Shaughnessy No.: 108801
Date Out of EFGWB: NOV 30 1989

Nov 30 1989

TO: J. Edwards
Product Manager
Registration Division (H7505C)

F.D. Rubis
Product Manager
Registration Division (H7508C)

FROM:

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

THRU:

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

Attached please find the EFGWB review of:

Reg./File # : 100-587, 108801

Chemical Name: Metolachlor

Product Type : Herbicide

Product Name : Dual

Company Name : CIBA-GEIGY

Purpose : Review results of the aerobic and anaerobic metabolism studies, and fish accumulation studies submitted in accordance with the metolachlor registration standard

Date Received: 2 August 89, 22 Feb 89 Action Code: 660, 400

Date Completed: _____ EFGWB No. 90719, 90368
90718

Total Reviewing Time (decimal days): 19.0

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

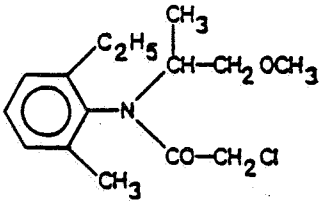
1.0 CHEMICAL:

Common name: Metolachlor

Chemical name: 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl) acetamide

Trade Name: Dual

Chemical Structure:



2.0 TEST MATERIAL: Analytical grade [U-phenyl-ring-^{14}C] metolachlor

3.0 STUDY/ACTION TYPE:

Evaluate the aerobic and anaerobic aquatic metabolism of Metolachlor

Request by CIBA-GEIGY for additional extension until June 1989 for submission of fish accumulation study EPA Guideline Reference 165-4.

Determine the bioconcentration and elimination of ^{14}C residues in fish exposed to metolachlor.

4.0 STUDY IDENTIFICATION:

Spare, W.C., 1989. Aerobic and Anaerobic Aquatic Metabolism of Metolachlor. Agrisearch Incorporated Agrisearch Project No. 1259 for CIBA-GEIGY Corp. MRID No. 411857-01

CIBA-GEIGY letter dated 6 January 1989 requesting an additional extension of fish accumulation studies for metolachlor registration standards until June 1989.

Fackler, P.H., 1989. Bioconcentration and Elimination of ^{14}C Residues by Bluegill (Lepomis macrochirus) Exposed to Metolachlor. Springborn Life Sciences, Inc., Laboratory Report Number 87-9-2505 for CIBA-GEIGY Corp. MRID No. 411542-01.

5.0 REVIEWED BY:

George Tompkins
Entomologist, Review Section 1
EFGWB/EFED

Signature: George Tompkins
Date: 30 Nov 1989

6.0 APPROVED BY:

Paul Mastradone
Section Chief, Review Section 1
EFGWB/EFED

Signature: Paul J Mastradone
Date:

7.0 CONCLUSIONS:

7.1 The aerobic and anaerobic aquatic metabolism studies on metolachlor are scientifically valid and will satisfy the requirement for an aerobic and anaerobic aquatic metabolism study as required under subdivision N of the Guidelines.

Based on the results of the study, EFGWB concludes that in microbiologically active sediment and water, the majority of the dose of metolachlor moved from the water to the sediment. The half-life of metolachlor in a flooded sandy loam sediment under aerobic and anaerobic conditions was 47 days and 78 days respectively.

Results of the study confirmed that metolachlor will metabolize in aquatic environments into several minor metabolites and these were identified as CGA-50720, CGA-51202, CGA-40919, CGA-40172,, CGA-46127, and CGA-41507. It was proposed that the metabolism was by hydrolysis of the methyl ether as the major pathway and by dechlorination with a subsequent substitution by a hydroxy or thio-methyl group.

7.2 EFGWB concludes that the laboratory studies of pesticide accumulation in fish (165-4) submitted is scientifically valid and satisfies the requirement for which the study was submitted.

Results of the study indicate that there is some bioconcentration of metolachlor in the edible tissues (15X), non-edible tissues (155X), and in the whole body of bluegill (69X) during the exposure period. Metolachlor was eliminated 70%, 96%, and 93%, respectively, from the edible, non-edible, and whole fish tissues by day 14 of the depuration period.

7.3 The registrant requested a time extension for completing the fish study. However, the completed report on fish accumulation studies has been received. No further extension is necessary for EFGWD # 90368. See report on EFGWB # 90718, MRID # 411542-01.

