DATA EVALUATION RECORD

STUDY 11

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Kimmel, E. C. 1992. Mobility and dissipation of [^{14}C-Phenyl]-CGA-169374 under actual field conditions. PTRL-West Project No.: 111W. Unpublished study performed by PTRL-West, Inc., Richmond, CA; and submitted by CIBA-GEIGY Corporation, Greensboro, NC.

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CONCLUSIONS

Field Dissipation - Terrestrial

1. This study is scientifically valid and provides useful supplemental information on the terrestrial field dissipation of difenoconazole in lysimeter-enclosed bareground plots of loamy sand soil in California. However, replicate samples were not utilized. Generally, a minimum of duplicate samples (lysimeters) is necessary for a valid determination of a half-life.

2. This study does not meet Subdivision N Guidelines for the partial fulfillment of EPA data requirements on terrestrial field dissipation for the following reason:

   (i) storage stability data were inadequate;

   (ii) the study did not represent actual field-use conditions.

3. Uniformly phenyl ring-labeled [^{14}C]difenoconazole (CGA-169374), applied at a nominal application rate of 51.8 g a.i./A (0.41 mg/lysimeter) to lysimeter-enclosed bareground plots of loamy sand soil in Reedley, California, dissipated with a registrant-calculated half-life of 252 days ($r^2 = 0.91$); however, the observed first half-life occurred between 93 and 182 days posttreatment. The half-life was determined from the parent detected in the 0- to 3-inch depth rather than the top 6 inches. Data are reported as percentages of the nominal application and are reviewer-calculated means of methanol:water plus oxalic acid:DMF extractions. Residue data were only reported for the 0- to 3-inch depth. The parent was initially 82.4% (0.1 ppm) of the applied radioactivity in the 0- to 3-inch depth, decreased to 49.7% (0.072 ppm) by 93 days posttreatment, and was 25.7% (0.03 ppm) at 363 days. Degradate data are reported in parent equivalents. The minor degradate CGA-190978 was a maximum of 1.3% (0.001 ppm; methanol:water extraction only) of the applied radioactivity at 61 days posttreatment and was 0.59% (0.001 ppm) at 363 days. The minor degradate CGA-189138 was a maximum of 2.7% (0.003 ppm) of the applied radioactivity at 61 days posttreatment and was 1.7% (0.002 ppm) at 363 days. The minor degradate CGA-205374 was a maximum of 3.3% (0.003 ppm; methanol:water extraction only) of the applied radioactivity at time 0 and was 1.2% (0.001 ppm) at 363 days. The minor degradate CGA-205375 was a maximum of 6.9% (0.009 ppm) of the applied radioactivity at 182 days posttreatment and was 6.6% (0.008 ppm) at 363 days. [^{14}C]Residues were not characterized below the 0- to 3-inch depth. In the 3- to 6-inch depth, total [^{14}C]residues were initially 0.56% (0.001 ppm) of the applied radioactivity at 7 days posttreatment, increased to a maximum of 5.1% (0.005 ppm) by 272 days, and were 2.5% (0.003 ppm) at 363 days. In the 6- to 9-inch depth, total [^{14}C]residues were $\leq$0.94% (0.001 ppm) of the applied radioactivity from 14 to 363 days posttreatment. In the 9- to 12-inch depth, total [^{14}C]residues were 0.26-0.47% (0.0003-0.0004 ppm) of the applied radioactivity from 182 to 363 days posttreatment. In the 12- to 18-inch depth,

total [^{14}C]residues were 0.30-1.3% (0.0001-0.0006 ppm) of the applied radioactivity from 182 to 363 days posttreatment. Total [^{14}C]residues detected in the leachate were 0.36% of the applied radioactivity throughout the study period.

