323 EE

Date Out EFB: OCT 14 1981

To Product Manager 21 Jacoby
TS-767

From Dr. Willa Garner
Chief, Review Section No. 1
Environmental Fate Branch

Attached please find the environmental fate review of:

Reg./File No.: 100-617

Chemical: Tilt (CGA-64250)

Type Product: Fungicide

Product Name: Tilt

Company Name: Ciba-Geigy

Submission Purpose: Bluegill study

ZBB Code: other

Date in: 9/2/81

Date Completed: OCT 14 1981

ACTION CODE: 400

EFB # 932

TAIS (level II)	Days
62	3

Deferrals To:

_____ Ecological Effects Branch

_____ Residue Chemistry Branch

_____ Toxicology Branch

1.0 INTRODUCTION

1.1 Purpose

Ciba-Geigy responded to the EPA letter of 8/3/81 and submitted the "Fish Accumulation Study" for Tilt Fungicide, now filed under accession No. 245708 on 8/20/81.

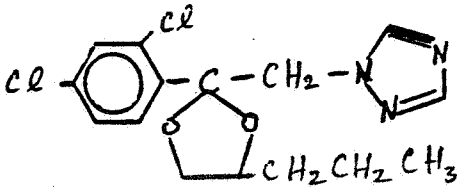
1.2 Previous Review

100 - ARI, ART 6/17/81

1.3 Chemical

Common name : none established (CGA-64250)
Trade : Tilt 3.6E
Chemical formula : 1-[2',4'-dichlorophenyl)-4-propyl-1,3-dixolan-2,yl-methyl]-1H-1,2,4-triazole

Chemical Structure :



2.0 DISSCUSSION OF DATA

Data submitted were filed under accession No. 245708, Reg. No. 100-617, on 8/20/81.

Research was conducted by EG and G, Bionomics Aquatic Toxicology Laboratory of Wareham, Massachusetts for Ciba-Geigy entitled: "Accumulation and elimination of ^{14}C-residues by bluegill sunfish (Lepomis Macrochirus) exposed to ^{14}C-CGA-64250. December, 1980".

EXPOSURE

Exposure was conducted in a 500-liter tank 40% full of well water characterized as having total hardness and alkalinity as Ca CO_3 of 25 and 22 ppm respectively, a pH of 6.7, a temperature of 20 °C, and a specific conductance range of 90-100 um hos/cm at rates of 32 turnover/day. Labelled ^{14}C-CGA-64250 was introduced to the tank to a final concentration of 1 ppm. The system was then allowed to reach equilibrium for 2 days. After equilibrium, 150 bluegills sunfish, averaging 7.1 gm in weigh and 77 cm in length, were introduced to the tank. Fifty other bluegills were introduced to a control tank.

Exposure was continuous for 28 days, after which the fish were transferred to a depuration tank. The depuration period continued for 14 days in order to estimate t 1/2 (elimination of 50% of accumulated ^{14}C-residues). Sampling for CGA-64250 residues in water were conducted on days 0, 1, 3, 7, 10, 14, 21, and 28 of exposure. In the edible and non-edible tissue of fish, sampling was on same days except 0 day of exposure, and on day 1, 3, 7, 10, and 14 of depuration. Control fish were sampled on days 1, 7, and 28 of exposure and day 14 of depuration.

Metabolism of CGA-64250 was studied by removing fish on day 14 and 21 of exposure and placing them under static conditions in a 10-liter tank containing 1.1 ppm of ^{14}C-CGA-64250 in water. The fish were transferred daily to similar static conditions and of the same radioactivity. After four days of static exposure, analysis was conducted to determine ^{14}C-residues in muscle, viscera and test solution.

ANALYSIS

For analysis, fresh samples were homogenized with liquid nitrogen, oxidized and combusted for radiometric analysis. The remaining tissue was extracted and combusted for radioassay. Portions of the homogenized fractions were then extracted with methanol/water (4/1). Extracts were concentrated and partitioned with methylene chloride. Samples from the aqueous and the organic phases were counted using LSC. Characterization of ^{14}C-residues in both phases was accomplished utilizing TLC and co-chromatography with known authentic samples. Solvent systems employed were: acetonitrile for organic soluble samples and ethyl acetate/acetic acid (9/1) for aqueous soluble samples. Spots were visulized using $AgNO_3$ spray solution.