8.0 RECOMMENDATIONS:

8.1 The data required for aerobic and anaerobic aquatic metabolism studies under subdivision N of the Guidelines that has been submitted is acceptable and this data requirement is satisfied.

8.2 The data required for laboratory studies of pesticide accumulation in fish (165-4) that has been submitted is acceptable and this data requirement is satisfied.

8.3 The request for an additional extension, EFGWB # 90368, on fish accumulation studies is not necessary as it has been sent and the review is included.

9.0 BACKGROUND:

Registration Division has requested EFGWB review the aerobic and anaerobic aquatic metabolism studies on metolachlor,and the laboratory study of pesticide accumulation in fish (165-4) data which CIBA-GEIGY has submitted in response to the Metolachlor Registration Standard.

10.0 DISCUSSION OF INDIVIDUAL STUDIES:

See attached DER

11.0 COMPLETION OF ONE-LINER:

One-liner updated

12.0 CBI APPENDIX:

CIBA-GEIGY makes no claim of confidentiality for the submitted study.

DATA EVALUATION RECORD

STUDY IDENTIFICATION:

Spare, W.C.1989. Aerobic and Anaerobic Aquatic Metabolism of Metolachlor. Agrisearch Incorporated Agrisearch Project No. 1259 for CIBA-GEIGY. MRID No. 411857-01.

TYPE OF STUDY:

Aerobic and Anaerobic Aquatic Metabolism study on metolachlor to determine the rate and pattern of metolachlor metabolism.

REVIEWED BY:

George Tompkins, Entomologist
Review Section 1, EFGWB, EFED

Signature: George Tompkins
Date: 30 Nov 1989

APPROVED BY:

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

Signature: Paul J Mastradone
Date: NOV 30

CONCLUSIONS:

The aerobic and anaerobic aquatic metabolism study on metolachlor is scientifically valid and will satisfy the requirement under Subdivision N of the Guidelines.

Based on the results of the study, EFGWB concludes that in microbiologically active sediment and water, the majority of the dose of metolachlor moved from the water to the sediment. The half-life of metolachlor was 47 days in a flooded sandy loam sediment under aerobic conditions,and the rate constant was 1.49×10^{-2} $days^{-1}$. Under anaerobic conditions the half life of metolachlor was 78 days and the rate constant was 8.85×10^{-3} $days^{-1}$.

Results of the study confirmed that metolachlor will metabolize in aquatic environments into several minor metabolites and these were identified. See Reported Results section for complete description of the metabolites formed. It was proposed that the metabolism was by hydrolysis of the methyl ether as the major pathway and by dechlorination with a subsequent substitution by a hydroxy or thio-methyl group.

MATERIALS AND METHODS:

A 97.3% pure sample of [U-Ring-^{14}C]-Metolachlor (CGA-24705)(See Figure 1 for position of radiolabels) with a specific activity of 26.2 uCi/mg was used in the aerobic and anaerobic aquatic

metabolism studies to determine the rate and pattern of metolachlor metabolism. Twelve analytical standards were used to monitor the metabolism(Table 1). The sediment used was obtained from Skunk Creek in Sioux Falls, South Dakota. The sediment was characterized as a sandy loam texture composed of 69.6% sand, 21.6% silt, 8.8% clay; a pH of 7.7 and a cation exchange capacity (meq/100g) of 14.4, and having 1.5% organic matter and 14.63% field capacity. The river water had a total alkalinity of 150, a total hardness of 440, a total suspended solids (mg/l) of 8, and a pH of 8.3.

Each test system consisted of a foil-covered 100 ml Erlenmeyer flask, stoppered with polyurethane foam plugs (aerobic) or Teflon coated rubber stoppers (anaerobic). For the assessment of $^{14}CO_2$ evolution, two flasks for each incubation (designated as day 30 for aerobic samples, 6 months for the sterile samples and 12 months for the anaerobic samples) were connected to a series of four traps (Figure 2). The anaerobic and sterile samples were aerated by using compressed nitrogen and the aerobic samples were aerated with compressed breathing air. The gases were bubbled through water before entering the flasks under positive pressure. The compressed nitrogen source for the sterile incubations was purified by bacterial filters prior to entering the flasks. All systems were maintained in a controlled temperature laboratory incubator at $25\pm1^{\circ}C$.

