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Record No.

83601
Shaughnessey No.

Review No.

EEB REVIEW

DATE: IN 03-21-88 OUT 08-26-88

FILE NUMBER 8340-17

PETITION OR EXP. NO.

DATE OF SUBMISSION 05-05-87

DATE RECEIVED BY HED 03-14-88

RD REQUESTED COMPLETION DATE 05-10-88

EEB ESTIMATED COMPLETION DATE 05-10-88

RD ACTION CODE 661

TYPE PRODUCT Fungicide

DATA ACCESSION NO. 40185901,40185902

PRODUCT MANAGER L. Rossi (21)

PRODUCT NAME TPTH

COMPANY NAME American Hoechst Corporation

SUBMISSION PURPOSE EAB deferral to EEB concerning adequacy of fish accumulation study

SHAUGHNESSEY NO.	CHEMICAL	%AI

REVIEW

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

AUG 26 1988

MEMORANDUM

SUBJECT: Triphenyltin hydroxide fish accumulation study

FROM: James W. Akerman, Chief
Ecological Effects Branch
Environmental Fate and Effects Division

TO: Lois Rossi, PM-21
Registration Division (TS-767C)

Information submitted by the registrant in Accession numbers 258234, 40185901, and 40185902 and reviewed by EAB are not considered adequate for defining the bioaccumulation of triphenyltin hydroxide (TPTH) in finfish for risk assessment purposes. No plateau was achieved over a 56-day exposure period and residues accumulated to 4900X in edible tissue, 8200X in nonedible tissue, and 6300X in whole body for bluegill sunfish. Also, the residues accumulated by finfish are almost exclusively parent TPTH. Given the stability of TPTH in water, additional testing is required to establish either a plateau or a body burden tolerance of TPTH in finfish.

cc. Emil Regelman

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Shaughnessy No.: 83601
Date Out of EAB: FEB 29 1988

To: Lois Rossi
Product Manager PM #21
Registration Division (TS-767)

From: Emil Regelman, Supervisory Chemist
Environmental Chemistry Review Section #3
Exposure Assessment Branch/HED (TS-769C)

Thru: Paul F. Schuda, Chief
Exposure Assessment Branch/HED (TS-769C)

Attached, please find the EAB review of...

Reg./File # : 8340-17

Chemical Name: Triphenyltin Hydroxide

Type Product : Fungicide

Product Name : TPTH

Company Name : American Hoechst Corporation

Purpose : Review Accumulation in Fish Study submitted in response to the TPTH Registration Standard.

Action Code: 661 EAB #(s): 80257

Date Received: 12/16/87 Total Reviewing Time: 3 days

Date Completed: 2/26/88

Monitoring Study Requested: _____

Monitoring Study Volunteered: _____

Deferrals to: X Ecological Effects Branch

____Residue Chemistry Branch

____Toxicology Branch

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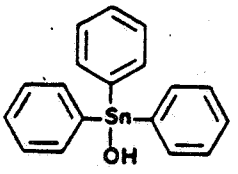
1. CHEMICAL:

chemical name: Triphenyltin Hydroxide

common name: TPTH

structure:



physical/chemical properties:

molecular formula-	$C_{18}H_{16}OSn$
molecular weight-	367.02
physical state-	crystalline
melting point-	118°C-120°C
solubility-	practically insoluble in water; moderately soluble in most organic solvents

2. TEST MATERIAL:

Active ingredient; uniformly phenyl-labeled [^{14}C] triphenyltin hydroxide. Specific activity- 23.17 mCi/g; radiochemical purity- >98%

3. STUDY/ACTION TYPE:

Review of a fish accumulation study which was submitted in response to the TPTH Registration Standard.

4. STUDY IDENTIFICATION:

A. Fischer, R. and W.L. Buerkle. "Fentin-hydroxide- ^{14}C (Identification Code: Hoe 029664 of ZE98 0003) Nature of Residues in Bluegill Sunfish After a 35-day Exposure in a Flow-Through System." Performed by Hoechst AG, Germany. Submitted by American Hoechst Corporation, New Jersey. Accession number: 40185901.

