

US EPA ARCHIVE DOCUMENT

CONCLUSIONS

Metabolism - Aerobic Soil

1. This study may not be scientifically valid and may not provide useful information on the aerobic soil metabolism of the lambda-cyhalothrin degradate Ref. XV. The presence of unreasonably high nonextractable [¹⁴C]residues by day 1 indicates that the analytical method, specifically extraction, may not have been adequate for the determination of Ref. XV; thus, the validity of the half-lives is questionable. Additionally, only single samples were incubated and removed for analysis at each sampling interval (except time 0) for each soil. Typically, a study is considered valid only if duplicate samples, at a minimum, are prepared and incubated for each sampling interval.
2. This study does not meet Subdivision N Guidelines for the fulfillment of EPA data requirements on aerobic soil metabolism for the following reasons:
 - (i) nonextractable residues were unreasonably high;
 - (ii) the analytical method may have been inadequate; and
 - (iii) the soil moisture content was not maintained at 75% of 0.33 bar.
3. Cyclopropyl ring-labeled [1-¹⁴C]Ref. XV (R211133), at a nominal application rate of 0.06 ppm, degraded with registrant-calculated half-lives (reported as DT₅₀'s; first-order multi-compartment model) of 4 days in sandy clay loam soil, 3 days in loamy sand soil, and 4 days in sandy loam soil (r² values not reported) incubated in darkness at 20 ± 2 °C for up to 53 days (sandy clay loam soil) or 49 days (loamy sand and sandy loam soils). However, the presence of unreasonably high nonextractable residues (for all three soils) precludes the accurate determination of half-lives. All data, reported as percentages of the applied, represent percentages of the nominal application. Reported residue concentration data (in ppm based on parent equivalents) were reviewer-calculated based on the nominal application rate and the reported percentages of applied radioactivity. In this review, the test compound (the degradate Ref. XV) is referred to as "the parent compound" for ease of reporting.

In the sandy clay loam soil, the parent compound was initially 97.5% (0.059 ppm; reviewer-calculated mean) of the applied radioactivity, decreased to 67% (0.040 ppm) by 3 days and 41% (0.025 ppm) by 7 days, was 19% (0.011 ppm) at 16 days, and was 8% (0.0048 ppm) at 53 days posttreatment. Nonextractable [¹⁴C]residues were initially (time 0) 4% of the applied radioactivity, increased to 17% by 1 day and 28% by 3 days, were a maximum of 45% at 16 days, and were 38% at 53 days posttreatment. Radioactivity removed by reflux and hexane partitioning of the post-extracted soil was ≤4% of the applied radioactivity throughout the incubation period. Evolved ¹⁴CO₂ initially (day 1)

accounted for 1% of the applied radioactivity, increased to 19% by 7 days and 38% by 16 days, and was 53% at 53 days posttreatment; [^{14}C]organic volatiles were negligible. Organic matter fractionation was not performed to determine the radioactivity associated with the humic acid, fulvic acid, and humin fractions.

In the loamy sand soil, the parent compound was initially 92.5% (0.056 ppm; reviewer-calculated mean) of the applied radioactivity, decreased to 67% (0.040 ppm) by 1 day and 43% (0.026 ppm) by 3 days, was 29% (0.017 ppm) at 12 days, and was 10-12% (0.0060-0.0072 ppm) from 19 to 49 days posttreatment. Nonextractable [^{14}C]residues were initially (time 0) 7% of the applied radioactivity, increased to 24% by 1 day, and were 40-48% from 7 to 49 days posttreatment. Evolved $^{14}\text{CO}_2$ initially (day 1) accounted for 1% of the applied radioactivity, increased to 15% by 7 days and 30% by 19 days, and was 40% at 49 days posttreatment; [^{14}C]organic volatiles were negligible. Organic matter fractionation was not performed to determine the radioactivity associated with the humic acid, fulvic acid, and humin fractions.

In the sandy loam soil, the parent compound was initially 93% (0.056 ppm; reviewer-calculated mean) of the applied radioactivity, decreased to 61% (0.037 ppm) by 3 days and 47% (0.028 ppm) by 7 days, was 20-22% (0.012-0.013 ppm) from 12 to 28 days, and was 14% (0.0084 ppm) at 49 days posttreatment. Nonextractable [^{14}C]residues were initially (time 0) 4.5% (reviewer-calculated mean) of the applied radioactivity, increased to 13% by 1 day and 29% by 3 days, and were 42-45% from 12 to 49 days posttreatment. Evolved $^{14}\text{CO}_2$ initially (day 1) accounted for 1% of the applied radioactivity, increased to 9% by 7 days and 26% by 19 days, and was 40% at 49 days posttreatment; [^{14}C]organic volatiles were negligible. Organic matter fractionation was not performed to determine the radioactivity associated with the humic acid, fulvic acid, and humin fractions.