The ^{14}C-metolachlor was dissolved in 5 ml acetone. For sterile incubation, 200 ml of sterile river water was dosed with 65 ul of dosing stock. For aerobic and anaerobic incubations, 1400 ml of river water was dosed as one batch with 455 ul of the dose stock solution. Zero time analysis was performed directly on dosed water. The final actual dose was 11.3 ppm. To each flask containing 25 g (dry weight) of sandy loam sediment, 50 ml of dosed river water was added. A total of 32 separate flasks were used in these tests. The individual flasks provided for 9 anaerobic, 5 aerobic, and 2 sterile sampling periods with 2 replicate flasks per sampling. The sterile incubation flasks were prepared as for the anaerobic incubations, autoclaved, and 50 ml of sterile river water dosed with metolachlor was added as was for anaerobic incubation. The flasks were then covered with aluminum foil and incubated anaerobically at $25\pm1^{\circ}$ C.

Zero time sampling involved analysis of dosed sterile and microbiologically active water. Prepared anaerobic test systems were removed from incubation at 1,3,7, and 14 days and 1,2,3,6,9, and 12 months. Aerobic flasks were sampled and analyzed at the same frequency through the one month sampling. Sterile flasks were sampled and analyzed at 29 days and 6 months. At each sampling, two replicate test systems were removed and subjected to analysis for non-volatile metabolite characterization as well sediment bound residues and parent decline. Trapping solutions from designated incubations were collected and analyzed for $^{14}CO_2$ evolution and volatile metabolite production.

Measurements of ^{14}C-radioactivity were made by a liquid scintillation counter(LSC). Sediment samples were oxidized and the resulting $^{14}CO_2$ collected in carbon-14 CO_2 trapping cocktail and counted. Confirmation of the products from aquatic metabolism were made by two dimensional thin layer chromatography (TLC), gas chromatography (GC) and mass spectroscopy (MS).

REPORTED RESULTS:

The results of microbiological plating on the test sediment and water at zero time, 29 days, 6 months, and 12 months to determine the presence of aerobic and anaerobic populations showed viable microbial populations in the aquatic water and sediment during the study (Table III). Radioactivity balance during the study averaged 101.6, 102.1 and 94.2% for anaerobic, aerobic, and sterile samples, respectively (Tables IV,V).

The relative retention times of metolachlor and standards as determined by TLC in two solvent systems are presented in Table VI. Calculated half lives and rate constants for anaerobic ($t_{1/2}$ = 78 days; k= 8.85 x 10^{-3}) and aerobic ($t_{1/2}$ = 47 days; k= 1.49 x 10^{-2}) aquatic treatments of metolachlor were different (Tables XV and XVI).

Single dimension TLC showed a low level production of several metolachlor metabolites (Table XVII and XVIII). Those products were at low levels for anaerobic incubation attaining a maximum 3-6% of dose at 29 days. Under anaerobic conditions products separated by TLC attained maximum levels at 89 to 270 days and these products were CGA-50720 and CGA-37735 at 7 to 18% of dose. Two dimensional TLC (Table XIX, Figures 9 and 10) confirmed metolachlor concentration at the final aerobic and anaerobic samplings.

Gas chromatography (Table XX, Figures 11 to 14) provided characterization of metabolites. Aerobic water contained low levels of unknown B and CGA-51202, as well as metolachlor. Aerobic sediment showed metolachlor, unknown B, unknown A, CGA-50720, and CGA-40172. Anaerobic waters showed a steady decline in metolachlor with a low detection of CGA-40172, CGA-37913, and unknowns A and B. Anaerobic sediment was similar with a decline in metolachlor, low detection of CGA-40172, CGA-37913, CGA-50720, CGA-40919, and increased detection of unknown A and B.

Mass spectroscopy, performed on the same samples as analyzed by gas chromatography confirmed the identities of unknowns A and B as CGA-46127 and CGA-41507, respectively (Appendix C, Figures 1 to 9).

A pathway proposed by the authors for aquatic metabolism of metolachlor is detailed in Figures 15 and 1. The metabolism followed a major pathway involving hydrolysis of the methyl-ether

and a minor pathway involving a substitution of the chlorine by a hydroxy or a thio-methyl group followed by additional oxidation.

DISCUSSION:

1. The aerobic and anaerobic aquatic metabolism study on metachlor is scientifically sound and will satisfy the requirements for this study as required under Subdivision N of the Guidelines.

