Shaughnessy Number: 129001

Date out of EFGWB: 9/28/90

To: Joanne Miller/Mary Erumsale
Product Manager 21
Registration Division (H7505C)

From: Henry Nelson, Acting Section Head H. Nelson
Environmental Fate Review Section #3
Environmental Fate and Ground Water Branch
Environmental Fate and Effects Division (H7507C)

Thru: Hank Jacoby, Chief Hank Jacoby
Environmental Fate and Ground Water Branch
Environmental Fate and Effects Division (H7507C)

Attached, please find the EFGWB review of...

Reg./File #: 59639-G

Chemical Name: 2-[1-[[(E--3-chloro-2-propenyl)oxy]-imino]propyl]-5-[2-(ethylthio) propyl]-3-hydroxy-2-cyclohexene-1-one Clethodim

Type Product: post emergent herbicide

Product Name: Select

Company Name: Chevron

Purpose: submission of revised aerobic soil metabolism study

Date Received: 6/25/90

Action Code: 100

EFGWB#(s): 90-0774

Total Reviewing Time (decimal days): 2

Deferrals to: ___Ecological Effects Branch, EFED

___Science Integration and Policy Staff, EFED

___Non-Dietary Exposure Branch, HED

___Dietary Exposure Branch, HED

___Toxicology Branch

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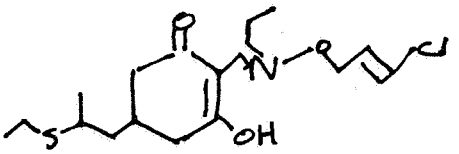
1. CHEMICAL:

chemical name: 2-[1-[[(E-3-chloro-2-propenyl)oxy]-imino]propyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexene-1-one
common name: clethodim
trade name: Select
structure:
CAS #: not available
Shaughnessy #: 129001



2. TEST MATERIAL: discussed in attached DER

3. STUDY/ACTION TYPE: aerobic soil metabolism

4. STUDY IDENTIFICATION:

Pack, D.E. 1988b. **The aeraobic soil metabolism of clethodim using [ring-4,6-^{14}C]- and [allyl-2-^{14}C] clethodim.** Lab project ID MEF-0015/0016/8819576. Unpublished study performed and submitted by Chevron Chemical Company, Richmond, CA. MRID # 409745-21. ***REVISED 1/5/90. MRID # 413768-01***

5. REVIEWED BY:

Typed Name: E. Brinson Conerly
Title: Chemist, Review Section 3
Organization: EFGWB/EFED/OPP

E.B. Conerly 9/11/90

6. APPROVED BY:

Typed Name: Henry Nelson, PhD
Title: Acting Section Head, Review Section 3
Organization: EFGWB/EFED/OPP

H Nelson 9/11/90

7. CONCLUSIONS:

This study ***as revised*** fulfills the aerobic soil metabolism data requirement for allyl and ring labelled clethodim. Satisfactory data on propyl labelled compound was previously supplied in MRID # 409745-22. Together the two studies (MRID #'s 409745-22 and 413768-01) completely fulfill the data requirement. No further aerobic soil metabolism data are needed.

8. RECOMMENDATIONS:

The attached DER replaces the previous DER on the same topic in the EFGWB science chapter for the new chemical Registration Standard on Clethodim. The attached executive summary and data table have also been revised to reflect the new information, and should be inserted in the appropriate places.

9. BACKGROUND:

The status of data requirements is set forth in the new chemical Registration Standard Chapter and is as follows:

hydrolysis -- fulfilled
photolysis in water -- fulfilled
soil photodegradation -- fulfilled
aerobic soil metabolism -- fulfilled with this submission
anaerobic soil metabolism -- not fulfilled

leaching/adsorption/desorption -- fulfilled
terrestrial field dissipation -- fulfilled
confined accumulation on rotational crops -- fulfilled
fish bioaccumulation -- fulfilled

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES: See DER.

