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TO: John Lee
Product Manager #31
Registration Division (H7505C)

FROM: Akiva D. Abramovitch, Ph.D., Section Head
Environmental Chemistry Review Section #3
Environmental Fate and Ground Water Branch, EFED (H7507C)

THRU: Henry M. Jacoby, Chief
Environmental Fate and Ground Water Branch/EFED (H7507C)

Attached, please find the EFGWB review of:

Reg./File #: 000707-RTL

Common Name: RH-5287

Chemical Name: 4,5-Dichloro-2-octylisothiazolone

Type product: Marine Antifoulant

Product Name: C-9211M

Company Name: Rohm & Haas

Purpose: Review of studies submitted for registration of the manufacturing product C-9211M (RH-5287 active ingredient), marine antifoulant.

Action Code: 116 EFGWB #: 91-0536 92-1036 Total Reviewing Time: 10.0 days

EFGWB Guideline/MRID Summary Table: The review in this package contains:

161-1		162-1		164-1		165-1		166-1	
161-2	41845001	162-2		164-2	Waiver Request	165-2		166-2	
161-3		162-3	41845002 42341101	164-3		165-3		166-3	
161-4		162-4	41845003 42341102	164-4		165-4		167-2	
201-1		163-1	41845004 41845005	164-5	41845006	165-5		167-3	
202-1		163-2/-3							

(1)

1. CHEMICAL:

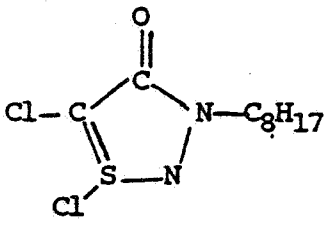
Common name: "RH-5287"

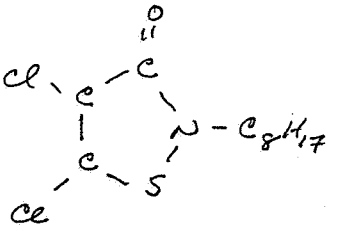
Chemical name(s): 4,5-Dichloro-2-n-octylisothiazolone
'4,5-dichloro-2-octyl-isothiazole

Chemical Abstracts Registry #: 64359-81-5

Trade name(s): Marine Antifoulant C-9211M; Kathon-287

Chemical structure:





Formulation*: 30-31% active ingredient (RH-5287)
70% inert ingredients

* To be used in the manufacturing of marine paints.

Physical/Chemical Properties (Technical Product):

Appearance: Tan brown waxy solid
Melting Point: 40-41 C
pH: Not applicable
Specific gravity: 1.28 (25 C)
Solubility:
Water (25 C)..... 14 ppm
Miscible in most organic solvents
Vapor pressure: 4.5×10^{-6} Torr
Octanol/water partition
coefficient: logP= 6.4

2. STUDY/ACTION TYPE:

Review of environmental fate studies submitted towards registration of this active ingredient.

3. STUDY IDENTIFICATION:

All studies (except 165-4) were performed by PTRL East, Inc. Richmond, KY and submitted by Rohm and Haas Company, Spring House, PA.

- 161-1 Photodegradation in Water

Kesterson, A., Lawrence, B., and Lawrence, L.J. 1990. Aqueous Photolysis of [$^{13/14}$C]RH-5287 in Natural Sunlight. PTRL Project 292, Report 1303. Rohm and Haas Technical Report 34-90-73.
MRID 41845001

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- 162-3 Anaerobic Aquatic Metabolism

Lawrence, L.J., Lawrence, B. and Kesterson, A. 1991. Anaerobic Aquatic Metabolism of $^{13/14}$CRH-5287. PTRL Project 295; Report No. 1313. Rohm and Haas Technical Report 34-91-06. Completed 3/21/91.
MRID 41845002

Kesterson, A. and Atkins, R. 1992. Supplemental Study to the Anaerobic Aquatic Metabolism of $^{13/1}$CRH-5287. PTRL Project 295; Report No. 1313. Rohm and Haas Technical Report No. 34-92-46. Completed 5/19/92.
MRID 42341101

