PC 700099

Data Evaluation Report on the aerobic biotransformation of safener of clodinafop-propargyl in soil

PMRA Submission Number {......} EPA MRID Number 46012929

Data Requirement: PMRA Data Code:
EPA DP Barcode: D215199
OECD Data Point:
EPA Guideline: 162-1

Test material:

Common name:	Cloquintocet-mexyl (Safener of clodinafop-propargyl).
Chemical name	
IUPAC:	5-Chloro-8-quinolinoxyacetic acid-1-methylhexylester.
CAS name:	1-Methylhexyl ester [(5-chloro-8-quinolinyl)oxy]-acetic acid.
CAS No:	99607-70-2
Synonyms:	CGA 185072.
SMILES string:	Clc1ccc(c2c1cccn2)OCC(=O)OC(CCCCC)C.

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CITATION: Ellgehausen, H. 2001. Rate of degradation of ^{14}C-quinolin CGA-185072 in two soils and availability of bound residues. Unpublished study performed by Syngenta Ag, Basel, Switzerland and submitted by Syngenta Crop Protection, Inc. Greensboro, NC. Study ID. 00EH01. Experiment start date August 21, 2000, and completion date November 29, 2000 (p. 8). Final report issued February 14, 2001.

EXECUTIVE SUMMARY

The biotransformation of [3-^{14}C]5-chloro-8-quinolinoxyacetic acid-1-methylhexylester (cloquintocet-mexyl; used as a safener with clodinafop-propargyl; radiochemical purity 99-100%) was studied in a silt loam soil (pH 7.2, organic carbon 2.35%) and a loamy sand soil (pH 7.5, organic carbon 1.0%) both from Switzerland for 56 days under aerobic conditions in darkness at 20 ± 0.1°C and a soil moisture of 40% of field moisture capacity. Cloquintocet-mexyl was applied at a nominal rate of 0.1 mg a.i./kg, reported to be equivalent to 65 g a.i./ha. This experiment was conducted in accordance with Commission Directive 95/36/EC Guidelines and in compliance with Swiss GLP Standards. The test system consisted of Erlenmeyer flasks (300 mL) containing treated soil (75 g) that were connected to a flow-through volatile trapping system consisting of two 2N NaOH traps and were incubated in a dark environmental chamber. Duplicate bottles were collected after 0, 0.21, 1, 3, 7, 14, 28 and 56 days of incubation. Soil samples were extracted with acetone:pH 4.65 buffer or acetone:water (80:20, v:v) by shaking at ambient temperature, followed by Soxhlet-extraction with acetone. Samples collected at the final sampling interval were further extracted by refluxing with acetonitrile:water (4:1, v:v) followed by acetonitrile:HCl (9:1, v:v). Soil extracts and extracted soil were analyzed for total radioactivity using LSC; the method of analysis for the NaOH was not reported.. The acetonitrile soil extracts were analyzed for [^{14}C]cloquintocet-mexyl and its transformation products by HPLC and TLC, and identified by comparison to the retention time of reference standards.

Test conditions specified in the study appear to have been maintained throughout the study.

Overall recoveries of [^{14}C]residues averaged 98.75 ± 0.90% (mean data range 97.76-100.49) of the applied in the loamy sand soil and 98.97 ± 0.64 (mean data range 97.95-99.86%) in the silt loam soil. There was no pattern of decline in either of the material balances during the study.

In the loamy sand soil, [^{14}C]cloquintocet-mexyl decreased from an average 98.90% of the applied at 0 days posttreatment to 41.62% at 0.21 days, 11.20% at 1 day and 5.33% at 56 days (study termination). The only major transformation product was CGA 153433 {[(5-chloro-8-quinolinyl)oxy]-acetic acid}, which averaged a maximum of 32.92% of the applied at 1 day posttreatment and decreased to 0.48-0.84% at 14-56 days. No minor transformation products were identified. Six unidentified HPLC peaks were each $\leq$5.05% of the applied. Extractable [^{14}C]residues decreased from an average 98.90% of the applied at 0 days posttreatment to 65.83% at 0.21 days and 8.24% at 56 days, while nonextractable [^{14}C]residues increased to 33.47% at 0.21 days and 84.69% at 56 days. At study termination, [^{14}C]residues trapped in the NaOH solution totaled 5.69% of the applied.

In the silt loam soil, [^{14}C]cloquintocet-mexyl decreased from an average 98.16% of the applied at 0 days posttreatment to 23.69% at 0.21 days, 9.26% at 1 day and 1.97% at 56 days. The only major transformation product was CGA 153433, which averaged a maximum of 19.30% of the applied at 0.21 day posttreatment and decreased to 5.18% at 14 days and 1.40% at 56 days. No minor transformation products were identified. Six unidentified HPLC peaks were each $\leq$3.84% of the applied. Extractable [^{14}C]residues decreased from an average 98.16% of the applied at 0 days posttreatment to 43.32% at 0.21 days and 5.49% at 56 days, while nonextractable [^{14}C]residues increased to 56.40% at 0.21 days and 82.63% at 14 days and were 79.44% at 56 days. At study termination, [^{14}C]residues trapped in the NaOH solution totaled 13.01% of the applied.