11. COMPLETION OF ONE-LINER: n.a.

12. CBI APPENDIX: attached to DER.

DATA EVALUATION RECORD

Study 5 (162-1 -- Aerobic soil Metabolism)

Pack, D.E. 1988b. **The aerobic soil metabolism of clethodim using [ring-4,6-^{14}C]- and [allyl-2-^{14}C]clethodim.** Lab Project ID MEF-0015/0016/8819576. Unpublished study performed and submitted by Chevron Chemical Company, Richmond CA. MRID #40974521 ***REVISED 1/5/90.*** MRID # 413768-01

REVIEWED BY: E. Hirsch TITLE: Staff Scientist

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APPROVED BY: W. Spangler TITLE: Project Manager

ORGANIZATION: Dynamac Corporation
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ORIGINAL DER APPROVED BY: H. Nelson, Ph.D.
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CONCLUSIONS:

(1) This study ***as revised*** fulfills the aerobic soil metabolism data requirement for allyl and ring labelled clethodim. Satisfactory data on propyl labelled compound was previously supplied in MRID # 409745-22. Together the two studies (MRID #'s 409745-22 and 413768-01) completely fulfill the data requirement. No further aerobic soil metabolism data are needed.

(a) Peak 18 in the ring-label, and Peaks 16 and 18 in the allyl-label extracts comprised up to 5.9% (0.59 ppm), 9.4% (0.94 ppm) and 6.0% (0.60 ppm) of the applied radioactivity, respectively, but were not identified. The retention times of peaks 16 and 18 are within less than 1 minute of a clethodim sulfoxide isomer and a clethodim sulfone isomer, respectively, and may also be isomers of those compounds. In the original report reference standards did not appear to have been run for all possible column separable isomers of those compounds. ***In the revised report the investigators have identified peak 16 as a clethodim sulfoxide isomer based on its retention time. Peak 18, present at a maximum of 6% of applied material, still has not been identified, but is discussed more fully. The applicants state that it is not persistent, does not match with any of the tested standards, and probably retains the intact molecular skeleton.***

(b) A parallel study was done on the aerobic soil metabolism of propyl labeled clethodim. The purpose of labeling the cyclohexene ring of

clethodim in this study was to identify degradates of clethodim that had lost the propyl group but still had the cyclohexene ring. However, the reference standards used which are listed in Table 1 do not include any containing the cyclohexene ring without the propyl group nor any containing the cyclohexanene ring without the sulfur containing side chain. Therefore, it does not appear to have been possible to identify such compounds by comparison of retention times to those of reference standards. In the review of the original report, EFGWB requested an explanation. ***The revised report states that all of the major metabolites have been identified and none of these had lost their side chains. Total reported accountability ranges from 84 to 102%.***

(c) The time 0 samples were collected from soil that had been treated separately from the soil from which the day 1 and subsequent samples were collected. ***In the revised submission, the investigators explain that due to clethodim's rapid degradation in soil, the time necessary to complete the work did not permit fortifying all samples on the same day. The same solution and pipette were used at all times.***

(d) The computation of applied radioactivity was based upon an analysis of the stock solution and the volume of solution added instead of the results of the time 0 samples. No explanation was provided in the original report. ***In the revised report the investigators have recomputed these values, with the effect of raising percent recovery, material balance, and percent-of-dose values about 10%. They further state that these differences do not materially affect the interpretation of the data. EFGWB agrees.***

(e) The total radioactivities recovered from the time 0 soil samples were only 90.1% (ring labeled) and 93.2% (allyl labeled) of that nominally applied to the soil based upon the radioactivity in the stock solution and the volume of stock solution added to the soil. No explanation was provided in the original report. ***The revised report has, as noted in d) above, recomputed values based on recoveries from time-0 samples.***