METHODOLOGY

Samples (50 g) of sieved (2 mm) sandy clay loam soil (collected from Berkshire, UK; 56% sand, 23% silt, 21% clay, 3.2% organic matter, pH 6.9, CEC 12.8 meq/100 g; Table 2, p. 21) OR loamy sand soil (collected from Suffolk, UK; 88% sand, 3% silt, 9% clay, 2.3% organic matter, pH 7.6, CEC 7.6 meq/100 g) OR sandy loam soil (collected from Surrey, UK; 74% sand, 15% silt, 11% clay, 2.6% organic matter, pH 6.6, CEC 8.1 meq/100 g) were weighed into centrifuge bottles, adjusted to pF 2 soil water tension (see Comment #3), and pre-incubated in darkness at $20 \pm 2^\circ\text{C}$ for up to 25 days prior to treatment (p. 12). Following the pre-incubation period, the samples were treated with cyclopropyl ring-labeled [^{14}C]Ref. XV {R211133; 1:1 mixture of (1*R*) *cis* α -(S) and (1*S*) *cis* α -(R) α -cyano-3-(4-hydroxyphenoxy)benzyl 3-(*Z*-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate; radiochemical purity ~95%, specific activity 2.2 GBq/mmol; pp. 11-12}, dissolved in acetone, at a nominal application rate of 0.06 ppm (p. 11). Uncapped samples were placed inside vacuum desiccators equipped with a

sidearm for air inlet and outlet, and incubated in darkness at $20 \pm 2^\circ\text{C}$ for up to 53 days (sandy clay loam soil) or 49 days (loamy sand and sandy loam soils) posttreatment (p. 15; Figure 1, p. 24). The soil moisture content was monitored gravimetrically throughout the study; data were not reported. Moist room temperature air was pumped through the desiccators and into a solid sorbent (Tenax) trap and two 1 M NaOH traps to capture volatiles. Duplicate samples were analyzed at time 0 for each soil; and single samples were removed for analysis at 1, 3, 7, 11, 16, 23, 32, and 53 days posttreatment for the sandy clay loam soil; and at 1, 3, 7, 12, 19, 28, and 49 days posttreatment for the loamy sand and sandy loam soils (p. 15). Volatile trapping solutions were replaced at each sampling interval.

At each sampling interval, soil samples were extracted twice by shaking with acetonitrile (p. 16; Figure 2, p. 25). The samples were centrifuged and the supernatants were decanted. The combined extracts were analyzed for total radioactivity by LSC; the limit of detection was <0.003 ppm (Appendix 2, p. 41). The extracts were filtered ($0.45 \mu\text{m}$), concentrated by rotary evaporation, and analyzed by TLC on silica gel plates developed in cyclohexane:diethyl ether:formic acid (60:40:2, v:v:v; p. 14). Samples were co-chromatographed with a nonradiolabeled reference standard of the metabolite Ref. XV which was visualized with UV (unspecified wavelength) light. Areas of radioactivity were quantitated using phosphoimage scanning. To confirm compound identities, selected samples (days 0 to 19) were analyzed by reverse-phase HPLC (Phenomenex Ultremex C18 column) using an isocratic mobile phase of CH_3CN :water (60:40, v:v) with UV (unspecified wavelength) and radioactive flow detection (p. 13). Samples were co-chromatographed with a nonradiolabeled reference standard of Ref. XV. Duplicate subsamples of the post-extracted soil were analyzed for total radioactivity by LSC following combustion (pp. 13, 16). To determine radioactivity remaining in post-extracted soil, subsamples of the sandy clay loam soil were refluxed with acetonitrile:water (25:10.7, v:v) and centrifuged (p. 16). The supernatant was partitioned with hexane (25 mL) and aqueous sodium chloride (45 mL). The hexane phase was analyzed for total radioactivity by LSC.

At each sampling interval, aliquots of the volatile trap solutions were analyzed for total radioactivity by LSC (p. 15); the method (if any) used to confirm the presence of $^{14}\text{CO}_2$ in the NaOH traps was not reported.