The observed DT50 for cloquintocet-mexyl was <5 hours; a valid half-life could not be calculated using first-order linear regression analysis. Using nonlinear regression analysis (two-compartment model), the study author determined a DT50 of 0.2 days in both soils for cloquintocet-mexyl and DT50s of 5.5 and 9.7 days for the transformation product CGA 153443 in the loamy sand and silt loam soils, respectively.

A transformation pathway was proposed by the study author. Cloquintocet-mexyl degrades via cleavage of the ester bond to CGA 153433. This compound in turn degrades to unidentified minor compounds which are incorporated into the organic material and mineralized to CO_2.

To determine the potential of the bound residues to leach, a study was performed using the treated aged soils (56 days posttreatment) that were subject to exhaustive extraction. Portions of the extracted soils were applied to the top of silt loam or loamy sand columns (30-cm length, 4-cm diameter). The columns were leached with 251 mL of deionized water (equivalent to 200 mm of rainfall). The leachate was analyzed by LSC and 2-cm soil column segment were analyzed by LSC following combustion. Overall recoveries of [^{14}C]residues from the loamy sand and silt loam soil columns totaled 98.52-98.94% of the bound residues that had been applied to the columns. [^{14}C]Residues were 93.49-93.62% of the applied in the top 2 cm (the treatment layer), 2.56-3.54% in the 2-4 cm section, and $\leq$0.87% in each of the 2-cm sections below the top two layers. In the leachate, [^{14}C]residues were 0.14-0.34% of the applied.

Results Synopsis:

Soil type: Pappelacker loamy sand.
DT50: <5 hours (observed).
Major transformation products:
  CGA 153433 {[(5-chloro-8-quinolinyl)oxy]-acetic acid}.
Minor identified transformation products:
  CO_2.

Soil type: Gartenacker silt loam.
DT50: <5 hours (observed).
Major transformation products:
  CGA 153433.
  CO_2.
Minor identified transformation products:
  None.

Study Acceptability: This study is classified as **unacceptable (upgradable)**. It cannot be used to meet the requirement for an aerobic soil metabolism study at this time because it was not reported whether the samples were stored prior to extraction and analysis. Also, the study cannot be used to fulfill data requirements because the test was conducted with the safener of clodinafop-propargyl rather than the parent and because

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was conducted in accordance with the Commission Directive 95/36/EC amending Council Directive 91/414/EEC (p. 8). One significant deviation from USEPA Subdivision N guidelines was noted:

> It was not reported whether the samples were stored prior to extraction and analysis. This does affect the validity of the study.
>
> The study was conducted with the safener of clodinafop-propargyl rather than the parent. This does not affect the validity of the study.

COMPLIANCE: This study was conducted in compliance with Swiss GLP Standards (pp. 3, 5). Signed and dated Data Confidentiality, GLP, Quality Assurance and Certification of Authenticity statements were provided (pp. 2, 3, 5-7).

A. MATERIALS:

1. Test Material:	[3-^{14}C]Cloquintocet-mexyl (safener of clodinafop-propargyl; p. 16).
Chemical Structure:	See DER Attachment 2.
Description:	White powder (p. 16).
Purity:	Radiochemical purity: 99-100% (p. 28). Batch No.: GAN-XLV-42-1 (p. 17). Analytical purity: 98.7% Specific activity: 2.04 MBq/mg (55.14 µCi/mg). Location of the radiolabel: 3-Carbon of the quinoline ring.
Storage conditions of test chemicals:	Between 0 and 5°C in the dark (p. 17).

Table 1: Physico-chemical properties of cloquintocet-mexyl.

Parameter	Values	Comments
Molecular weight:	335.83 g/mole	
Molecular formula:	$C_{18}H_{22}ClNO_3$	
Water solubility:	590 μg/L	At 25°C.
Vapor pressure/volatility (Pa):	5.31×10^{-6} Pa	At 25°C.
UV absorption:	Not reported.	
pK_a:	3.5-4	Basic
Log P_{ow}:	5.03	At 25°C.
Stability of compound at room temperature:	Not reported.	

Data obtained from pp. 16-17 of the study report.

2. Soil Characteristics:

Table 2: Description of soil collection and storage.

Description	Pappelacker loamy sand	Gartenacker silt loam
Geographic location:	Les Barges, Vouvry, Switzerland	
Pesticide use history at the collection site:	Not reported.	
Collection date:	The "batch no." for both soils was reported to be May 2000.	
Collection procedures:	Not reported.	
Sampling depth:	Not reported.	
Storage conditions:	Soils were stored at 4°C.	
Storage length:	Stored <4 months, if the "batch no." refers to the collection date.	
Preparation:	The soils were sieved (2 mm).	

Data obtained from p. 18, Table 2, p. 32 of the study report.

Table 3: Properties of the soil.

