(UNDATED)

DATA EVALUATION RECORD

STUDY 4

CHEM 112602 Cimectacarb §165-4

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 41869542
Fackler, P.H. 1990. Bioconcentration and elimination of ^{14}C-residues by bluegill (Lepomis macrochirus) exposed to CGA-163935. Laboratory Report No. 90-2-3236. Ciba-Geigy Protocol No. 144+ 145-89. Unpublished study performed by Springborn Laboratories, Inc., Wareham, MA, and submitted by Ciba-Geigy Corporation, Greensboro, NC.

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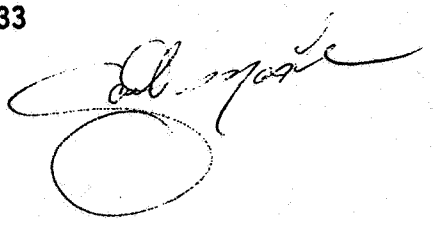

CONCLUSIONS:

Laboratory Accumulation - Fish

1. This study can not be used towards the fulfillment of data requirements.

2. Cimectacarb residues (uncharacterized) accumulated in bluegill sunfish exposed to 1.4 ppm of cimectacarb, with maximum mean bioconcentration factors of 2.7x, 13.6x, and 7.1x in edible, nonedible, and whole fish tissues, respectively (See Table IV). The maximum mean concentrations of total [^{14}C]residues were 3.8 ppm in edible tissues (day 28), 19 ppm in nonedible tissues (day 21), and 10 ppm in whole fish (day 21). Depuration was rapid, with 100% of the

accumulated [^{14}C]residues eliminated from the fish tissues by day 7 of the 14-day depuration period.

3. This study is scientifically sound, but does not meet Subdivision N guidelines for the following reason:

   [^{14}C]residues in the fish tissues were not characterized.

4. This study provides information on the accumulation of total [^{14}C]cimectacarb residues in fish. Because the fish tissues partially degraded before residue characterization was initiated, the registrant repeated a portion of the study (Study 5, MRID 41869543) to obtain fresh fish tissue samples for metabolite identification. If the criticisms of Study 5 are adequately addressed, this study plus Study 5 can be used to fulfill the accumulation in laboratory fish data requirement.

METHODOLOGY:

Juvenile bluegill sunfish (Lepomis macrochirus; mean length and weight 53 mm and 1.9 g, respectively) were held in culture tanks on a 16-hour photoperiod (Vita-Lite fluorescent lights) for ≥14 days prior to the initiation of the study. Flow-through aquatic exposure systems were prepared using two aquaria (76 x 40 x 30 cm). Aerated well water (17 ± 1 C, pH 6.9-7.6, dissolved oxygen content unspecified, total hardness 25-36 mg/L as $CaCO_3$, and alkalinity 22-30 mg/L as $CaCO_3$), was provided to each aquarium at a rate of 8.3 turnovers per day (90% replacement/6 hours). The flow-through systems were equilibrated for several weeks prior to the start of the study.

Then, 175 fish were transferred into each aquarium, one of which was continually treated at 1.4 ppm with ring-labeled [1,2,6-^{14}C]cimectacarb (radiochemical purity 96.2%, specific activity 21.4 uCi/mg, Ciba-Geigy) plus unlabeled cimectacarb (purity 96.2%) dissolved in acetone. The remaining aquarium served as an untreated solvent-only control. The fish were fed a commercial fish meal once daily at a rate of 2% of their total biomass, except during the 24 hours prior to sampling. The treated water was sampled (5 mL) during equilibration on days 4 and 3 prior to the introduction of the fish. During the exposure period, water samples (5 mL) and fish (5) were collected from the treated aquarium on days 0 (water only), 1, 3, 7, 10, 14, 21, and 28; and from the control aquarium on days 0 (water only) and 28. Unexposed fish were also sampled initially (day 0) and analyzed for background [^{14}C]residues. Following a 28-day exposure period, 35 fish from the treated aquarium were transferred to an untreated aquarium for a 14-day depuration period. During the depuration period, water samples (5 mL) and fish (5) were collected from the treated aquarium on days 1, 3, 7, 10, and 14; and from the control aquarium on day 14.

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The water samples were analyzed for total radioactivity by LSC. Recovery efficiencies from fortified water samples ranged from 91.4 to 122% (Table II). The detection limit was 0.15 ppm.

Two water samples collected from the treated aquarium on day 28 of the exposure period were analyzed to determine the radiochemical purity of the [^{14}C]activity in the test water. The water samples (500 mL) were acidified to pH 3 with 0.1 N hydrochloric acid and extracted three times with methylene chloride; the extraction efficiency was determined to be approximately 85%. The methylene chloride was filtered through sodium sulfate and rotary-evaporated to dryness. The residues were reconstituted in acetone and analyzed by one-dimensional TLC on silica gel plates developed in toluene:acetone:formic acid (75:25:1, v:v:v). Radioactive zones on the plates were located using autoradiography, scraped, and analyzed by LSC.

The fish samples were divided into edible (muscle) and nonedible (viscera and carcass) tissue. Each tissue sample was air-dried for $\geq$24 hours at ambient temperature, then analyzed for total radioactivity by LSC following combustion. Recovery efficiencies from fortified fish tissues ranged from 80.4 to 117% (Table III). The detection limits were not reported.