2. Based on the results of the study it can be concluded, that in microbiologically active sediment and water, the majority of the dose of metolachlor moved from the water to the sediment. A decline in the percent dose in the water occurred with a corresponding increase in the percent dose in the sediment. Metolachlor had a half-life of 47 days under aerobic conditions with a flooded sandy loam sediment and a rate constant of 1.49×10^{-2} $days^{-1}$. The half-life of metolachlor under anaerobic conditions was 78 days and the rate constant was 8.85×10^{-3} $days^{-1}$.

3. Characterization data of the products from aquatic metabolism of metolachlor by two dimensional TLC, GC, and MS confirmed metolachlor and several minor metabolites. Based on the results, the authors concluded that metolachlor will metabolize in aquatic environments. The metabolism was by hydrolysis of the methyl ether as the major pathway and by dechlorination with a subsequent substitution by a hydroxy or thio-methyl group.

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Pages 9 through 38 are not included.

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DATA EVALUATION RECORD

STUDY IDENTIFICATION:

Fackler,P.H. 1989. Bioconcentration and Elimination of 14C Residues by Bluegill (Lepomis macrochirus) Exposed to Metolachlor. Springborn Life Sciences, Inc., Laboratory Report Number 87-9-2505 for CIBA-GEIGY. MRID No. 411542-01.

TYPE OF STUDY:

Laboratory study to determine the pesticide accumulation in fish for metolachlor.

REVIEWED BY:

George Tompkins, Entomologist
Review Section 1, EFGWB, EFED

Signature: George Tompkins
Date: 30 Nov. 1989

APPROVED BY:

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

Signature: Paul J Mastradone
Date: NOV 30 1989

CONCLUSIONS:

EFGWB concludes that the submitted study on bioconcentration and elimination of residues by bluegill exposed to metolachlor is scientifically valid and fulfills the data requirement for laboratory studies of pesticide accumulation in fish (165-4).

The results of the study demonstrated a mean equilibrium bioconcentration factor for ^{14}C-Metolachlor of 15X in the edible tissue, 155X in the non-edible tissue, and 69X in the whole body of bluegill fish. Continuous elimination of ^{14}C-residues occurred in the selected tissue portions of bluegill during the depuration period. Metolachlor was eliminated 70%,96% and 93% respectively from the edible, non-edible, and whole fish tissues by day 14 of the depuration period.

Metolachlor metabolizes into several metabolites, which were identified in bluegill fish at levels above 0.05 ppm. Parent metolachlor accounted for 18.0% of the total ^{14}C found in the edible portion, CGA-41638 accounted for 1.5%, glucuronide conjugates of CGA-41638 accounted for 2.2% and the glucuronide conjugate of hydroxy-parent accounted for 2.9% of total ^{14}C. In the viscera, parent metolachlor accounted for 3.2% of total ^{14}C, CGA-41638 accounted for 5.0%, and numerous other metabolites were also present.

MATERIALS AND METHODS:

This study was done in two separate parts. The first study utilized radiolabeled [U-ring-^{14}C] metolachlor (radiopurity of 97.3%, a total of 1.57 mCi) and nonradiolabeled metolachlor that contained 97.8% a.i. A stock solution of 10.714 mg/ml (a.i.) was prepared by adding 5.477 g of nonradiolabeled metolachlor to acetone, and adding 0.06 g of 14C-Metolachlor. The theoretical specific activity of this stock was 58164 dpm/ug for ^{14}C-Metolachlor with an actual measured specific activity of ^{14}C-Metolachlor of 62962 dpm/ug(±141), 108% of theoretical.

The treatment and control aquarium each contained 75 L of water and to each aquarium 225 juvenile bluegill with a mean wet weight of 2.1 g were added. The water which flowed into the tank was characterized as having total hardness and alkalinity ranges as calcium carbonate of 30-38 mg/L and 29-32 mg/L, respectively, and a specific conductance range of 110-120 micromhas per centimeter (umhos/cm). The pH of the water was 6.8 and the temperature was maintained at 17±1° C. A chemical introduction system delivered 0.014 ml of a 10.714 mg/ml (a.i.) ^{14}C-Metolachlor stock solution to the treatment aquarium with each cycling of the diluter.