Property	**Pappelacker loamy sand**	**Gartenacker silt loam**
Soil texture [1]:	Loamy sand	Silt loam
% sand:	71.5	38.18
% silt:	22.1	50.46
% clay:	6.5	11.36
pH (KCl)	7.5	7.2
Organic carbon (%):	1.0	2.35
CEC (meq/100 g):	6.2	15.7
Moisture content (g water/100 g):	44.1	67.9
Moisture content (%) at 1/3 bar:	Not reported.	
Bulk density (disturbed; g/cm^3):	1.26	0.95
Soil Taxonomic classification:	Not reported.	
Soil Mapping Unit:	Not reported.	

Data obtained from Table 2, p. 32 of the study report.

[1] The range of particle sizes defining sand, silt, and clay was not reported. The soil was characterized in Switzerland, and therefore the particle size distribution may not be equivalent to that used by the USDA Soil Classification System.

B. EXPERIMENTAL CONDITIONS:

1. Preliminary experiments: No preliminary studies were described.

2. Experimental conditions:

Table 4: Study design.

Criteria		**Pappelacker loamy sand**	**Gartenacker silt loam**
Duration of the test		56 days.	
Soil condition (air dried/fresh):		Fresh.	
Soil (g/replicate)		75 g dry wt equivalent.	
Test concentrations (mg a.i./kg soil and equivalent g a.i./ha):		0.102 mg a.i./kg dry soil; equivalent to 0.049 kg a.i./ha.	0.102 mg a.i./kg dry soil; equivalent to 0.065 kg a.i./ha.
Control conditions, if used		Sterile controls were not used.	
No. of Replications:	Controls	Sterile controls were not used.	
	Treatments	Duplicate samples were collected at each interval.	
Test apparatus (Type/material/volume):		Erlenmeyer flasks (300 mL) containing treated moistened soil (75 g dry wt equivalent) were attached to individual volatile trapping systems via inlet/outlet ports in the flask cap. The flasks were maintained in a dark environmental chamber. The test apparatus is illustrated in Figure 1, p. 39.	
Details of traps for CO_2 and organic volatiles, if any:		Humidified air was continuously drawn (*ca.* 50 mL/min) through individual flasks, then through two tubes of 2N NaOH.	
If no traps were used, is the system closed/open?		Volatile traps were used.	
Identity and concentration of co-solvent:		Acetone, *ca.* 0.5% by volume.	
Test material application:	Vol. of test solution used/treatment:	371 µL/75 g	
	Application method:	Applied to the soil surface dropwise via Hamilton syringe, then the soils were "carefully mixed".	
	Co-solvent evaporated:	Not reported.	
Any indication of the test material adsorbing to the walls of the test apparatus?		None.	
Microbial biomass of the control:		Sterile controls were not used.	
Microbial biomass of soil treated with acetone: (mg C/kg)	Initial	29.4	65.3
	56 days	22.6	55.9

Criteria		**Pappelacker loamy sand**	**Gartenacker silt loam**
Microbial biomass of the treated soil: (mg C/kg)		Not analyzed.	
Experimental conditions:	Temperature (°C):	20 ± 0.1°C	
	Moisture content (%):	40% of maximum water holding capacity	
	Moisture maintenance method:	Flasks were weighed every 1-2 weeks and remoistened if necessary.	
	Continuous darkness:	Yes	
Other details, if any:		None.	

Data obtained from pp. 18, 19, 20, 32; Table 2, p. 32, Figure 1, p. 39 of the study report.

3. Aerobic conditions: Humidified air was continuously drawn (*ca.* 50 mL/min) through the flasks containing the treated soil (p. 18; Figure 1, p. 39). No determinations such as redox potentials were made to verify that aerobic conditions were maintained in the soil.

4. Supplementary experiments: To determine if bound residues of cloquintocet-mexyl were likely to leach, the extracted soils from the definitive metabolism study were applied to the top of silt loam or loamy sand columns (30-cm length, 4-cm diameter; p. 23, Figure 3, p. 41). It was estimated that the residues (2-cm depth) were applied at a rate of 0.08 mg a.i./kg, which was equivalent to 0.04-0.05 kg a.i./ha. The upper surface of the columns were covered with filter disks of sintered glass, then the columns were leached with 251 mL of deionized water (equivalent to 200 mm of rainfall). Following leaching, leachate samples were collected in two fractions and the soil columns were divided into 15 sections of approximately 2 cm each. The leachate was analyzed by LSC and the soil was analyzed by LSC following combustion (p. 24).

5. Sampling:

Table 5: Sampling details.

Criteria	**Pappelacker loamy sand**	**Gartenacker silt loam**
Sampling intervals:	0, 0.21, 1, 3, 7, 14, 28 and 56 days.	
Sampling method:	Duplicate samples were collected at each sampling interval.	
Method of collection of CO_2 and volatile organic compounds:	Trapping solutions were collected at each sampling interval or every two weeks.	
Sampling intervals/times for: Sterility check: Moisture content: Redox potential/other:	 Sterile controls were not used. Flasks were weighed every 1 week during the first month and then 2 weeks until termination Redox potential and other parameters were not measured.	
Sample storage before analysis:	Not reported.	
Other observations, if any:	None.	

Data obtained from p. 20, Table 3, p. 33 of the study report.