To confirm the viability of the soil, the microbial biomass was measured at the initiation and termination of the study using a modified version of the Anderson and Domsch method (1978; p. 14); data indicated that the soil samples were viable (Table 2, p. 21).

DATA SUMMARY

Cyclopropyl ring-labeled [^{14}C]Ref. XV (R211133; radiochemical purity ~95%), at a nominal application rate of 0.06 ppm, degraded with registrant-calculated half-lives (reported as DT_{50} 's; first-order multi-compartment model) of 4 days sandy clay loam soil, 3 days in loamy sand soil, and 4 days in sandy loam soil (r^2 values not reported) incubated in darkness at $20 \pm 2^\circ\text{C}$ for up to 53 days (sandy clay loam soil) or 49 days (loamy sand and sandy loam soils; p. 18; Figures 6-8, pp. 29-31). However, the presence of unreasonably high nonextractable residues (for all three soils) precludes the accurate determination of half-lives. All data, reported as percentages of the applied, represent percentages of the nominal application. Reported residue concentration data (in ppm based on parent equivalents) were reviewer-calculated based on the nominal application rate and the reported percentages of applied radioactivity. In this review, the test compound (the degradate Ref. XV) is referred to as "the parent compound" for ease of reporting.

Sandy clay loam soil

The parent compound was initially present at 97.5% (0.059 ppm; reviewer-calculated mean) of the applied radioactivity, decreased to 67% (0.040 ppm) by 3 days and 41% (0.025 ppm) by 7 days, was 19% (0.011 ppm) of the applied at 16 days posttreatment, and was 8% (0.0048 ppm) of the applied at 53 days posttreatment (Table 3, p. 22). Nonextractable [^{14}C]residues were initially (time 0) 4% of the applied radioactivity, increased to 17% by 1 day and 28% by 3 days, were a maximum of 45% of the applied at 16 days posttreatment, and were 38% of the applied at 53 days posttreatment (Table 4, p. 23). Radioactivity removed by reflux and hexane partitioning of the post-extracted soil was $\leq 4\%$ of the applied radioactivity throughout the incubation period (Table 3, p. 22). Evolved $^{14}\text{CO}_2$ initially (day 1) accounted for 1% of the applied radioactivity, increased to 19% by 7 days and 38% by 16 days, and was 53% of the applied at 53 days posttreatment (Table 4, p. 23); [^{14}C]organic volatiles were negligible. Organic matter fractionation was not performed to determine the radioactivity associated with the humic acid, fulvic acid, and humin fractions.

Material balances (based on LSC analysis) were 102-107% of the applied radioactivity (with the exception of 112% at day 1) throughout the incubation period (Table 4, p. 23; see Comment #4).

Loamy sand soil

The parent compound was initially present at 92.5% (0.056 ppm; reviewer-calculated mean) of the applied radioactivity, decreased to 67% (0.040 ppm) by 1 day and 43% (0.026 ppm) by 3 days, was 29% (0.017 ppm) of the applied at 12 days posttreatment, and was 10-12% (0.0060-0.0072 ppm) of the applied from 19 to 49 days posttreatment (Table

3, p 22). Nonextractable [^{14}C]residues were initially (time 0) 7% of the applied radioactivity, increased to 24% of the applied by 1 day posttreatment, and were 40-48% of the applied from 7 to 49 days posttreatment (Table 4, p. 23). Evolved $^{14}\text{CO}_2$ initially (day 1) accounted for 1% of the applied radioactivity, increased to 15% by 7 days and 30% by 19 days, and was 40% of the applied at 49 days posttreatment; [^{14}C]organic volatiles were negligible. Organic matter fractionation was not performed to determine the radioactivity associated with the humic acid, fulvic acid, and humin fractions.

Material balances (based on LSC analysis) were 95-108% of the applied radioactivity throughout the incubation period, with no observed pattern of decline (Table 4, p. 23).

Sandy loam soil

The parent compound was initially present at 93% (0.056 ppm; reviewer-calculated mean) of the applied radioactivity, decreased to 61% (0.037 ppm) by 3 days and 47% (0.028 ppm) by 7 days, was 20-22% (0.012-0.013 ppm) of the applied from 12 to 28 days posttreatment, and was 14% (0.0084 ppm) of the applied at 49 days posttreatment (Table 3, p. 22). Nonextractable [^{14}C]residues were initially (time 0) 4.5% (reviewer-calculated mean) of the applied radioactivity, increased to 13% by 1 day and 29% by 3 days, and were 42-45% of the applied from 12 to 49 days posttreatment (Table 4, p. 23). Evolved $^{14}\text{CO}_2$ initially (day 1) accounted for 1% of the applied radioactivity, increased to 9% by 7 days and 26% by 19 days, and was 40% of the applied at 49 days posttreatment; [^{14}C]organic volatiles were negligible. Organic matter fractionation was not performed to determine the radioactivity associated with the humic acid, fulvic acid, and humin fractions.