(f) The total radioactivity recovered decreased with time to marginal levels (see discussion). EFGWB comments on the original report speculated that the gradual decrease in total recovered radioactivity could possibly be due to inefficient trapping of volatile organic degradates or inefficient extraction of the polyurethane plugs used for the trapping since no significant radioactivity was detected in extracts from the plugs. EFGWB requested further discussion on the trapping efficiency of polyurethane plugs and the method used to extract them, and noted that since no organic volatiles were identified, trapping and extraction efficiency data on such compounds obviously could not be provided. Therefore, a general discussion might suffice. ***In the revised report, the applicant noted that only low levels of radioactivity were trapped, and combustion of the plugs yielded no additional material. The applicant's position is that no volatile degradates went undetected. Based on the data, this seems to be correct.***

(2) Given the somewhat complex chemistry of clethodim and its degradates, this study was a very good one despite the deficiencies listed above. The original EFGWB review stated that the study could probably be made to partially satisfy the aerobic soil metabolism data requirement by the submission of acceptable information addressing at least most of the above listed deficiencies. ***As revised***, this study taken together with study 3 (409745-22) completely satisfies the aerobic soil metabolism (162-1) data requirement.

(3) Ring and allyl ^{14}C labeled incubated at 25°C at initial concentrations of 10 ppm in a sandy loam soil degraded with half-lives of approximately one day. The major degradate at the end of the 4 month incubation period was CO_2 which represented 57% of the ring labeled and 45% of the allyl labeled applied radioactivity. Clethodim sulfoxide which was initially the major degradate peaked at 62-72% of the applied radioactivity at 3-7 days post-treatment and then declined (half-life approximately 30 days) to 0.2-0.5% of applied at 121 days post-treatment. Clethodim sulfone which was formed from the oxidation of the sulfoxide peaked at 15% of applied at 30 days post-treatment and then declined to 5-7% of applied at 121 days post-treatment. The proposed degradative pathway for clethodim in soil under aerobic conditions is given in Figure 17.

MATERIALS AND METHODS:

Fifty-gram samples of sandy loam soil (0.9% organic matter, pH 7.5)(Tables II and III) were weighed into biometer flasks, moistened to 75% of field capacity, and treated at a nominal concentration of 10 ppm with either [ring-4,6-^{14}C]clethodim dissolved in acetone or [allyl-2-^{14}C]clethodim dissolved in ethanol (radiochemical purities ≥99%; specific activities 56.5 and 57.1 mCi/mMole, respectively; Wizard Labs). The treated soil samples were stirred with a spatula to mix. A "low pressure" oxygen source was connected to the biometer flasks; volatiles were trapped in a polyurethane foam plug located in the connecting arm and a 0.5 N sodium hydroxide solution located in the side well. The flasks were maintained in dark at 25°C. Duplicate flasks of soil were collected for analysis at 0, 1, 3, 7, 14, 30, 60-62, 94-99, and 121-125 days posttreatment; the sodium hydroxide trapping solutions were changed at each sampling interval.

The soils were extracted once with methanol containing unlabeled clethodim on an Omni-Mixer for 5 minutes, followed by three extractions with clethodim-free methanol; the samples were centrifuged and the extract removed after each extraction. The extracts were combined, and aliquots were analyzed for total radioactivity by LSC. The remainder was concentrated in a vacuum rotary evaporator at ambient temperature; the solvent vapors were condensed onto a dry ice-cooled cold finger trap to insure that no material was lost during condensation. The concentrated residues were diluted with methanol and again concentrated, this time under a stream of nitrogen. Aliquots of the methanol concentrate and the trapped distillates were analyzed for radioactivity by LSC. The methanol-extracted soils were further extracted three times with a clethodim-free 10 mM calcium sulfate solution on an Omni-mixer as described; the calcium sulfate extracts were combined and analyzed for radioactivity by LSC. The methanol concentrate and calcium sulfate extract were analyzed using reversed-phase HPLC with radioactive flow detection. Reference compounds were cochromatographed with the extracts, and retention times for the standards were determined by UV detection. In addition, the methanol concentrates were analyzed using TLC on silica gel plates developed in either chloroform:acetic acid (9:1) or hexane:acetone:acetic acid (50:50:1). Radioactive areas on the plates were detected by autoradiography. Reference compounds were cochromatographed with the samples and visualized by quenching of UV fluorescence. The twice-extracted soils were analyzed for unextractable radioactivity by LSC following combustion.