Edible tissues from fish sampled on day 28 of the exposure period were analyzed in order to determine the relative distribution of nonpolar and polar [^{14}C]residues. Each of three sets of approximately 10 fish were homogenized with dry ice, mixed with hexane, and then centrifuged for 10 minutes. The hexane extract was decanted, concentrated under a stream of nitrogen, and analyzed for total radioactivity using LSC. The hexane-extracted tissues were then extracted with acetonitrile. The acetonitrile extract was filtered (0.7 um), concentrated under a stream of nitrogen, and analyzed for total radioactivity using LSC. The extracted tissues were analyzed for unextracted radioactivity by LSC following combustion.

DATA SUMMARY:

[^{14}C]Cimectacarb residues accumulated in bluegill sunfish exposed to ring-labeled [1,2,6-^{14}C]cimectacarb (radiochemical purity 96.2%) at 1.4 ppm for 28 days under flow-through conditions. The maximum mean bioconcentration factors were 2.7x for edible tissues (muscle), 13.6x for nonedible tissues (viscera and carcass), and 7.1x for whole fish (Table 1). Maximum mean concentrations of total [^{14}C]residues were 3.8 ppm for edible tissues (day 28), 19 ppm for nonedible tissues (day 21), and 10 ppm for whole fish (day 21; Table IV). Of the accumulated [^{14}C]residues in 28-day edible tissues, an average 51.5% of the recovered was extractable (6.5% with hexane and 45% with acetonitrile) and 32% was unextracted [^{14}C]residues (Table VI). By day 7 of the 14-day depuration period, 100% of the accumulated

[^{14}C]residues had been eliminated from the fish tissues (Table IV). The apparent half-life for elimination of [^{14}C]residues from whole fish was between 1 and 3 days.

Throughout the study, the temperature of the treated water was 16-18 C, the pH ranged from 6.2 to 6.9, and the dissolved oxygen content ranged from 6.1 to 8.5 mg/L; values were comparable for the control aquarium. Total [^{14}C]residues in the treated water ranged from 1.3 to 1.6 ppm during the exposure period (Table IV). Based on TLC analyses of the 28-day water samples, the study author stated that cimectacarb comprised 95% of the extracted [^{14}C]residues (data not provided).

COMMENTS:

1. Radioactive residues were not characterized in the fish tissues and were characterized in the water samples only at 28 days.

   [^{14}C]Residues in water and fish samples were characterized in Study 5 (MRID 41869543) reviewed in this report. Study 5, however, provides only supplemental information at this time because residues in one HPLC peak, which contained up to 1.6 ppm of radioactivity, were incompletely characterized. If the criticisms of Study 5 are adequately addressed, this study plus Study 5 can be used to fulfill the accumulation in laboratory fish data requirement for cimectacarb.

2. Bioconcentration factors for edible, nonedible, and whole fish tissues were calculated by the reviewer by dividing the mean measured concentration of [^{14}C]residues in the fish tissue by the mean measured water concentration up to and including the respective sampling day during the exposure period (Table 1). This method enabled the reviewer to determine the maximum mean bioconcentration factors for each tissue by providing bioconcentration factors for each sampling interval. In contrast, the registrant calculated mean steady-state bioconcentration factors by dividing the mean measured equilibrium [^{14}C]tissue concentration for each tissue type by the mean measured water concentration for the entire exposure period. Based on the reviewer's calculations, the bioconcentration factors were 2.5x for edible tissues, 11x for nonedible tissues, and 6x for whole fish (Study Author(s)'s Results and/or Conclusions).

3. The detection limits for the tissue samples were not reported. It was stated that the detection limits varied for both the water and fish samples, and were dependent upon counting efficiency, sample size, and background levels of radiation for the liquid and combusted samples.

4. During the exposure and depuration periods, two fish died in the control aquarium; there were no deaths in the treated or depuration aquaria. The fish appeared healthy and exhibited normal behavior during the study period.

5. A preliminary study was conducted to determine the acute toxicity of cimectacarb to bluegill sunfish. The 96-hour LC_{50} was calculated to be 140 ppm. Based on this result, the registrant chose an exposure level of 1.4 ppm for the bioaccumulation study (1/100 of the 96-hour LC_{50} value).

Table 1. Bioconcentration (BCF) of [^{14}C]residues in bluegill sunfish during 28 days of exposure to [^{14}C]cimectacarb at 1.4 ppm in a flow-through aquarium, followed by 14 days of depuration.

		Fish					
	Water	Edible		Nonedible		Whole Fish	
Day	mg/L	mg/kg	BCF[1]	mg/kg	BCF	mg/kg	BCF
Exposure							
0	1.5	<3.7	---	<3.8	---	NA	---
1	1.5	2.7	1.8	12	8.0	6.5	4.3
3	1.4	3.5	2.3	12	8.0	7.2	4.8
7	1.6	3.7	2.5	17	11.3	9.5	6.3
10	1.4	3.4	2.3	13	8.7	7.8	5.2
14	1.3	3.5	2.5	13	9.3	7.4	5.3
21	1.4	3.7	2.6	19	13.6	10	7.1
28	1.4	3.8	2.7	17	12.1	9.8	7.0
Depuration							
1	≤0.15	3.6		12		7.1	
3	≤0.15	1.3		2.4		1.8	
7	≤0.15	<1.9		<1.9		NA	
10	≤0.15	<1.0		<1.6		NA	
14	≤0.15	<1.4		<1.6		NA	

[1] Daily bioconcentration factor (BCF) obtained by dividing the tissue concentration by the mean measured water concentration up to and including the respective sampling day.

NA = Not applicable. These values could not be calculated.

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