- 162-4 Aerobic Aquatic Metabolism

Lawrence, L.J., Lawrence, B., Jackson, S. and Kesterson, A. 1991. Aerobic Aquatic Metabolism of $^{13/14}$CRH-5287. PTRL Project 294; Report No. 1291. Rohm and Haas Technical Report No. 34-91-01. Completed 3/26/91.
MRID 41845003

Kesterson, A. and Atkins, R. 1992. Supplemental Study on the Aerobic Aquatic Metabolism of $^{13/14}$C RH-5287. PTRL Project 294; Report No. 1291; Completed 5/1/92.
MRID 42341102

- 163-1 Mobility in Soil

Olson, G.L. and Lawrence, L.J. 1991. Soil Adsorption/Desorption of [^{14}C]RH-5287 by the Batch Equilibrium Method. PTRL Project 296; Report No. 1246. Rohm and Haas Technical Report No. 34-90-28. Completed 1/2/91.
MRID 41845004

Olson, G.L. and Lawrence, L.J. 1991. Leaching of $^{13/14}$C RH-5287 in Four Soil Types Following 30 Days or One Half-Life Aerobic Aging in Sandy Loam Soil. PTRL Project 297; Report No. 1296. Rohm and Haas Technical Report 34-90-67. Completed 1/30/91.
MRID 41845005

- 165-4 Bioaccumulation in Fish

Derbyshire, R.L., Jacobson, O'Dowd, M.L. and Santangelo. 1991. Metabolism of RH-5287 in Bluegill Sunfish. Rohm and Haas Technical Report 34-90-71 Completed 3/27/91. Performed by Rohm & Haas.
MRID 41845006

4. REVIEWED BY:

Silvia C. Termes, Chemist
Review Section #3
OPP/EFED/EFGWB

Signature: _____

Date: February 5th, 1992

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5. APPROVED BY:

Akiva D. Abramovitch, Ph.D.
Section Head, Review Section #3
OPP/EFED/EFGWB

Signature: Akiva Abramovitch

Date: FEB 8 1990

6. CONCLUSIONS:

a. Administrative (Studies reviewed in this data package)

The 165-4 (Bioaccumulation in Fish, Metabolite Identification) and the 163-1 (Mobility in Soil, unaged) are acceptable. The other reviewed studies (161-1, Photodegradation in Water; 162-3, Anaerobic Aquatic Metabolism; 162-4, Aerobic Aquatic Metabolism) are not acceptable at this time. However, the studies may be upgradable. To upgrade the studies, the registrant must respond to the "Recommendations and/or Comments" section in each corresponding Data Evaluation Record (DER). Therefore, all the DERs must be made available to the registrant, including the batch equilibrium adsorption/desorption study with parent RH-5287, Study 4; and the 165-4 identification of metabolites in the Bioaccumulation in Fish study, Study 5).

The aged soil column leaching, although acceptable, lacks information on the mobility of aged residues in a marine sediment. Inclusion of sediments was recommended in the review of the protocol for this study (EFGWB #90498; 8/28/89). In addition, it was noticed that in the mobility studies (which were conducted with a Ca^{2+}/"fresh water" solution as the aqueous phase) it was possible to extract parent RH-5287 from the soils/sediment. This is in contrast with the aquatic metabolism studies conducted with seawater, in which residues (presumably ring-open materials) appear to bind readily and strongly to marine sediments after rapid degradation of parent RH-5287. The Branch believes that the registrant must demonstrate that the proposed open-ring structures are actually involved in the strong binding of residues to marine sediments. Batch-equilibrium adsorption/ desorption studies should be conducted with each of the individual, proposed ring-open degradates.

The status of data requirements for this chemical is summarized in Table A.

b. Potential Concerns

The Ecological Effects Branch (EEB) should be made aware of the tendency of RH-5287 residues to bind strongly to marine sediments in the presence of seawater and the potential for long term accumulation of residues on sediments.

Although data indicate that RH-5287 degrades/dissipate readily in marine sediments/seawater systems incubated under anaerobic or aerobic conditions, degradation products/residues (which were not definitively identified) bind strongly to the sediment phase. The extent (and reversibility) of binding of the proposed open-ring degradates is not fully understood at this point. The important conclusion that can be reach at this time is that in marine sediments/seawater systems residues of RH-5287 are strongly bound

to the sediment phase and that microbial as well as chemical processes may be involved in the degradation of RH-5287 in seawater.