The polyurethane foam plugs were extracted three times using sonication with methanol; aliquots of the combined methanol extracts were analyzed by LSC. Aliquots of the sodium hydroxide solutions were analyzed for total radioactivity by LSC.

The detection limit appeared to be 0.1% of the applied.

RESULTS: [revised values are in brackets in bold type]

Ring- and allyl-labeled [^{14}C]clethodim (radiochemical purities ≥99%), at a theoretical application rate 10 ppm, degraded with half-lives of approximately 1 day in sandy loam soil incubated in the dark at 25°C and 70-75% of field capacity for 4 months (Figure 15). At the end of the 4-month study, evolved $^{14}CO_2$ was the major degradate and totaled 52% **[57%]** of the ring-labeled radioactivity and 40% **[45%]** of the allyl-labeled radioactivity (Table IV and Figure 16). Nonvolatile degradates included clethodim sulfoxide, clethodim sulfone, clethodim imine sulfoxide, clethodim oxazole sulfoxide, and clethodim oxazole sulfone.

In the soil treated with ring-labeled [^{14}C]clethodim, [^{14}C]clethodim decreased from 89% **[96%]** of the applied at day 0 to 49% **[50%]** at day 1, 17% at day 3, and 0.2% at day 121-125 (Table V). [^{14}C]Degradates isolated from the soil included (Table V and Figure 16):

clethodim sulfoxide (maximum concentration 64% **[65%]** of the applied at 7 days posttreatment)
clethodim sulfone (15% at 30 days posttreatment);
clethodim imine sulfoxide (2% at 7-14 days posttreatment);
clethodim oxazole sulfoxide (2% at 7 through 4% at 125 days posttreatment);
clethodim oxazole sulfone (8% **[9%]** at 125 days posttreatment).

At 121-125 days posttreatment, $^{14}CO_2$ totaled 52 **[57%]** % of the applied radioactivity and unextractable [^{14}C]residues were 11% **[13%]** of the applied. Throughout the study, the material balance ranged from 75 to 90% **[84 - 102%]** of the applied.

In the soil treated with allyl-labeled [^{14}C]clethodim, [^{14}C]clethodim decreased to 58% **[60%]** of the applied at day 1, 10% at day 3, and 0.2% at day 121-125 (Table V). [^{14}C]Degradates isolated from the soil included (Table V and Figure 16):

clethodim sulfoxide (maximum concentration of 70% **[73%]** of the applied at 3 days posttreatment)
clethodim sulfone (15% **[16%]** at 30 days posttreatment).

At 121-125 days posttreatment, $^{14}CO_2$ totaled 40% **[45%]** of the applied radioactivity and unextractable [^{14}C]residues were 26% **[29%]** of the applied. Throughout the study, the material balance ranged from 72 to 92% **[86 - 102%]** of the applied.

DISCUSSION:

(1) In the original report, data were expressed, as customary, as "% of the applied radioactivity". However, application rates were not determined using the typical procedure -- i.e., analysis of treated soil at time 0 (although there was a time 0 soil sample), using the resulting concentration as "100% of the applied". Instead, these rates (10.1 and 10.4 ppm) were determined by pipetting (automatic pipette) aliquots of the stock solution at the start and finish of soil treatment into 250-mL volumetric flasks, diluting the samples to volume, and analyzing the diluted stock solution. The application rates in terms of "dpm" that were used by the study author to convert soil data into "% of the applied" (Appendix Tables II-A and II-B) were:

ring-labeled: 177950000 dpm--0 time;
181550000 dpm--all samples except 0 time;
allyl-labeled: 171950000 dpm--0 time;
177950000 dpm--all samples except 0 time.

In the revised report, these values were recalculated on the basis of recovery from time-zero samples.