The fish were initially fed a dry pelleted food equal to 2% of the mean organism body weight. This was modified later to feeding fish only as much food as they could consume in 15 minutes to avoid the problem of unconsumed food. The exposure of bluegill to ^{14}C-Metolachlor at a concentration of 0.10 mg/L was continuous for 28 days or until a steady-state tissue residue concentration was established. After 28 days exposure, approximately 35 of the remaining fish in the treatment aquarium were transferred to a clean aquarium into which uncontaminated dilution water was introduced at a rate equal to the flow rate during exposure. Nineteen fish were removed from the treatment aquarium for metabolite characterization and 25 fish for methanol/hexane extraction. The remaining fish in the treatment aquarium were maintained for an additional 7 days to provide fish for a second metabolite charaterization. The depuration period continued for 14 days to estimate the half-life.

To monitor the concentration of ^{14}C-residues in water of the ^{14}C-Metolachlor treatment aquarium, water samples were collected on days 1 and 2 of equilibrium and days 0,1,3,7,10,14,21, and 28 of exposure and on days 1,3,7,10, and 14 of depuration. Water in the control aquarium was sampled on days 1 and 2 of equilibration and days 0 and 28 of exposure and day 14 of depuration.

In order to quantitate the accumulation and elimination of ^{14}C-residues in the edible and non-edible tissue of bluegill, five fish were collected from the treatment aquarium, eviscerated and filleted on days 1,3,7,10,14,21, and 28 of exposure and on days 1,3,7,10, and 14 of depuration. Five control fish were removed,

eviscerated and filleted on day 0 and 28 of exposure and on day 14 of depuration to quantitate background ^{14}C-residues as metolachlor in fish tissue.

The ^{14}C-activity of the water samples was measured by liquid scintillation counting(LSC) and recording the number of disintegrations per minute(dpm). The respective tissue portions from the five fish at each sampling interval were individually wet weighed in pre-tared Combusto- Cones. Each sample was then air-dried for approximately 24 hours and then combusted. The resulting $^{14}CO_2$ was trapped as a carbonate salt in a mixture of Carbasorb (a basic amine) and scintillation fluid and each vial then placed in a liquid scintillation spectrometer and the dpm determined.

The second study, to characterize the metabolites of ^{14}C-Metolachlor in the tissues of exposed bluegill, was performed to generate sufficient tissue for metabolite identification and was reported in Appendices II,III,and IV of the report. Radiolabeled [U-ring^{14}C] Metolachlor (specific activity= 22.7 uCi/mg) at a concentration of 1.0 mg/L was continuously exposed to bluegill sunfish for 33 days to expose a sufficient amount of fish to allow for purification, identification and determination of the relative distribution of metabolites in the tissue.

The well water flowing into the holding tank of the bluegill was characterized as having total hardness and alkalinity ranges of 27-38 mg/L $CaCO_3$ and 22-25 mg/L $CaCO_3$ respectively, and a specific conductance range of 100-140 umhos/cm; a dissolved oxygen concentration of 83-86% of saturation and a flow rate of 7.6-8.8 tank volume replacements per day. The temperature ranged from 17-18° C. During the test exposure these water quality parameters were maintained.

The nominal concentration for the exposure was selected to be 1.0 mg/L Metolachlor based on the acute toxicity of Metolachlor to bluegill and previous bioconcentration studies. This concentration was approximately 1/10 the 96 hour acute LC_{50} for bluegill, and allowed for the maximum accumulation of metabolite residues in tissue.

Initially 620 bluegill were placed in the test tank and an attempt was made to feed the fish commercial fish feed at the rate of 2% of their biomass, but excess food clouded the water. From day 6-33 fish were fed fish food twice daily; the amount they would consume in 10-15 minutes, up to a maximum of 2% of their biomass. A photoperiod of 16 hours light and 8 hours darkness was maintained by ambient laboratory lighting.

After exposure of bluegill to metolachlor at a concentration of 1.0 mg/L continuously for 33 days all fish were removed and dissected into 3 tissue portions (fillets, viscera, carcass). To monitor the concentration of ^{14}C-residues in the exposure solution, three 5 ml water samples were collected once during the equilibration period and on days 0,7,14,21,28 and 33 during the exposure. Each

5 ml sample was removed by pipette from midpoint of the exposure tank and transferred into glass scintillation vials for LSC.

