $^{14}CO_2$.

Test solutions without soil were shaken for 24 hours to measure any loss of radioactivity due to adhesion of RH-7592 to the vessel walls during the study.

Adsorption and desorption coefficients were calculated based on the Freundlich Equation.

The organic material from the adsorption supernatant was passed through Sep-paks (adsorption chromatography), eluted from the column with methanol, evaporated to dryness and redissolved in methanol. Extracted radioactivity was analyzed by normal phase thin-layer chromatography (TLC). Radioactive areas were located by autoradiography then quantitated by scrapping the plate of the radioactive areas and quantitating by LSC. High performance liquid chromatography was also used to identify ^{14}C-RH-7592 in the supernatant of the adsorption test.

REPORTED RESULTS:

The author reported the material balance averaged 95.8% (range 86.2-107.5%) of the applied ^{14}C-RH-7592. Table V

The author reports that TLC and HPLC analysis that RH-7592 was stable under the test conditions. Based on the results of the study, the following K_d values were calculated:

Soil	% OM	K_d Values		K_{oc}
		Adsorption	Desorption	
Clay	0.4	5.07	7.09	2185
Loam	2.4	75.21	147.66	5402
Sand	0.5	7.56	2.33	2607
Sandy loam	2.2	115.40	132.20	9042
Silty Clay Loam	1.2	20.08	33.0	2884

Based on these results, the author concluded that RH-7592 varied from slightly mobile in clay, sand and silty clay loam soils to being immobile in sandy loam and loam soils.

DISCUSSION:

EFGWB concludes that this study satisfies the data requirement for 163-1 adsorption/desorption study.

Based on the results of the study, EFGWB concludes that RH-7592 will be only slightly mobile to immobile in soils. Adsorption appears to be associated with percent organic matter present. RH-7592 will be slightly mobile in soils containing a low percent of organic material ($\leq$ 1%) and relatively immobile in soils with

higher levels or organic material

While no reports on various equilibrium times were reported, the results of the study indicate the 24 hour equilibration time used in this study was sufficient.

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DATA EVALUATION RECORD

STUDY IDENTIFICATION:

Schieber, C. 1988. Aged Leaching Study of RH-7592. Technical Report No. 34S-88-09. Rohm and Haas Company. MRID No. 410312-48

TYPE OF STUDY: 163-1 Mobility/Leaching-Aged Residues

REVIEWED BY:

Clinton Fletcher, Chemist
Review Section 1, EFGWB, EFED

Signature: Clinton Fletcher
Date: 10-3-89

APPROVED BY:

Paul J. Mastradone, Section Chief
Review Section 1, EFGWB, EFED

Signature: Paul J. Mastradone
Date: OCT 12 1989

CONCLUSIONS:

EFGWB concludes that the study is acceptable and satisfies the data requirement for 163-1 mobility/leaching-aged residue study.

Based on the results of the study, EFGWB concludes that RH-7592 residues have only a slight potential to leach in the soil environment.

MATERIALS AND METHODS:

^{14}C-triazole-RH-7592 (specific activity 20.95 mCi/g, radiopurity 98.6%) and ^{14}C-phenyl-RH-7592 (specific activity 20.83 mCi/g, 98.0% radiopurity) sorbed onto cellulose were added to Pasquotank sandy loam soil (sieved through 2 mm mesh screen) to level of 1.0 ppm. Soil was aged under aerobic soil conditions in biometer flasks for 30 days in an environmental chamber maintained at 25 $\pm$ 1° C. Flasks were equipped with side arm containing 0.5 N NaOH solution to trap any volatilized $^{14}CO_2$. See Table II for soil characteristics

Prior to incubation, one soil sample was taken and frozen for later analysis, one sample was taken for combustion. A control blank soil sample was also maintained.

Four soil columns (5.5 cm dia.) were prepared using 6 cm segments of glass rings taped together. Sufficient soil was added for a final column height of 30 cm soil, pre-wetted and allowed to drain. After ageing, duplicate soil samples were taken and added to complete final 30 cm column height. A soil subsample was taken and frozen for later analysis.

Columns were eluted with 997 ml of water placed onto column in 200-300 ml aliquots over a 5-7 day period. Columns were maintained at

ambient temperature of 22° C. Elution time varied from 7 to 14 days.

After elution period, columns were divided into 5 6-cm segments and the soil air-dried then frozen at -6° C until analysis. Leachate and aqueous extraction fractions were refrigerated at 36° F prior to analysis.

The radioactivity in leachate fractions was quantitated by liquid scintillation counting (LSC), and in the soil by combustion and quantitation of $^{14}CO_2$. Volatilized radioactivity was quantitated by LSC and verified as $^{14}CO_2$ by barium chloride precipitation. Soil was extracted with 70:30 acetonitrile/1.0 M acetic acid twice, decanted and soil filtered. Soil was later re-extracted with the solution under heat (60° C) to remove additional radioactivity. The extraction fraction was partitioned with ethyl acetate, evaporated, re-dissolved in methanol then analyzed by normal phase thin-layer chromatography (TLC). Identity of extracted residues was by co-chromatography with known standard reference compounds. Separated radioactive areas were located with autoradiography. Located radioactivity was quantitated by scrapping the TLC plates and analyzing the scrapings by LSC.