Time 0 samples were collected from soil that had been treated separately from the soil from which the day 1 and subsequent samples were collected, because *per the revised report* the rapid rate of disappearance of clethodim on soil did not allow processing of all samples at once.

(2) At time 0, an average of only 90.1% of the applied radioactivity was recovered from the soil treated with ring-labeled [^{14}C]clethodim (Appendix Table II-A) and an average 93.2% from the soil treated with allyl-labeled [^{14}C]clethodim (Appendix Table II-B). ***In the revised report, these values were taken as 100% and the other samples recalculated on the basis of time-zero samples.***

(3) As originally reported, the material balances were incomplete; up to 25.8% of the allyl-labeled and 25.4% of the ring-labeled radioactivity that was applied to the soil (applied computation based upon an analysis of stock solutions) were not recovered. The EFGWB review speculated that this might be at least partially due to inefficient trapping of volatile organics by the polyurethane plugs. ***In the revised report, the applicant noted that only low levels of radioactivity were trapped, and combustion of the plugs yielded no additional material. The applicant states that no volatile degradates went undetected. The data bear this out, with accountability ranging from 85 to 102%.***

(4) Initially, all degradates >0.01 ppm (≈0.1% of the applied) were not identified (Appendix Tables V-A and V-B). In the HPLC analysis of the ring-labeled [^{14}C]clethodim-treated soil, eleven [^{14}C]compounds each representing 0.2-5.9% of the applied were isolated but not identified. In the HPLC analysis of the allyl-labeled [^{14}C]clethodim-treated soil, twelve [^{14}C]compounds were isolated at 0.1-9.4% of the applied but not identified. Of special concern is Peak 18 in the ring-label, which comprised up to 5.9% of the applied (0.59 ppm), and Peaks 16 and 18 in the allyl-label, which comprised up to 9.4 and 6.0% of the applied (0.94 and 0.60 ppm), respectively.

Also, it was unclear whether peak numbers in Appendix Table V-A (ring label) correspond to peak numbers in Appendix Table V-B (allyl label). In both tables, clethodim is peak 23, clethodim sulfoxide is peaks 12, 13, and 17, and clethodim sulfone is peaks 15 and 19. However, peaks 6-11 are identified in Table V-A as clethodim imine sulfoxide, clethodim oxazole sulfoxide, and clethodim oxazole sulfone, but these peaks are not similarly identified in Table V-B. If the peak numbers do correspond, then the unidentified [^{14}C]compound measured by peak 18 is an important degradate of both labels.

In the revised report the investigators have identified peak 16 as a clethodim sulfoxide isomer because of its retention time. Peak 18, present at a maximum of 6% of applied material, still has not been identified. The applicants state that it is not persistent, does not match with any of the tested standards, and probably retains the intact molecular skeleton.

(5) Recovery efficiencies from fortified soil samples were not reported. ***No additional data were provided in the revised report.***

(6) The study was terminated before patterns of decline of the degradates clethodim oxazole sulfoxide and clethodim oxazole sulfone were established. However, a second aerobic soil metabolism study (Study 6) submitted in this data package was conducted for 1 year and provides the additional necessary information on the formation and decline of these two degradates.

(7) It appeared that the accountability for the HPLC analysis was >100%, based on a comparison between the HPLC totals (Appendix Tables V-A and V-B) and the

total extractable radioactivity (Table IV). ***In the revised report where these values have been recalculated, the recoveries are not significantly more than 100%.***

(8) Isomers (geometrical and optical isomers; tautomers) of clethodim and its degradates resulted in multiple HPLC peaks and streaking on the TLC plates. A very thorough discussion on the possible isomers of clethodim and its degradates was provided in the Appendix.

(9) The study author stated (Studies 5 and 6) that when low concentrations of clethodim are present in soil, considerable oxidation of clethodim to clethodim sulfoxide occurs during extraction. Methanol gave the lowest amount of conversion of the solvents tested, and the addition of unlabeled clethodim to the extracting solution repressed air oxidation completely. No numerical data were provided to support these statements.