Results

1. ^{14}C-Residues In Water
   The concentrations of ^{14}C-residues, calculated as CGA-64250, measured in the water of the exposure aquarium during the 28-day exposure period and the 14 day depuration period are presented in Table 1. These data indicate that the mean concentration of ^{14}C-residues in aqueous solution prior to the introduction of bluegill into the system (i.e. equilibration period) was 0.93 ± 0.01 ppm. Radiometric analyses performed during the depuration phase in which previously exposed fish were held in ^{14}C-CGA-64250-free water are also presented in Table 1.

These data indicate that a decreasing concentration of ^{14}C-CGA-64250 was measured in the water during the initial 10 days of depuration. By day 14, the ^{14}C-residues in the water had decreased to below detectable limits of 0.0055 ppm. These aqueous ^{14}C-residues were obviously a result of the elimination of the ^{14}C-residues previously accumulated in the fish tissues. Analyses of control water samples indicated that no ^{14}C-residues were present above the detection limit throughout the study period.

2. Accumulation of ^{14}C-Residues in Fish Tissues

The mean ^{14}C-residue concentrations measured in the selected portions of bluegill, i.e., edible (muscle) and non-edible (viscera-carcass), during 28 days of continuous exposure to ^{14}C-CGA-64250 and during the 14 day depuration period, are presented in Table 1. and Figures 1-3. These data suggest that, despite some fluctuation of the ^{14}C-residue content in the edible tissue, an apparent period of equilibrium between the rates of accumulation and elimination of ^{14}C-residues in the edible tissue existed throughout the exposure period (day 1-28, Figure 1). The fluctuation of ^{14}C-residues in the edible tissue was directly proportional to the varying concentrations of aqueous ^{14}C-residues. Based on a mean concentration of 16 $\pm$ 5.2 ppm, measured in the muscle tissue during days 1-28 of exposure and a mean concentration of 0.66 $\pm$ 0.11 ppm ^{14}C-CGA-64250 measured in the water during the period 0-28 days of exposure, the mean equilibrium bioconcentration factor for ^{14}C-CGA-64250 in bludgill muscle tissue was 24X.

Radiometric analyses of the non-edible tissues (viscera-carcass) of bluegill continuously exposed to ^{14}C-CGA-64250 indicate that a substantial fluctuation of ^{14}C-residue content was evident throughout the 28-day exposure period (Figure 2). Based on maximum mean concentration of 330 $\pm$ 28 ppm measured in the combined viscera-carcass on day 21 of exposure and a mean concentration of 0.64 $\pm$ 0.10 ppm ^{14}C-CGA-64250 measured in the water during the period 0-21 days of exposure, the mean maximum bioconcentration factor for ^{14}C-CGA-64250 in bluegill viscera and carcass was 516X. During the remaining 7 days of exposure, the concentration of ^{14}C-residues rapidly decreased to 180 ppm, 45% of the concentration measured in the viscera-carcass at the point of maximum accumulation. In light of the substantial fluctuation of ^{14}C-residues in the non-edible tissue, the average bioconcentration factor for ^{14}C-CGA-64250 in bluegill viscera-carcass during the 28-day study period was 257X with a range of 138X to 516X.

These analyses were also performed to estimate the total ^{14}C-residue content on a whole fish basis. These data are expressed as mean calculated ^{14}C-residue concentrations and are based on a summation of the mean concentrations of ^{14}C-residues measured in each tissue portion and the total weight of each tissue portion from the four bluegill sampled at each interval during the entire study (Table 1). The calculated data suggest that the pattern of accumulation and elimination of ^{14}-residues in the whole fish was similar to that observed in the non-ebible tissue (Figure 3). Based on a maximum mean calculated ^{14}C-residue concentration in whole fish of 130 ppm (day 21) and a mean concentration of 0.64 $\pm$ 0.10 ppm ^{14}C-CGA-64250 measured in the water during the period 0-21 of exposure, the mean maximum biocontration factor for ^{14}C-CGA-64250 in the whole body of bluegill was 203X. The average bioconcentration factor for ^{14}C-CGA-64250 in the whole body of bludgill during the 28-day study period was 116X with a range of 68X to 203X.