C. ANALYTICAL METHODS:

Extraction/clean up/concentration methods: Approximately 50 mL of either acetone:pH 4.65 buffer (80:20, v:v; 0-7 days) or acetone:water (80:20, v:v; 14-56 days) were added to the sample flask, and the soil was extracted at ambient temperatures by 30 minutes of vigorous shaking (300 rpm, (pp. 20-21, Figure 2, p. 40). The mixture was centrifuged (2000 g) and the supernatant decanted; the soil pellet was extracted three additional times as described. The supernatants were analyzed using LSC, then combined and concentrated under reduced pressure. Aliquots of the concentrates were analyzed by HPLC and TLC.

The extracted soil was Soxhlet-extracted for 2-3 hours using acetone. The samples collected at study termination (56 days) were further extracted by refluxing while stirring at 80°C with acetonitrile:water (4:1, v:v) for 4 hours. The samples were centrifuged, the supernatant was decanted through filter paper, and portions of the extract and extracted soil were analyzed using LSC and LSC following combustion. The remaining extracted soil was extracted by refluxing with acetonitrile:0.1N HCL (9:1, v:v) for 2 hours and analyzed as described.

Nonextractable residue determination: The extracted soil was air-dried and homogenized, and portions were analyzed for total radioactivity by LSC following combustion (p. 22).

To separate unextracted [^{14}C]residues into humin, humic acids and fulvic acids fractions in the "harsh extraction" 56-day soil samples, the extracted soils were further extracted by shaking for 17 hours at ambient temperatures with 0.5N NaOH (p. 22). The sample was centrifuged, and the extract was decanted and acidified to pH ≤ 1 using HCl. The resulting precipitate (humic acids) were removed by centrifugation. The supernatant (fulvic acids) was analyzed using LSC. The precipitate pellet (humic acid) was dissolved in 0.5N NaOH and analyzed using LSC. The concentration of [^{14}C]residues remaining in the extracted soil (humins) was determined by subtracting the concentration of extracted residues (fulvic plus humic acids) from the concentration of residues in the soil prior to extraction.

Volatile residue determination: The procedure used to determined the concentration and identity of [^{14}C]residues in the NaOH trapping solution was not reported.

Total ^{14}C measurement: Total [^{14}C]residues were determined by summing the concentrations of residues measured in the soil extracts, extracted soil, and volatile trapping solutions (Table 3, p. 33).

Derivatization method, if used: A derivatization method was not employed.

Identification and quantification of parent compound: Soil extracts were analyzed using HPLC under the following conditions (pp. 25-26): Nucleosil C-18 column (250 cm x 4.6 mm, 5 µm) gradient mobile phase combining (A) water acidified to pH 2.9 with H_3PO_4 (B) acetonitrile [percent A:B at 0.0-7.0 minutes, 30:70; 7.0-9.0 minutes, 5:95; 9.0-16.0 minutes, 5:95, 16.0-17.0 minutes, 30:30, 17.0-20.0 minutes 30:30 (Reviewer's Comment #12)] with a flow rate of 1 mL/minute and UV (226 nm) and radioactive flow detection. [^{14}C]Cloquintocet-mexyl was identified by comparison to the retention time of an unlabeled reference standard (Rt 12.72 minutes).

Also, the soil extracts were analyzed using two-dimensional TLC on silica gel plates developed in methylene chloride:methanol:formic acid (80:15:5, v:v:v, SS1) in the first direction and ethyl acetate:n-hexane (60:30, v:v, SS2) in the second (p. 24). Following development, radioactive areas on the plate were located and quantified using a radioanalytical scanner, and the reference standard was located using UV light (254 nm, Rf 0.94 SS1, 0.82 SS2; p. 25).

Identification and quantification of transformation products: Transformation products were quantified and identified using the HPLC and TLC methods described for the parent. The only references standard used was CGA 153433 (Rt 3.26 minutes, Rf 0.29 SS1, 0.00 SS2; pp. 25-26).

Detection limits (LOD, LOQ) for the parent compound: The Limit of Detection was twice background and the Limit of Quantification was three times background (Appendix C, p. 65).

Detection limits (LOD, LOQ) for transformation products: The LOD and LOQs were the same as for the parent.

II. RESULTS AND DISCUSSION:

A. TEST CONDITIONS: The temperature in the incubation chamber averaged 19.99 ± 0.05°C (Figure 7, p. 45). The soil aerobicity and moisture were reportedly maintained during the experiment; no supporting data were provided for review.

B. MATERIAL BALANCE: The study author provided only averaged data for each sampling interval. Overall recoveries of [^{14}C]residues averaged 98.75 ± 0.90% of the applied (range 97.76-100.49%) in the loamy sand soil and 98.97 ± 0.64% (97.95-99.86%) in the silt loam soil (Table 3, p. 33). There was no significant loss of radioactivity over time with either soil.

Table 6a: Biotransformation of [^{14}C]cloquintocet-mexyl in loamy sand soil, expressed as percentage of applied radioactivity (n = 2), under aerobic conditions.