Samples of edible tissue, non-edible tissue and carcass were analyzed to determine the metabolites in bluegill sunfish after 33 days continuous exposure to metolachlor. Metolachlor and CGA-41638 standards were dissolved in methanol to a concentration of 1 ug/ul and used for HPLC, thermospray HPLC/MS, EI/MS, and CI/MS analyses. The schemes for the extraction of radioactivity from edible and non-edible tissues are shown in Figures 2 and 3.

REPORTED RESULTS:

The results of the study indicate that there was a mean equilibrium bioconcentration factor for ^{14}C-Metolachlor of 15X in the edible tissue, 155X in the non-edible tissue and 69X in the whole body of bluegill during the 28 days of exposure (Table 3). The percentage extractibility of the ^{14}C-residue accumulated in the edible tissue of bluegill exposed to metolachlor was 13% with hexane, 23% with methanol and approximately 63% non-extractable with either solvent.

During the depuration period continuous elimination of ^{14}C-residues occurred from the selected tissue portions of bluegill and on a whole fish basis. Half-life of the ^{14}C-residues present in the non-edible tissue and whole body portions of bluegill on the last day of exposure occurred during the first twenty-four hours of depuration, and between day 1 and day 3 for the ^{14}C-residues in the edible tissue portion (Fig. 1,2,3). By day 14 of the depuration period, the ^{14}C-residues present on the last day of exposure in the edible, non-edible and whole fish tissues had been eliminated by 70%, 96%, and 93%, respectively.

The residue concentrations present in the bluegill tissue after 28 days exposure to metolachlor were 1.4 ppm in the edible, 16 ppm in the non-edible and 7.2 ppm in the whole body (Table 3). This exceeds the 0.05 ppm specified in the EPA guideline (165-4) and a second study was initiated to characterize and identify the metabolites since insufficient amounts of radioactivity were present in the first study.

The results of the metabolite study indicate that the radioactive levels in the edible tissue of fish exposed to 1.0 mg/L of ^{14}C-metolachlor for 33 days was 13.9 ppm and in the viscera 220-250 ppm equivalents to ^{14}C-metolachlor. Grouping of the metabolites identified by HPLC and quantification yielded numerous metabololites in excess of 0.05 ppm. These metabolites were further characterized by mass spectroscopy identification (Fig. 47-65), and quantitation of the metabolites in excess of 0.05 ppm are listed in Tables IV and V. The authors proposed that the metabolic pathway includes demethylation of the methoxy group at the N-alkyl substituent, hydroxylation of the aromatic alkyl group followed by extensive glucuronide conjugation and reductive dechlorination with subsequent glutathione conjugation (Fig. 66). Demethylation and hydroxylation appeared to be the major metabolic pathway.

DISCUSSION:

1. EFGWB concludes that the submitted studies on bioconcentration and elimination of ^{14}C-residues by bluegill exposed to metolachlor satisfy the requirements for laboratory studies of pesticide accumulation in fish (165-4).

2. EFGWB concludes that from the results of the studies submitted metolachlor was bioconcentrated 15X in the edible tissue, 155X in the non-edible tissue, and 69X in the whole body of bluegill during the exposure period. Metolachlor was eliminated 70%,96% and 93% respectively from the edible, non-edible, and whole fish tissues, by day 14 of the depuration period.

3. Parent metolachlor accounted for 18.0% of the total ^{14}C found in the edible portion, CGA-41638 accounted for 1.5%, glucuronide conjugate of CGA-41638 accounted for 2.2% and the glucuronide conjugate of OH-parent accounted for 2.9% of total ^{14}C (Table IV). In the viscera parent metolachlor accounted for 3.2% of the total ^{14}C, CGA-41638 accounted for 5.0%, and numerous other metabolites were also present (Table V).

4. EFGWB notes that the write up of the study with accompanying tables and figures is not well organized for efficient review.

5. Also, the registrant should be informed that future studies should be properly edited. Several editing mistakes were not corrected, i.e., in the materials and methods (page 98) and results and discussion (p 107) it is mentioned that 35 days exposure occurred, although the second study was run for 33 days (p80). In the Table of Contents (p89) no page numbers were listed although a column headed by page numbers is listed and the summary in the test was deleted, yet appeared in the table of contents. These inconsistencies, however, did not affect the results or conclusions, but do make it difficult to review the study.

11/30/89 EFED Memo — Metolachlor

Page____ is not included in this copy.

Pages 44 through 75 are not included.

The material not included contains the following type of information:

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