REPORTED RESULTS:

The author reports that material balance for the four columns averaged 98% (range was 89.6% to 102.2%). Extractability of radioactivity from the soil before and after leaching was greater than 90%. Tables IVa and IVb

During the aging period, less than 1% of the applied radioactivity had volatilized as $^{14}CO_2$. Also, 99.0%-99.5% and 89.1%-101.7% of the ^{14}C-triazole- and ^{14}C-phenyl-RH-7592, respectively, applied to the soil column was found in the 0-6 cm soil column segment. (Note: 0-2 cm was applied fortified soil and 3-6 cm was upper portion of soil column.) No significant radioactivity (> 1%) was found below segment 1 of the soil column. The leachate contained 0.1-0.2% of the applied radioactivity. Tables IVa and IVb

Of the radioactivity in segment 1 of the column, 93.4%-94.8% and 78.0%-89.8% was extracted from the soil. Of this amount, 78.0% to 89.8% was parent RH-7592. Three degradation products ["1"-RH-99129 (diastereomer A); "2"-RH-99130 (diastereomer B); "3"-RH-96467] accounted for 1.5%-12.8% of the radioactivity applied. Table VI See Table VII for structures

Based on the results of the soil column study, the author calculated the sorption coefficient (K^{oc}) (correlating leaching potential with the sorption coefficient in soil column experiments) for RH-7592 to be 3445, indicating a slight potential for leaching. Compare values in Table VIII

DISCUSSION:

EFGWB concludes that the study is acceptable and satisfies the data requirement for 163-1 mobility/leaching-aged residue study.

Based on the results of the study, EFGWB concludes that aged RH-7592 residues have only a slight potential to leach in the soil environment.

EFGWB notes:

1. RH-7592 was adsorbed to cellulose then added to the soil for the aerobic aging period. This could affect the leaching potential. However, in this case, the adsorption study showed that RH-7592 adsorbed strongly to the same sandy loam soil (K_d of 115.4) as used here. Thus, EFGWB does not believe the use of celulose affected the results of this study. EFGWB does not recommend this practice for this study.

2. That the author did not report the time period that samples were stored prior to analysis and results of the storage stability study. However, the lack of these results do not affect the conclusions drawn from the study. The registrant should provide such data in future studies submitted to support registration.

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DATA EVALUATION RECORD

STUDY IDENTIFICATION:

O'Dowd, M. L. 1988. Laboratory Studies of Pesticide Accumulation in Fish; RH-7592 Metabolism in Bluegill Sunfish. ABC Laboratories for Rohm and Haas. MRID No. 410735-09.

TYPE OF STUDY: 165-4 Fish Accumulation

REVIEWED BY:

Clinton Fletcher, Chemist
Review Section 1, EFGWB, EFED

Signature: Clinton Fletch
Date: 10-3-89

APPROVED BY:

Paul J. Mastradone, Section Chief
Review Section 1, EFGWB, EFED

Signature: Paul J Mastradone
Date: OCT 12 1989

CONCLUSIONS:

EFGWB concludes that this study partially satisfies the data requirement for a fish accumulation study.

The results of this study indicated that bluegill sunfish had maximum bioaccumulation factors of 170X, 50X and 330X in whole fish, fillet and viscera tissues, respectively, after 28 days exposure and that 95-98% of these residues were eliminated during the 14 day depuration period. Based on the results of the study, EFGWB concludes that RH-7592 will not bioaccumulate in fish and any residues that are taken up will be depurated when fish are no longer exposed to RH-7592 residues.

In order to satisfy the data requirement for this study, the registrant should provide additional characterization of the unknown polar metabolite identified in the study as "metabolite 3".

MATERIALS AND METHODS:

In-life phase

Bluegill Sunfish [7.7 (± 1.5)g weight; 62 (± 3.8) mm length] maintained in a flow-through system were exposed for 28 days to nominal water concentration of 0.01 ppm ^{14}C-triazole-RH-7592 (specific activity 20.95 mCi/g, 98% radiopurity)/technical RH-7592 (96.8% purity) followed by a 14 day depuration period. The exposure tank, with flow of aerated well water (See Table 1 for characteristics), was maintained at 21° C during the test duration. A control tank was also maintained under identical conditions.

Fish and water were sampled at time 0 and after 0.17, 1, 3, 7, 14,

21, 28 days of exposure. During the depuration period, fish were sampled after 1, 3, 7, 10, and 14 days depuration. Fish were dissected into fillet (edible) and viscera (inedible) tissues, homogenized, and frozen until analysis.

Note: In addition, additional fillet and viscera tissues were generated by a supplemental uptake study wherein the tissues were used in methods development and metabolite identification. In this second in-life phase study bluegill sunfish were exposed to a nominal concentration of 0.045 ppm residues of RH-7592.