Compound	Sampling times (days)							
	0	0.21	1	3	7	14	28	56
[^{14}C]Cloquintocet-mexyl (CGA 185072)	98.90	41.62	11.20	8.96	8.05	7.80	10.35	5.33
CGA 153433	0.00	23.93	32.92	21.73	22.59	0.48	0.35	0.84
UK1	0.00	0.00	2.38	0.25	0.00	5.05	0.00	0.80
UK2	0.00	0.00	0.62	0.21	0.29	0.49	0.25	0.37
UK3	0.00	0.00	0.00	0.09	0.07	0.25	0.00	0.00
UK4	0.00	0.00	0.00	0.00	0.00	0.12	0.00	0.00
UK5	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.18
UK6	0.00	0.00	0.00	0.00	0.00	0.00	0.21	0.71
NA*	0.00	0.28	0.23	0.00	0.00	0.00	0.00	0.00
Total extractable residues	98.90	65.83	47.33	31.25	30.99	14.19	11.15	8.24
Nonextractable residues	1.59	33.47	51.91	66.95	66.63	83.08	84.09	84.69
CO_2	0.00	0.00	0.02	0.12	0.31	1.03	2.52	5.69
Volatile organics	Not reported.							
Total % recovery	100.49	99.31	99.27	98.32	97.93	98.31	97.76	98.63

Only mean data were reported by the study author. Data obtained from Table 3, p. 33 and Table 4, p. 34 of the study report.

* NA was not defined by the study author.

Table 6b: Biotransformation of [^{14}C]cloquintocet-mexyl in silt loam soil, expressed as percentage of applied radioactivity (n = 2), under aerobic conditions.

Compound	Sampling times (days)							
	0	0.21	1	3	7	14	28	56
^{14}C]Cloquintocet-mexyl (CGA 185072)	98.16	23.69	9.26	4.10	4.05	3.72	4.44	1.97
CGA 153433	0.00	19.30	15.84	18.41	15.75	5.18	0.98	1.40
UK1	0.00	0.00	0.87	0.33	1.50	3.84	0.20	0.74
UK2	0.00	0.00	1.64	0.12	0.15	0.49	0.62	0.69
UK3	0.00	0.00	0.68	0.00	0.33	0.36	0.00	0.00
UK4	0.00	0.00	0.22	0.00	0.00	0.27	0.00	0.00
UK5	0.00	0.00	0.00	0.00	0.00	0.29	0.24	0.00
UK6	0.00	0.00	0.00	0.00	0.00	0.00	3.67	0.69
NA*	0.00	0.33	0.09	0.00	0.00	0.00	0.00	0.00
Total extractable residues	98.16	43.32	28.60	22.97	22.77	14.15	10.15	5.49
Nonextractable residues	1.70	56.40	70.12	76.26	75.46	82.63	82.50	79.44
CO_2	0.00	0.00	0.01	0.17	0.55	1.89	6.03	13.01
Volatile organics	Not reported.							
Total % recovery	99.86	99.71	98.74	99.40	98.78	98.66	98.69	97.95

Only mean data were reported by the study author. Data obtained from Table 3, p. 33 and Table 4, p. 34 of the study report.

* NA was not defined by the study author.

C. TRANSFORMATION OF PARENT COMPOUND: In the loamy sand soil, [^{14}C]cloquintocet-mexyl decreased from an average 98.90% of the applied at 0 days posttreatment to 41.62% at 0.21 days, 11.20% at 1 day and 5.33% at 56 days (study termination; Table 4, p. 34).

In the silt loam soil, [^{14}C]cloquintocet-mexyl decreased from an average 98.16% of the applied at 0 days posttreatment to 23.69% at 0.21 days, 9.26% at 1 day and 1.97% at 56 days (study termination; Table 4, p. 34).

HALF-LIVES: Because cloquintocet-mexyl degraded very rapidly, so that <55% of the applied remained undegraded after 5 hours (first sampling interval after time 0) in both soils, an accurate half-life could not be calculated using first-order linear regression techniques (see DER Attachment 1). The observed DT50 was <5 hours. An accurate half-life could not be calculated for the transformation product CGA 153443 because the sampling intervals were too few and infrequent during the period of interest; in both soils, >50% of the measured CGA 153443 dissipated between the 7- and 14-day sampling intervals (Table 4, p. 34).

The study author determined that cloquintocet-mexyl degraded with a DT50 of 0.2 days in both soils using a two-compartment model with MicroCal Origin (v. 6.0) software (pp. 26, 27, 29; Table 6, p. 36). The DT50 for the transformation product CGA 153443 was determined to be 5.5 and 9.7 days in the loamy sand and silt loam soils, respectively (p. 29).

Half-life/DT50 values:

Soil	First order Linear			DT50 (days)	DT90 (days)
	Half-life	Regression equation	r^2		
Loamy sand	Not determined; observed DT50 <5 hours.			0.2	1.0
Silt loam	Not determined; observed DT50 <5 hours.			0.2	1.0

DT50 and DT90 values were obtained from Table 6, p. 36 of the study report.