B. LeBlanc, G.A. and J.D. Mastone. AMENDMENT- "Accumulation and Elimination of ^{14}C-Residues by Bluegill Sunfish Exposed to ^{14}C-Triphenyltin Hydroxide." Performed by EG & G Bionomics, Massachusetts. Submitted by American Hoechst Corporation, New Jersey. Accession number 40185902.

5. REVIEWED BY:

Dana Spatz
Chemist, ECRS #3
EAB/HED/OPP

Date: FEB 26 1988

6. APPROVED BY:

Emil Regelman
Supervisory Chemist, ECRS #3
EAB/HED/OPP

Date: FEB 29 1988

7. CONCLUSIONS:

The Accumulation in Fish requirement is satisfied, pending concurrence by the Ecological Effects Branch.

The registrant has submitted two Fish Accumulation studies, one in 1985 (accession number 258234), and the current study, relying on the combined merits of both studies to fulfill the Study Requirements.

The 1985 study was originally considered unacceptable for fulfilling EPA data requirements for registering pesticides for the following reasons:

a. The purity of the test substance was unspecified.

b. Radioactive residues were not characterized.

A further inadequacy of the 1985 study was that the accumulation of residues did not plateau over the 56-day exposure period. We, therefore, have no indication as to the extent of accumulation that can occur. Consequently, bioconcentration factors for edible, nonedible, and whole fish are actually greater than the 4900x, 8200x, and 6300x respectively, as were reported in the 1985 study.

The current submission, (Vol. 2; acc. no. 40185902), addresses the purity of the test substance. It indicates that the triphenyltin hydroxide [ring-^{14}C(u)] was determined to be $\geq$ 97% radiochemically pure.

The intent of Volume 1 of the current submission was to address the characterization of radioactive residues.
This study indicates that after the 35-day exposure period, residues accumulated by the fish were almost exclusively the unchanged parent compound, TPTH.

Because the residue accumulation did not plateau over the length of the study, EAB must defer to EEB on whether sufficient information is provided by these two studies to make an assessment on the effects of TPTH accumulation in fish. If EEB feels that a determination of the total possible accumulation of TPTH in fish is necessary, then a new fish accumulation study should be submitted to EAB for review.

8. RECOMMENDATIONS:

EEB should be consulted on whether a new Fish Accumulation study is necessary, in light of the fact that residue accumulation in the 56-day study did not reach a plateau. If EEB is satisfied with the results of this submission, then the Fish Accumulation study requirement will be fulfilled.

9. BACKGROUND:

This study was submitted in response to the TPTH Registration Standard, which was issued in September, 1984.

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

A. Study Identification:

Fischer, R. and W.L. Buerkle. "Fentin-hydroxide- ^{14}C (Identification Code: Hoe 029664 of ZE98 0003) Nature of Residues in Bluegill Sunfish After a 35-day Exposure in a Flow-Through System." Performed by Hoechst AG, Germany. Submitted by American Hoechst Corporation, New Jersey. Accession number: 40185901.

B. Materials and Methods:

Bluegill sunfish (average length and weight of 4.8 cm and 3.1g respectively) were held in culture tanks on a 16-hour daylight photoperiod for 4 weeks prior to the initiation of the study. Flow-through aquatic exposure systems were prepared using 36-L chemically inert stainless steel tanks. Aerated tap water (pH 7.6-8.3, dissolved oxygen 5.3-10.7 ppm, temperature 21.8-23°C, total hardness 308-339 mg/L as $CaCO_3$, total alkalinity 256-272 mg/L as $CaCO_3$, chlorine <0.05 mg/L, nitrate <0.1 mg/L) was provided to each aquarium at a rate of 8 turnovers per day.

Bluegill sunfish (50) were placed in one aquarium which was continuously treated with uniformly phenyl-labeled [^{14}C] triphenyltin hydroxide (radiochemical purity >98%, specific activity 23.17 mCi/g, at 0.5 ppb. A control aquarium

contained 95 bluegill. Water samples were taken daily from the middle of the tank and from the inflow. All fish were sampled at the end of the exposure phase (35 days).