The impact of RH-5287 on terrestrial environments (as a result of application/ removal of the antifoulant paint in maintenance facilities and nearby drydocks) is not fully understood at this time, but data included in the soil-column leaching studies (aged) shows that the half-life of incubation in soils under aerobic conditions is about 21 days. This suggests that RH-5287 may be more persistent in terrestrial than in marine environments. Unaged RH-5287 is not very mobile in soils, but are more mobile than in sediments. Degradates that form on soil are not characterized at this time.

Considerations should be taken to the fact that this active ingredient will be sold as a formulated product for use in the manufacturing of marine paints. Ultimately the environmental/ecological impact of this chemical would be determined by the leaching rate of RH-5287 from the surface of the painted vessels. The presence of other active ingredients (such as copper) in the paint product may affect the rate of leaching of RH-5287 from the painted surface and/or the subsequent fate of RH-5287.

c. Summary of Scientific Conclusions for Individual Studies

These summaries appear under DISCUSSION OF INDIVIDUAL STUDIES.

7. RECOMMENDATIONS:

a. Inform the registrant that, although not acceptable at this time, the 161-1, 162-3/-4 are upgradable. All DERs should be made available to the registrant to upgrade these studies.

b. Additional data is being requested for the 163-1 (Mobility in Soil/ Sediments) requirement (inclusion of a sediment; batch-equilibrium adsorption/desorption studies with each individual ring-open degradate postulated by the registrant in the aquatic metabolism studies).

c. Provide supporting data for the degradates of RH-5257 formed by abiotic hydrolysis at pH 9.

d. The Surface Water Section is independently looking at the modelling study submitted by the registrant and will respond in a separate action.

e. Provide the registrant the status of environmental fate data requirements as summarized in Table A.

f. Studies on leaching rates from paint matrices will be required for each end-use products.

g. The Aquatic Field Dissipation (164-2) study can be waived for the manufacturing use product, but may be required for end-use products if

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the leaching rates indicate that significant amounts of the chemical may be release into the environment.

h. The registrant should clarify if the product is intended for marine uses only or if registration will also extend to uses in vessels navigating in freshwaters in the future.

i. The impact on terrestrial environments (as a result of application/removal of the antifoulant paint in maintenance facilities and nearby drydock) is not well established. It was understood by EFGWB (6/21/90 meeting) that the registrant intended to provide such information. Data on degradates formed on soils from aerobic incubation is not available at this time.

8. BACKGROUND:

Rohm & Haas is seeking the registration of RH-5287 in the formulated product C-9211M (marine antifoulant). This is a manufacture use product intended for use in marine paints. The product is intended for distribution to the largest formulators/painters involved in the painting of large military and commercial ships. The products containing RH-5287 as an active ingredient will not be available to private boat owners or small commercial establishments.

The Branch had previously reviewed environmental fate data on this chemical, but most of the data was deemed unacceptable and new studies were requested (see reviews 8/11/83, 12/3/87, 11/21/88, 8/28/89). Several meetings between EFGWB members and Rohm & Haas were held throughout the development of the database.

9. DISCUSSION OF INDIVIDUAL STUDIES: Refer to Data Evaluation Records (DERs) attached to this review.

Summaries of Scientific Conclusions

a. Abiotic Degradation (Hydrolysis and Photolysis in Water)

An earlier hydrolysis study (buffered solutions) indicated that RH-5287 degraded with half-lives of 9 days at pH 5 and 2.5 days at pH 9, but that very little degradation occurred at pH 7 during the 30-day study (23 $\pm$ 2) C. The major product of degradation at pH 5 after 100 days was the ring-open degradate 2-chloro-n-octyl-acetamide. The registrant should present data on degradates formed at pH 9 to completely assess the effect of hydrolysis on this chemical. Date of review 8/11/83; EFGWB #3332; EPA Accession #249934.

Although the photodegradation in water study (pH 7 buffer; natural sunlight) indicates a half-life of degradation of 13.3 days (as opposed to 80 days under dark conditions), complete degradate identification was not feasible. There are evidences that ring-open degradates and $^{14}CO_2$ form upon irradiation.