3. Elimination of ^{14}C-Residues From Fish Tissue

Radiometric analyses of the edible and non-edible portions of bluegill transferred to flowing, uncontaminated water after 28 days of aqueous exposure to ^{14}C-CGA-64250 indicate that in each case there was significant elimination of ^{14}-day depuration phase (Table 2). Half-life of the ^{14}C-residues in the edible (muscle) tissue occurred within 24 hours after transfer to flowing, uncontaminated (^{14}C-CGA-64250) water. observations of the elimination of ^{14}C-residues from the non-edible (viscera-carcass) tissues and on a whole fish basis indicate that half-life of these residues occurred approximately by day 7 of depuration. At termination of the depuration period (day 14), bludgill had eliminated 99%, 98% and 98% of the ^{14}C-residues present in the edible tissue, non-edible tissues and whole fish, respectively, on the last day of exposure.

4. Metabolism of ^{14}C-CGA-64250 by Bluegill.

The mean measured ^{14}C-residue concentration in the muscle of bluegill after 4-day static exposure were as follow:

	^{14}C-residue concentration in ppm			
Test#	muscle	viscera	carcuss	whole body
1	22	1200	40	120
2	17	1400	37	120

The above data indicate no increased uptake or elimination of ^{14}C-CGA-64250 once the fish were transferred from the flow-through 28-day esposure to the static 4-day esposure.

Results of the characterization of residues in fish tissues by extraction and partition are presented in Table 3 and 4. During both tests, approximately 5 times more ^{14}C-residue was extracted in the orginic phase as compared to the aqueous phase in both muscle and carcass. However, 3 to 4 times more ^{14}C-residue were extracted from the vircera in the aqueous phase as compared to the organic phase. The characterization of water, sampled During the static exposures, by extraction and partition, indicate that the majority (83-100%) of the ^{14}C-residues were extracted in the organic phase (Table 5).

Thin layer chromatographic characterization of organic soluble ^{14}C-residues extracted from fish and water is presented in Tables 6 and 7. In all samples analyzed (muscle, viscera, carcass and water) the parent compound CGA-64250, was the predominant compound detected. In muscle and water samples CGA-64250 constituted virtually all of the ^{14}C-residue present. An appreciable quantity of the metabolite 1,2,4-triazole was detected in visceral tissue during the first test. In addition, the carcass samples analyzed in both tests were found to contain appreciable quantities of the metabolite CGA-77502 (See Fig. 4 for structual formulas of parent and metabolites).

3.0 SUMMARY

Bluegill sunfish (Lepomis macrochirus) were continuously exposed to a nominal concentration of 1.0 ppm of the triazole-labelled ^{14}C-CGA-64250 in well water for 28 days after which all remaining fish were transferred to flowing, uncontaminated water for a 14 day depuration period. In addition, two 4-day static exposures were conducted in an effort to identify the metabolism of ^{14}C-64250 by bluegill. Radiometric analyses of the water and selected fish tissues revealed that ^{14}C-CGA-64250 accumulates in edible tissue at a maximum concentration of 24 ppm, in non-edible tissue at 257 ppm, and whole fish at 116 ppm. A continuous elimination of ^{14}C-residues from edible tissue, as well as whole fish, was observed throughout the depuration. By day 14 of depuration, 99% and 98% of the ^{14}C residue present in edible tissue and whole fish, respectively, had been eliminated.

Thin layer characterization of the organic soluble ^{14}C-residues from exposure water and selected fish tissues showed predominately CGA-64250. ^{14}C-1,2,4-triazole was dected as a metabolite in viscera tissue while x-(2,4-dichlorophenyl)-1H-1,2,4-triazole-1-ethanol was detected as a metabolite in carcass tissue (See Tables 1-7 and Figures 1-4).

COMMENTS

The Environmental Fate Branch has no adverse comments on the fish accumulation study for Tilt Fungicide, submitted by Ciba-Geigy on 8/20/81 under accession No. 245708.

Sami Malak

Sami Malak, Chemist
Review Section #1
Environmental Fate Branch/HED

TILT CGA-64250 Reviews

The next // page(s) is/are not included in this copy of the TILT reviews.

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 product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commerical/financial information

___ A draft product label

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