Radioactivity in the water samples was quantified using LSC.

To determine the total radioactive residues in the fish, 3 fish were cut into pieces and analyzed by LSC following combustion. The remaining fish were dissected into edible and nonedible tissues. The samples were pooled and homogenized with dry ice. After warming to room temperature, aliquots of the samples were analyzed by LSC.

The edible tissue was further analyzed by reductive cleavage with zinc-hydrochloric acid, extraction with n-hexane, and extraction with an acid solvent mixture. In the reductive cleavage procedure, the phenyltin bond is cleaved quantitatively by reaction with zinc and hydrochloric acid, resulting in benzene which can be evaporated from the reaction mixture. The reaction was carried out in a flow-through device shown in Figure 1. Excess zinc dust and water were added to the tissue sample placed in the reaction flask. The mixture was heated to 80°C and stirred magnetically. Within a one-half hour period, 50 ml of 5 M hydrochloric acid was slowly added. The volatiles that were formed were passed through anhydrous calcium chloride and trapped in cooled methanol. In order to reduce the volume, the adsorbed benzene was extracted with methylene chloride after addition of water, saturated sodium chloride solution, and sulfuric acid. Benzene was identified by GC-MS. The samples were analyzed for another possible volatile compound, phenol, by reextraction with 1 M sodium hydroxide solution.

In another procedure, an aliquot of homogenized tissue was extracted three times with n-hexane. The extracts were combined, dried with sodium sulfate, concentrated, and purified by TLC. The radioactive area was scraped from the TLC plate, desorbed with acetone, concentrated, and analyzed by TLC. The sample was co-chromatographed with reference parent compound on silica gel plates developed in toluene:acetic acid ethyl ester:water:glacial acetic acid (30:60:0.5:1). The radioactive areas were quantified by linear analyzer.

In the acid solvent extraction procedure, both edible and nonedible samples were extracted three times with methanol:hydrobromic acid (400 g/L):water:acetone (20:10:40:80). The solid residue was dried and analyzed by LSC following combustion. The extract was diluted with sodium chloride solution and reextracted with n-hexane four times and with acetic acid ethyl ester. The combined organic

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phases were dried with sodium sulfate, concentrated, and analyzed by TLC as previously described.

C. Reported Results:

No mortality of the fish was reported.

Table 1 contains data on the concentrations of TPTH found in the water.

The following is a summary of the results of the current submission:

The residues of TPTH taken up and metabolized by bluegill sunfish can be presented as follows:

1. **TOTAL RADIOACTIVE RESIDUES AFTER A 35 DAYS EXPOSURE to 0.5 ug/l**

whole body	**: 0.83 mg equiv/kg**
edible tissue	**: 0.66 mg equiv/kg**
non-edible tissue	**: 1.63 mg equiv/kg**

2. **CHARACTERIZATION OF THE RESIDUES IN THE EDIBLE TISSUE:**

- 96	**% of total residues:**	**phenyltin groups determined via benzene split off reductively**
- 95.5	**% of total residues:**	**extractable**
- 4.5	**% of total residues:**	**non-extractable, bound**
- 87	**% of total residues:**	**parent compound TPTH**
- 19	**% of total residues:**	**physically dissolved TPTH extractable with n-hexane**
- 7	**% of total residues:**	**water soluble polar degradates probably, di- and monophenyltin compounds**

3. **CHARACTERIZATION OF THE RESIDUES IN THE NON-EDIBLE TISSUE:**

- 99	**% of total residues:**	**extractable**
- 1	**% of total residues:**	**non-extractable, bound**
- 97	**% of total residues:**	**parent compound TPTH**
- 0.3	**% of total residues:**	**water soluble, polar**

Below are the results of the 1985 study:

Mean measured (standard deviation) [^{14}C]residue concentrations, calculated as triphenyltin hydroxide (TPTH) in the edible tissue (muscle) and nonedible tissue (viscera/carcass) of bluegill (Lepomis macrochirus), during 56 days of continuous aqueous exposure to [^{14}C]TPTH at a mean measured concentration of 0.49 0.019 ppb and during an additional 56 days depuration in flowing, uncontaminated water.