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b. Biodegradation

Aquatic metabolism studies (anaerobic and aerobic conditions) report a degradation/dissipation half-life of less than 1-hour. Both studies were conducted with silt loam aquatic sediment and seawater from the York River, VA (pH of sediment, 6.6; pH of seawater 7.4). While under aerobic conditions $^{14}CO2$ formation was rapid (>12% by day 30), mineralization (oxidation) is hindered under anaerobic conditions. In both cases, degradation products tend to partition (bind) strongly onto the sediment phase. These bound degradates were hard to extract and were characterized by their chromatographic behavior (polarity). Data suggest that degradates form by cleavage of the N-S bond followed by subsequent oxidation. Proposed degradation products include n-octylmalonamic acid and n-octyloxamic acid (particularly under aerobic conditions). Under anaerobic conditions, other proposed ring-open degradates include species containing a terminal aldehyde or alcohol functional group or a beta-ketone. Besides the role of microorganism in the degradation of RH-5287, the presence of nucleophiles and electrophiles in marine sediments/seawater environments is also believed to catalyze the cleavage of the labile -N-S- bond.

In aerobically incubated soils it appears that RH-5287 is more persistent than in marine sediments/seawater systems. The aged mobility study (soil column leaching) reports half-lives of degradations of 21 days. Data on degradates forming in soils incubated under aerobic conditions are not available at this time.

c. Mobility in Soil/Sediments

Batch-equilibrium adsorption/desorption conducted with four different soils and one aquatic sediment (parent RH-5287, unaged) report Freundlich adsorption constants (K_{ads}) ranging from 31.5 to 76.4 for the soils and 625.4 for the sediment; data suggest (values of n, slope) that the adsorption process was non-linear. Unlike the data presented in the metabolism studies, where rapid and strong binding to the marine sediment in the presence of seawater was noted, the batch-equilibrium adsorption/desorption study showed that a fraction as high as 34% could be desorbed form soils and sediment. In addition, parent RH-5787 was found to be the major component found in soils/sediment/aqueous phase (89 to 98%) even after 24 hrs of contact with the sediment in contrast to the apparent rapid degradation (possible by ring cleavage followed by subsequent oxidation) found in the aquatic metabolism studies. This suggests that the presence of chemical species characteristic of marine sediments and/or seawater may contribute significantly to the degradation of RH-5287. Table 1 summarizes the results.

The "aged" soil column leaching study (21-day aerobic incubation in silty clay and silt loam soils) indicate that between 80.2 to 100% of the applied ^{14}C-residues remained in the upper 6-cm and that RH-5287 was the only compound identified (47-64%) and that the remaining (uncharacterized) radioactivity was basically unextractable. The data in this study do not address the mobility in an aquatic sediment nor conclusively show that the degradation products reported as non-extractables are associated with ring-cleavage/subsequent oxidation products proposed to bind strongly to marine sediments in the presence of seawater.

d. Bioaccumulation in Fish

Carbon-14 residues of RH-5287 showed maximum accumulation at 21 to 28 day exposure of Lepomis macrochirus to 0.76-1.5 ppb concentrations (pH 7.9-8.3; dissolved oxygen content 5.9-8.8 mgL^{-1}. Bioconcentration factors were 170-200x (edible tissues), 1100-1200x (nonedible tissues) and 660-680x (whole fish), with water at 21 and 28 days containing 0.028 to 0.004 ppb of parent RH-5287. Maximum concentration of radioactive residues at during the exposure period were 0.23 ppm in edible tissues, 1.4 ppm in nonedible tissues and 0.8 ppm in whole fish. After 21-days depuration, residues in edible and nonedible tissues and whole fish were 0.093, 0.28, and 1.28 ppm, respectively. Although the attempt to characterize metabolites in the earlier uptake/depuration study (EPA Accession #265912; EFGWB #70104; 12/3/87) was unsuccessful, the registrant repeated the metabolite characterization study (0.99 ppm exposure). The results are as follows,