Analytical phase

Total radioactivity in samples was quantitated by combustion of samples and liquid scintillation counting (LSC) of $^{14}CO_2$ trapped during combustion. During extraction and analysis procedures radioactivity in aliquots of partition supernatants and thin-layer chromatograms scrapings was quantitated by LSC.

The 21 and 28 day viscera samples were extracted with methanol, partitioned with hexane then with deionized millipore filtered water followed with ethyl acetate. The ethyl acetate was evaporated, residues re-dissolved in methanol for analysis by TLC. The aqueous phase was partitioned with n-butanol, then the n-butanol evaporated and residues were re-dissolved in methanol for TLC analysis.

The 7 and 28 day fillet samples were extracted with methanol in blender (28 day sample) or hand blended (7 day sample), then centrifuged. The methanol supernatant was decanted and concentrated, then deionized millipore filtered water was added. The aqueous solution was partitioned with ethyl acetate for analysis by TLC. The aqueous phase was partitioned with n-butanol, then the n-butanol evaporated and residues re-dissolved in methanol for TLC analysis.

Extracted radioactive residues were separated by TLC using reverse phase chromatography. Separated radioactive areas on the TLC plate were located with proportional scanner. Separated radioactive spots were identified by co-chromatography with known standards. Quantitation of radioactivity was accomplished by scrapping the TLC plates and quantitating the radioactivity by LSC. High performance liquid chromatography (HPLC) was used as additional aid to identify the residues. Confirmation of the identity of residues was attempted by gas chromatography/mass spectroscopy but was not successful.

REPORTED RESULTS:

The sampling schedule is presented in Figure 2. The nominal water concentration was 0.01 ppm (ranging from 0.0073 to 0.012 ppm) during the uptake phase.

During the uptake phase, ^{14}C-RH-7592 residues ranged from 0.089 ppm

(day 0) to 0.50 ppm (maximum, day 7) to 0.44 ppm at day 28 for fillet tissue; 0.24 ppm (day 0) to 1.6 ppm (maximum, day 21) to 1.4 ppm at day 28 for whole fish; and from 0.41 ppm (day 0) to 4.1 ppm (maximum, day 21) to 3.3 ppm at day 28 for viscera tissue samples. Table 5

The maximum bioaccumulation factors were 170X for whole fish at 7 days exposure, 50X for fillet tissue at 7 days exposure and 330X for viscera at 28 days exposure. Based on the results and using the BIOFAC non-linear kinetic fish accumulation computer model, the author calculated the bioconcentration factor (BCF) for RH-7592 to be 160. Table 5

During the 14 day depuration period, accumulated ^{14}C-RH-7592 residues dropped 95, 98, and 98% of the observed concentration at day 28 of uptake exposure in the fillet, whole fish and viscera, respectively. Table 3

The identity of accumulated residues were determined on the samples with the highest concentration of residues (found in the 7 and 28 days fillet samples and the 21 and 28 day viscera samples).

Material balance averaged 90% (range 76.1%-96.6%) for radioactive residues taken up during the exposure period. The majority of the residues were extracted from the fish samples. The radioactivity extracted by ethyl acetate was identified by TLC and HPLC co-chromatography with known standards as three compounds: parent RH-7592, lactone A (RH-9129) and the ketone (RH-6467). See Figure 1 for structures. The n-butanol extract contained an additional amount of these compounds and, in addition, three unknown areas, described as "polar unknowns 1, 2, and 3".

About 10-15% of the radioactivity was unextractable and remained in the fish tissue samples. Also, 2.6 - 9.5% of the extracted radioactivity remained in the aqueous phases of the extraction procedures and could not be identified. Table 2

Parent RH-7592 constituted 20-23% of the residue; the ketone 9-13%; and the lactone 7-10% and the polar unknown 3 8-13% of the radioactivity extracted from the fillet samples. Polar unknowns 1 and 2 accounted for 4-10% each of the radioactivity extracted from the fillet sample. Table 2

In the viscera, parent RH-7592 and the ketone accounted for 7-11% of the radioactivity extracted from the viscera sample. Polar compounds unknowns 2 and 3 accounted for 9-10% and 23-29%, respectively, of the radioactivity extracted from the viscera.

In the summary statement, the author concluded that the polar unknown 3 has been tentatively identified as a conjugate (probably the glucuronide) of the benzyl alcohol proposed to be an intermediate in the formation of the lactone and ketone metabolite. The proposed metabolic pathway for RH-7592 in fish is given in Figure 3.

DISCUSSION:

EFGWB concludes that this study partially satisfies the data requirement for a fish accumulation study. It is adequate to support the application for the EUP. However, for registration the registrant should identify more conclusively the residues associated with the polar unknown metabolite 3.

The results of this study indicated that bluegill sunfish had maximum bioaccumulation factors of 170X, 50X and 330X in whole fish, fillet and viscera tissues, respectively, after 28 days exposure and that 95-98% of these residues were eliminated during the 14 day depuration period. Based on the results of the study, EFGWB concludes that RH-7592 will not bioaccumulate in fish and any residues that are taken up will be depurated when fish are no longer exposed to RH-7592 residues.

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