Period	Day	Concentration in water (ppb)[a]	[^{14}C]residue concentration (ppm)					
			Edible[b]	BCF (x)[c] / % change[d]	Nonedible	BCF (x) / % change	Whole fish[e]	BCF (x) / % change
Pre-exposure	-1	0.50(0.0058)	--	--	--	--	--	--
Exposure	0	0.50(0.000)	--	--	--	--	--	--
	1	0.45(0.010)	0.045(0.013)	94	0.14(0.030)	290	0.087(0.020)	180
	3	0.47(0.010)	0.093(0.024)	200	0.31(0.064)	660	0.19(0.030)	400
	7	0.50(0.015)	0.24(0.046)	500	0.71(0.19)	1500	0.46(0.11)	960
	10	0.47(0.006)	0.35(0.076)	730	0.0(0.17)	2100	0.67(0.14)	1400
	14	0.50(0.021)	0.45(0.095)	940	0.0(0.084)	2300	0.76(0.087)	1600
	21	0.47(0.006)	0.63(0.19)	1300	0.7(0.53)	3500	1.1(0.34)	2300
	28	0.51(0.006)	1.1(0.19)	2300	2.3(0.32)	4800	1.7(0.23)	3500
	35	0.50(0.031)	1.5(0.29)	3100	2.4(0.44)	4900	2.0(0.40)	4100
	42	0.50(0.053)	1.9(0.33)	3900	3.2(0.40)	6500	2.6(0.36)	5300
	49	0.47(0.015)	1.5(0.24)	3100	2.8(0.31)	5700	2.1(0.26)	4300
	56	0.50(0.030)	2.4(0.47)	4900	4.0(0.44)	8200	3.1(0.44)	6300
Depuration	1	--	2.7(0.48)	+12[d]	3.7(0.56)	-8	3.2(0.51)	+3
	3	--	1.7(0.23)	-29	3.0(0.32)	-25	2.3(0.20)	-26
	7	--	1.4(0.29)	-42	--[e]	--	--[f]	--
	14	--	1.5(0.11)	-38	1.9(0.28)	-52	1.6(0.20)	-48
	21	--	1.4(0.23)	-42	2.0(0.15)	-50	1.7(0.19)	-45
	28	--	1.0(0.19)	-58	1.6(0.34)	-60	1.3(0.24)	-58
	35	--	1.1(0.11)	-54	1.6(0.10)[h]	-60	1.3(0.10)	-58
	56	--	0.75(0.11)	-69	1.1(0.18)[h]	-72	0.87(0.10)	-72

[a] Mean (S.D.) based on the radiometric analyses of triplicate water samples.

[b] Mean (S.D.) based on the radiometric analyses of five muscle tissues and five viscera/carcass tissues, unless otherwise specified.

[c] Bioconcentration factor.

[d] Percent change, relative to day 56 of exposure, of [^{14}C]residues measured in fish tissues during depuration.

[e] Mean (S.D.) calculated whole body [^{14}C]residue concentrations based on the radiometric analyses of the individual tissue portions of five fish, unless otherwise specified.

[f] Sample oxidizer malfunction resulted in a spurious analysis.

[g] [^{14}C]Residue concentration based on the summation of analyses from five viscera and five remaining carcass sampled individually.

[h] [^{14}C]Residue concentration based on six muscle tissues from three fish or the summation of analyses from three viscera and three remaining carcass sampled individually.

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D. Study Author's Conclusions:

"Even after extended exposure periods, the main portion of residues taken up by fish is the unchanged parent compound TPTH."

E. Reviewer's Discussion and Interpretation of Study Results:

The results indicate that the residues that accumulate in the fish are predominantly the parent compound, TPTH. The extent of this accumulation is at least 4900x, 8200x, and 6300x; in edible, nonedible, and whole fish, respectively.

11. COMPLETION OF ONE-LINER:

Not applicable.

12. CBI APPENDIX:

Not applicable.