- No parent RH-5287 and its degradates were detected in edible and nonedible tissues
- In edible fish tissue, 35.5% of the radioactive residues were extracted with water (17.8% as protein; 12.9% as trichloroacetic acid [TCA] soluble); 9.6% was extracted with methanol; 47.0%, was nonextractable.
- In nonedible tissue, 82.4% was water extractable (60.6% as protein and 29.9% as TCA soluble.; 4.7% methanol extractable residues, and 15.9% nonextractable.
- TCA-soluble residues were further partitioned into ethyl acetate/water, were 50% of the residue remained in the ethyl acetate phase and 50% in the water phase, but were not further characterized.
- Further analyses of the TCA-precipitated protein indicated the authors that the residues is likely to involve a disulfide bond, most likely a cisteine adduct. This suggested the authors that cleavage of the isothiazoline ring is involved in the metabolism of RH-5287 in fish (biologically and or chemically mediated), followed by formation of amino acids adducts and subsequent incorporation into protein.

10. COMPLETION OF ONE-LINER: The One-Liner has been updated.

11. CBI APPENDIX: No CBI.

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TABLE 1. Soil/Water Partitioning (as Freundlich Constants)

	Adsorption Phase			Desorption Phase		
	K_d	K_{oc}	Slope (n)	K_d	K_{oc}	Slope (n)
Loamy Sand Soil %OM 0.8; pH 7.7 CEC* 3 83% sd; 9% st. 8% cl.	31.46	7865	0.61 (1.64)	48.45	12114	0.602 (1.66)
Sandy Loam Soil %OM 2.3; pH 7.4 CEC 8 74% sd; 18% st; 8% cl	73.33	6377	0.609 (1.64)	96.73	8412	0.536 (1.86)
Silt Loam Soil %OM 2.7; pH 6.8 CEC 18 16% sd; 67% st; 17% cl.	76.43	5662	0.600 (1.66)	102.26	7575	0.522 (1.91)
Silty Clay Loam Soil %OM 1.3; pH 7.9 CEC 29 10% sd; 51% st; 39% cl	42.49	6538	0.596 (1.75)	63.76	9809	0.592 (1.68)
Aquatic Sediment %OM 8.1; pH 6.6 CEC 35 20% sd; 60% st; 20% cl	625.37	15441	0.677 (1.47)	872.42	21541	0.697 (1.43)

CEC, in meq/100g; sd=sand; st= silt; cl= clay
K_{oc}= K_d x 100/% OC n= 1/slope

TABLE A. Status of Data Requirements for RH-5287

Data Requirement	MRID #/Review Date	Status/Comments
161-1 Hydrolysis	Accession #249934; 8/11/83	Satisfied, but registrant must present data on degradates at pH 9 to fully assess the effect of hydrolysis on RH-5287
161-2 Photodegradation in Water	41845001/This review	Not satisfied at this time, but study can be upgraded by responding to the Recommendations and Comments sections in DER.
162-3 Anaerobic Aquatic Metabolism	41845002/This review 42341101/This review	Not satisfied at this time, but study can be upgraded (see comments for 161-2)
162-4 Aerobic Aquatic Metabolism	41845003/This review 42341102/This review	Not satisfied at this time, but study can be upgraded (see comments for 161-2)
163-1 Mobility in Soil	41845004/This review batch.eq. study, unaged	Study is acceptable and partially satisfies 163-1 data requirement.
	41845005/This review soil column leaching, aged	Study acceptable, but was conducted with soil and not aquatic sediment. The study can be used towards partially satisfying 163-1 requirements for mobility of aged RH-5287 in soils. Registrant must present additional data as indicated in the RECOMMENDATIONS section, (b).
164-2 Aquatic Field Dissipation	Waiver Request, 4/10/91	Waived for the manufacturing use formulation only. RESERVED for end-use product (anti-foulant paint).
165-4 Bioaccumulation in Fish	#265912; 12/3/87 (Uptake/Depuration) 41845006/This review, (Metabolite identification)	Satisfied

TABLE A. Data Requirements for RH-5287,

Continued,

Data Requirement	MRID #/Review Date	Status/Comments
165-5 Bioaccumulation in Aquatic Non-target		RESERVED
Surface Water Monitoring		RESERVED
Special Studies:		
Leaching-from-the-matrix (dynamic study)		REQUIRED for all end-use products (that is, for the antifoulant paints).

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Page _____ is not included in this copy.

Pages 12 through 15 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.