TRANSFORMATION PRODUCTS: The only transformation product identified was CGA 153433, which was a major transformation product in both soils with maximum concentrations at 0.21-1 day posttreatment (Table 4, p. 34). In the loamy sand soil, CGA 153433 averaged a maximum of 32.92% of the applied at 1 day posttreatment and decreased to 0.48-0.84% at 14-56 days. In the silt loam soil, CGA 153433 averaged a maximum of 19.30% of the applied at 0.21 day posttreatment and decreased to 5.18% at 14 days and 1.40% at 56 days. No minor transformation products were identified. In both soils, six unidentified HPLC peaks [UK1 (Rt = 3.35 minutes), UK2 (Rt = 4.15 minutes), UK3 (Rt = 4.53 minutes), UK4 (Rt = 5.12 minutes), UK5 (Rt = 6.70 minutes) and UK6 (Rt not reported)] were each ≤5.05% of the applied.

NONEXTRACTABLE AND EXTRACTABLE RESIDUES: In the loamy sand soil, extractable [^{14}C]residues decreased from an average 98.90% of the applied at 0 days posttreatment to 65.83% at 0.21 days and 8.24% at 56 days, while nonextractable [^{14}C]residues increased to 33.47% at 0.21

days and 84.69% at 56 days (Table 3, p. 33). In extracted 56-day soil samples, 16.6% of the applied was associated with fulvic acids, 6.2% with humic acids, and 52.6% with humins (Table 5, p. 35).

In the silt loam soil, extractable [^{14}C]residues decreased from an average 98.16% of the applied at 0 days posttreatment to 43.32% at 0.21 days and 5.49% at 56 days, while nonextractable [^{14}C]residues increased to 56.40% at 0.21 days and 82.63% at 14 days and were 79.44% at 56 days (Table 3, p. 33). In extracted 56-day soil samples, 13.7% of the applied was associated with fulvic acids, 4.8% with humic acids and 60.6% with humins (Table 5, p. 35).

VOLATILIZATION: At study termination, [^{14}C]residues trapped in the NaOH solution totaled 5.69% of the applied from the loamy sand soil and 13.01% from the silt loam (Table 3, p. 33). These residues were characterized as $^{14}CO_2$ by the study author; no methodology was provided to determine if the identification was definite or assumed. No data were provided on volatile organics were not reported.

TRANSFORMATION PATHWAY: A transformation pathway was proposed by the study author. Cloquintocet-mexyl degrades via cleavage of the ester bond to CGA 153433 (p. 29, Figure 14, p. 52). This compound in turn degrades to unidentified minor compounds which are incorporated into the organic material and mineralized to CO_2.

Table 7: Chemical name for the transformation product of cloquintocet-mexyl.

Applicant's Code	CAS Number	Chemical Name	Chemical formula	Molecular weight (g/mol)	SMILES string
CGA 153433	88349-88-6	[(5-chloro-8-quinolinyl)oxy]-acetic acid			

Data obtained from Appendix 2, Figure 1, p. 298 of MRID 46012939.

D. SUPPLEMENTARY EXPERIMENT-RESULTS: In the column leaching experiment, overall recoveries of [^{14}C]residues from the loamy sand and silt loam soil columns totaled 98.52-98.94% of the bound residues that had been applied to the columns (Table 8, p. 38). [^{14}C]Residues were 93.49-93.62% of the applied in the top 2 cm (the treatment layer), 2.56-3.54% in the 2-4 cm section, and ≤0.87% in each of the 2-cm sections below the top two layers. In the leachate, [^{14}C]residues were 0.14-0.34% of the applied.

III. STUDY DEFICIENCIES:

1. It was not reported whether the samples were analyzed immediately, or were stored prior to extraction and analysis. Because of the apparent rapid degradation of cloquintocet-mexyl and its transformation product, any delay in stabilizing the sample would be expected to have a significant affect on the study results. It was not demonstrated that cloquintocet-mexyl was stable in soil extracts during storage and analysis.

2. Sampling intervals were insufficient to allow the reviewer to calculate an accurate and precise half-life for cloquintocet-mexyl and its transformation product CGA 153433. Cloquintocet-mexyl decreased by approximately 90% of the applied by the third sampling interval, from an average 98.16-98.90% of the applied immediately posttreatment to 23.69-41.62% at 5 hours and approximately 10% at 1 day. The majority of the CGA 153433 detected in the soil degraded between the 7- and 14-day sampling intervals.

3. The study was conducted with a safener of clodinafop-propargyl rather than the parent.

IV. REVIEWER'S COMMENTS:

1. The soils were maintained at 40% of water holding capacity at atmospheric pressure. Since the water holding capacity of the soil at 1/3 bar was not reported, it could not be determined whether they were more or less moist than if they had been maintained at the specified 75% of 1/3 bar. This is not expected to have had a significant effect on the rate or pattern of degradation.

2. The procedure used to determine the concentration and identity of [^{14}C]residues in the NaOH trapping solution was not reported. It is likely that the NaOH solutions were analyzed using LSC. Also, it was not reported if precipitation with barium chloride was used to confirm the identity of CO_2.

3. The chemical name and CAS number for CGA 153433 were not reported in this study; however, its chemical name and CAS number were reported as [(5-chloro-8-quinolinyl)oxy]-acetic acid and 88349-88-6, respectively, in Appendix 2, Figure 1, p. 298 of MRID 46012939 (a clodinafop-propargyl field dissipation study).