Clethodim environmental fate review

Page _____ is not included in this copy.

Pages 10 through 12 are not included in this copy.

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 commercial/financial information

___ A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

X FIFRA registration data

___ The document is a duplicate of page(s) _____

___ The document is not responsive to the request

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

TABLE A -- GENERIC DATA REQUIREMENTS FOR CLETHODIM TERRESTRIAL FOOD USE

Data Requirement	Composition [1]	Use Pattern	Does EPA have data to satisfy this requirement	Bibliographic Citation	Must additional data be submitted?
158.290 Environmental Fate					
DEGRADATION STUDIES-LAB:					
161-1 - Hydrolysis	TGAI or PAIRA	A	Yes	409745-20	No
Photodegradation					
161-2 - In Water	TGAI or PAIRA	A	Yes	410301-33, -34	No
161-3 - On Soil	TGAI or PAIRA	A	Yes	410301-35	No
161-4 - In Air	TGAI or PAIRA	A	No		Reserved [3]
METABOLISM STUDIES-LAB:					
162-1 - Aerobic Soil	TGAI or PAIRA	A	Yes	409745-21, -22 413768-01	No
162-2 - Anaerobic Soil	TGAI or PAIRA	A	Partial	410301-36	YES [4]
162-3 - Anaerobic Aquatic	TGAI or PAIRA	N.A.	No		No
162-4 - Aerobic Aquatic	TGAI or PAIRA	N.A.	No		No
MOBILITY STUDIES:					
163-1 - Leaching/ads/des unaged and aged	TGAI or PAIRA	A	Yes	409745-23	No
163-2 - Volatility (Lab)	TEP	A	No		Reserved [3]
163-3 - Volatility (Fld)	TEP	A	No		Reserved [3]
DISSIPATION STUDIES-FIELD:					
164-1 - Soil	TEP	A	Yes	410302-07, -08	No
164-2 - Aquatic (Sed)	TEP	N.A.	No		No
164-3 - Forestry	TEP	N.A.	No		No
164-4 - Cmbn/Tank Mixes	TEP	N.A.	No		No
164-5 - Soil, Long-term	TEP	N.A.	No		No
ACCUMULATION STUDIES:					
165-1 - Rotational Crops (Confined)	PAIRA	A	Yes	410302-11	No
165-2 - Rotational Crops (Field)	TEP	A	No		Reserved [6]

TABLE A -- GENERIC DATA REQUIREMENTS FOR CLETHODIM TERRESTRIAL FOOD USE

Data Requirement	Composition[1]	Use[2] Pattern	Does EPA have data to satisfy this requirement?	Bibliographic Citation	Must additional data be submitted?
ACCUMULATION STUDIES:					
165-3 - Irrigated Crops	TEP	N.A.	No		No
165-4 - In Fish	TGAI or PAIRA	A	Yes	4097545-24, -31	No
165-5 - In Aq. Nontarget	TEP		No		No
158.440 Spray Drift					
201-1 - Drift Field Evaluation	TEP	A	No		YES
202-1 - Droplet Size Spectrum	TEP	A	No		YES

FOOTNOTES:

1/ Composition: TGAI = Technical grade of the active ingredient; PAIRA = Pure active ingredient, radiolabeled; TEP = Typical end-use product.

2/ The use patterns are coded as follows: A = Terrestrial, Food Crop; B = Terrestrial, Non-Food: C = Aquatic, Food Crop; D = Aquatic, Non-Food; E = Greenhouse, Food Crop; F = Greenhouse, Non-Food; G = Forestry; H = Domestic Outdoor; I = Indoor.

3/ These data are required if the vapor pressure of the compound so indicates. The vapor pressure of Clethodim (per personal communication via M. Erumsale) is less than $1x10^{-7}$ torr @ 25° C, and therefore this requirement does not apply.

4/ The soils were not flooded and it was uncertain whether anaerobic conditions actually existed in the cited study.

5/ The applicant should petition for a tolerance through Dietary Exposure Branch.