Material balances (based on LSC analysis) were 99-107% of the applied radioactivity (with the exception of 88% at day 12) throughout the incubation period (Table 4, p. 23; see Comment #4).

COMMENTS

1. Nonextractable [^{14}C]residues were unreasonably high for all three soils by 1 day posttreatment, precluding the accurate determination of half-lives. Nonextractable [^{14}C]residues were 17%, 24%, and 13% of the applied radioactivity in the sandy clay loam, loamy sand, and sandy loam soils, respectively, by day 1, and were respective maximums of 45%, 48%, and 45% of the applied (Table 4, p. 23). The presence of unreasonably high nonextractables by day 1 (for each soil) indicates that the analytical method, specifically extraction, may not have been adequate for the determination of Ref. XV. Without the appropriate extraction procedures to ensure quantitative recovery of the compounds of interest, the validity of the reported half-lives is questionable. Following preliminary extractions, selected soil samples (sandy clay loam soil only) were re-extracted.

and partitioned in order to determine radioactivity associated with the post-extracted soil (p. 16); radioactivity removed by reflux and hexane partitioning of the post-extracted soil was $\leq 4\%$ of the applied radioactivity throughout the incubation period (Table 3, p. 22). Unless appropriate extraction procedures are utilized, it cannot be confirmed that additional Ref. XV residues were not present in the fraction of the applied radioactivity that was reported as nonextractable. Generally, soil samples are extracted to sufficiently remove any extractable residues, and the initial extracts are analyzed for the primary characterization of the parent and its degradates. Then, soil samples are often further extracted, perhaps using harsh methods such as reflux or Soxhlet extraction, in an attempt to remove bound residues; the harsh extracts are not usually characterized due to the compound-altering effects of the extractions on the residues. Additionally, organic matter fractionation was not performed to determine the radioactivity associated with the humic acid, fulvic acid, and humin fractions; generally, such data are reported for aerobic soil metabolism studies.

2. Single test samples were utilized for each sampling interval, except time 0 (p. 15). The use of single test samples is generally not considered to be sound scientific practice; at a minimum, duplicate samples for each sampling interval and each treatment are necessary in order to accurately determine the decline of the parent.
3. The reviewer could not confirm that the soil moisture content was maintained at 75% of the soil moisture at 0.33 bar during the incubation period, as required by Subdivision N Guidelines. The study authors reported that the soil moisture content was adjusted to pF 2 soil water tension during the pre-incubation period and was monitored gravimetrically throughout the incubation period (p. 12). However, the study authors did not report the relationship between the two moisture contents. Clarification by the registrant is necessary. The study authors reported in Table 2 (p. 21) that pF 2.5 is one-third bar; however, the relationship between pF 2 and pF 2.5 was not reported. Subdivision N Guidelines require that aerobic soil metabolism studies be performed at 75% of the soil moisture content at 0.33 bar in order to ensure aerobic conditions and soil viability.
4. The study authors stated that the maximum expected concentration of the metabolite Ref. XV in the soil was 0.06 ppm (hop-use pattern; p. 10).
5. Residue data were reported only as percentages of the nominal application; concentration data were not reported. All concentration data (in ppm based on parent equivalents) were reviewer-calculated from the nominal application rate and the reported percentages of the applied radioactivity. In future studies submitted to the EPA, it is necessary that data be reported as both percentages of the applied radioactivity and in units of concentration such as ppm.

6. The study authors reported that the study was conducted to fulfill requirements of the European Union. The study authors also stated that the study was submitted under FIFRA (p. 2) and conducted under EPA Good Laboratory Practice standards (p. 3).
7. The limit of detection was reported for LSC, but was not reported for TLC or HPLC analyses. Both limits of detection and quantitation should be reported for each analytical method utilized to allow the reviewer to evaluate the adequacy of the methods for the determination of the parent and degradates.
8. The aqueous solubility of Ref. XV was reported as <0.01 ppm (unspecified temperature and pH; p. 15).

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