4. The concentration of [^{14}C]residues remaining in the extracted soil following organic matter fractionation (humin) was determined by subtracting the concentration of extracted residues (fulvic plus humic acids) from the concentration of residues in the soil prior to extraction, rather than by combustion of the extracted soil. Since the concentration of residues in the soil prior to organic matter fractionation was determined by LSC following combustion, it could not be determined why the concentration of humin was not also measured directly.

5. The range of particle sizes defining sand, silt, and clay was not reported. The soil was characterized in Switzerland, and therefore the particle size distribution may not be equivalent

to that used by the USDA Soil Classification System. Also, information about the source, collection, and storage of the soils was incomplete.

6. Although a significant fraction of the applied [^{14}C]residues were not extracted from the soils (82.63-84.69%), it is not likely that the use of extraction procedures harsher than those used (Soxhlet extraction and refluxing at 80°C) in the study would have been nondestructive.

7. Duplicate samples were collected at each sampling interval, however, the study author reported only averaged data for all sampling intervals. It is preferred that individual sample data be provided for each sampling interval, so that the between-replicate variability can be assessed.

8. The study author stated that extracts were analyzed by HPLC and/or TLC. Although the reviewer described the TLC method present by the study author, it is not clear if TLC was used since no TLC results or chromatograms were provided.

9. The study author lists NA in Table 4 (p. 34). NA was not further described. Also, only chromatograms from time 0 and day 56 were provided for review and NA was reported as 0.00 at those sampling intervals. Therefore, the reviewer could not determine if this was an isolated peak or some other reference.

10. The study author reported that the nominal application rate chosen for this study corresponded to a field application rate of 65 g a.i./ha (p. 17). The rate chosen was 3.25 times the maximum field application rate (20 g a.i./ha) and was chosen for analytical reasons. The study author stated that this was based on the test substance being homogeneously distributed in the top 5 cm of a soil with a bulk density of *ca.* 1.3 g/cm^3 (p. 19).

11. The radiochemical purity of [^{14}C]cloquintocet-mexyl in the treatment solution was determined to be 99-100% via HPLC and 2D-TLC analyses (p. 28; Figures 4-5, pp. 42-43).

12. The IUPAC name of cloquintocet-mexyl, 5-chloro-8-quinolinoxyacetic acid-1-methylhexylester, was reported on p. 16 of the study report. The CAS chemical name and number of cloquintocet-mexyl were reported as 1-methylhexyl ester [(5-chloro-8-quinolinyl)oxy]-acetic acid and 99607-70-2, respectively, in Appendix 2, Figure 1, p. 297 of MRID 46012939 (a clodinafop-propargyl field dissipation study).

13. A typographical error listed the HPLC gradient at 16.0-17.0 minutes and 17.0-20.0 minutes as 30% A and 30% B (p. 26).

V. REFERENCES:

1. U.S. Environmental Protection Agency. 1982. Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate, Section 162-1. Aerobic soil metabolism. Office of Pesticide and Toxic Substances, Washington, DC. EPA 540/9-82-021.

2. U.S. Environmental Protection Agency. 1989. FIFRA Accelerated Reregistration, Phase 3 Technical Guidance. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 540/09-90-078.

3. U.S. Environmental Protection Agency. 1993. Pesticide Registration Rejection Rate Analysis - Environmental Fate. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 738-R-93-010.

Attachment 1

Excel Spreadsheets

Chemical: Cloquintocet-mexyl, a safener used with clodinafop-propargyl
MRID: 46013929
PC: 125203
Guideline: 162-1

Pappelacker loamy sand

Mass Balance	
0	100.49
0.21	99.31
1	99.27
3	98.32
7	97.93
14	98.31
28	97.76
56	98.63
Average	98.75
SD	0.90

Data from Table 3, p. 33 of the study report.

Gartenacker silt loam

Mass Balance	
0	99.86
0.21	99.71
1	98.74
3	99.4
7	98.78
14	98.66
28	98.69
56	97.95
Average	98.97
SD	0.64

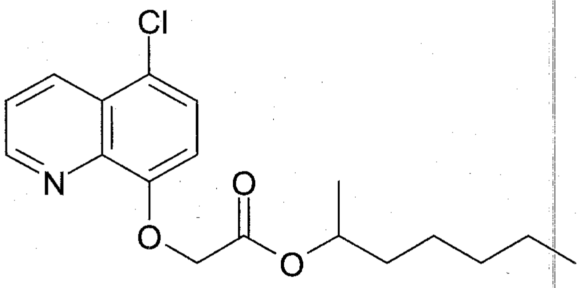
Attachment 2

Structures of Test Material and Transformation Products

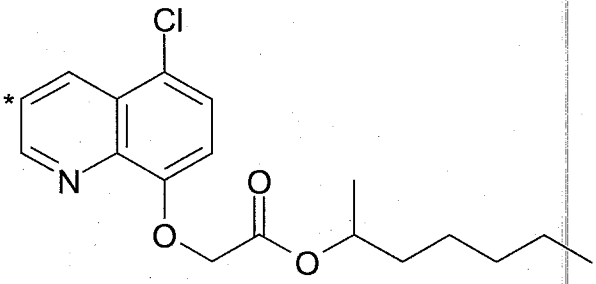
Cloquintocet-mexyl (CGA-185072; Safener of clodinofop-propargyl)

IUPAC name: 5-Chloro-8-quinolinoxyacetic acid-1-methylhexylester.
CAS name: 1-Methylhexyl ester [(5-chloro-8-quinolinyl)oxy]-acetic acid.
CAS No: 99607-70-2
SMILES string: Clc1ccc(c2c1cccn2)OCC(=O)OC(CCCCC)C

Unlabeled



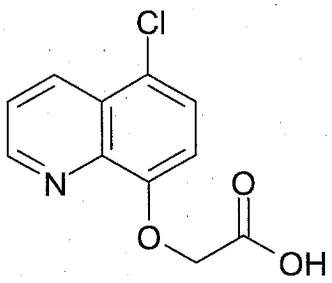
[3-^{14}C]Cloquintocet-mexyl



* Position of the radiolabel.

CGA 153433

IUPAC name:	Not reported.
CAS name:	[(5-Chloro-8-quinolinyl)oxy]-acetic acid.
CAS No:	88349-88-6



Attachment 3

Transformation Pathway Presented by Registrant
Illustration of Test System

Figure 14: Proposed Degradation Pathway

(simplified)

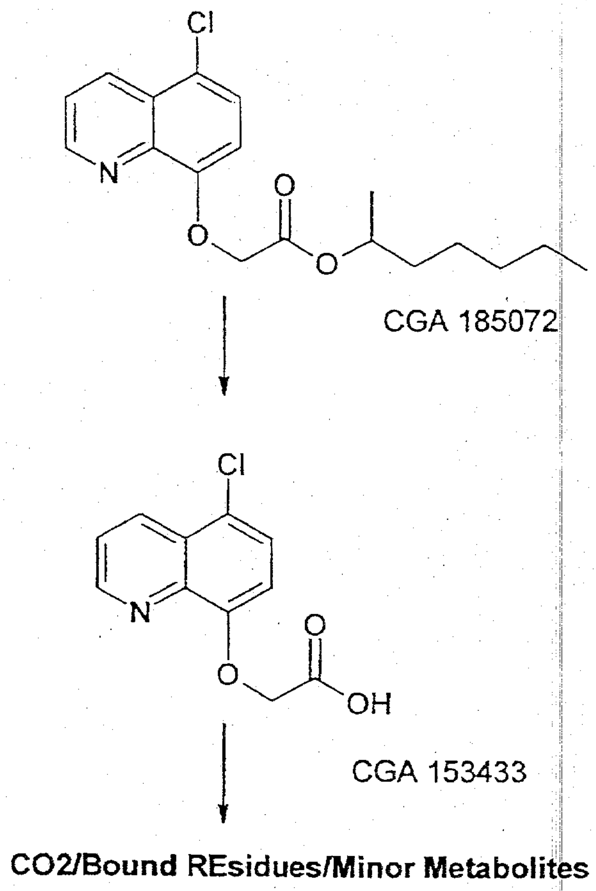
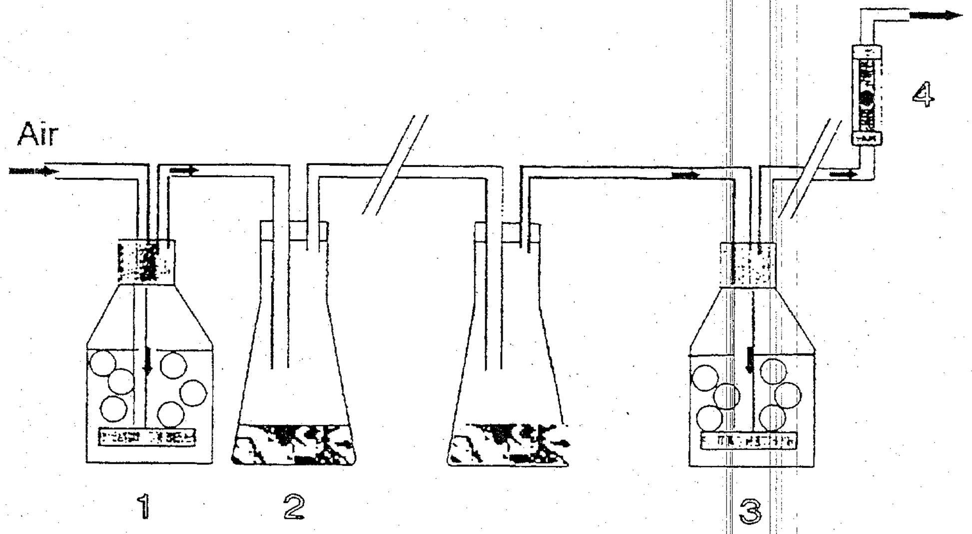


Figure 1: Incubation Apparatus.



1	Gas washing bottle containing water to saturate the incoming air (flow rate: about 50 ml / min).
2	Soil metabolism flasks
3	2N NaOH (2x) traps.
4	Flow meter

Figure 3: Leaching Apparatus