METHODOLOGY

Uniformly phenyl ring-labeled [^{14}C]difenoconazole (CGA-169374; radiochemical purity ≥98.2%; specific activity 74.4 μCi/mg; p. 19; Figure 1, p. 61), dissolved in acetone, was applied once at a nominal application rate of 51.8 g a.i./A (0.41 mg/lysimeter; Table III, p. 46; Table III, p. 46) to 8-inch diameter steel lysimeter-enclosed bareground plots of loamy sand soil (0-12 inch depth; 84.9% sand, 14.9% silt, 0.2% clay, 0.1% organic matter, pH 7.7, CEC 6 meq/100 g; Table I, p. 36) in Reedley, California (p. 21). The plot contained 59 cylindrical, steel lysimeters (36-inch length) inserted vertically into the soil (leaving the rim one inch above the soil surface). An access trench (5 feet x 100 feet x 3 feet) was dug parallel to the row of lysimeters (1 foot apart; Figure 3, p. 64) and plastic funnels were placed under the lysimeters; leachate was collected in glass jars. The soil surfaces within 11 lysimeters were individually treated drop-wise with the test solution using a Pasteur pipette (p. 23). Each lysimeter received 75 mL of water following application of the test solution. A untreated control plot (6 feet x 6 feet) was located 25 feet from the treated plot (p. 21). Maintenance pesticides were not applied during the in-life phase of the study. Vegetation (grasses and weeds) inside the lysimeters was cut back manually to the height of the rim (p. 22). A three-year plot history indicated no prior use of difenoconazole or related compounds (Appendix A5, p. 132). Environmental data were collected on-site (Appendix A4, pp. 114-131). The depth to the water table was approximately 55 feet (p. 22). Precipitation data were collected approximately one mile from the test site (Table IIa, p. 44). Precipitation was supplemented with irrigation; total water input (40.6 inches) was approximately 340% (reviewer-calculated) of the 10-year mean annual precipitation (Table IIa, p. 44). Total pan evaporation was 76.9 inches (reviewer-calculated) during the study period (Appendix A4, pp. 115-130).

Soil lysimeters were collected at 0, 1, 3, 7, 14, 31, 61, 93, 182, 272, and 363 days posttreatment (p. 23). At each sampling interval, a single lysimeter was collected by removing the entire lysimeter from the plot. For samples collected at 0, 1, and 3 days posttreatment, the top three inches of soil were collected (by spooning) prior to removing the lysimeter from the field; samples were immediately placed on dry ice. For samples collected at 7-93 days posttreatment, the top six inches of soil were collected by the same method; samples were immediately placed on dry ice. All other lysimeters were sealed (top and bottom) intact and shipped to the analytical laboratory. The soil columns within the lysimeters were divided into 3-inch (0- to 12-inch depth) or 6-inch (12- to 36-inch depth) sections and homogenized (p. 24). Soil subsamples were stored frozen for 1.5-2.5 years prior to analysis (p. 24). Prior to extraction, three soil subsamples from each

sampling interval and depth were analyzed for total radioactivity by LSC following combustion; the limit of detection was 0.14 ppb (pp. 24, 28).

Selected 0- to 3-inch depth soil samples (0 and 14-363 days) were extracted three times by vortexing with methanol:water (9:1, v:v; initial extraction), sonicating, and centrifuging (p. 25; Figure 4, p. 65); aliquots of the supernatants were analyzed for total radioactivity by LSC following each extraction. Selected post-extracted soil samples (14-363 days) were further extracted by refluxing with methanol:water (pH 5.5; 9:1, v:v; second extraction) and centrifuged; aliquots of the supernatants were analyzed by LSC. Extracts from the initial and second methanol:water extractions were combined, concentrated by rotary evaporation and by nitrogen, and analyzed by two-dimensional TLC using silica gel plates developed with chloroform:methanol (9:1; v:v) followed by toluene:ethyl formate:formic acid (5:7:1, v:v:v; p. 26); radiolabeled residues were detected with a radioimaging scanner or X-ray film. Samples were co-chromatographed with nonradiolabeled reference standards of the parent and potential degradates CGA-190978, CGA-189138, CGA-205374, and CGA-205375, which were visualized by UV light (wavelength not specified). Radiolabeled areas were scraped and quantified by LSC. Soil samples (14-363 days) were further extracted with 0.1 *N* oxalic acid:dimethylformamide (1:1, v:v), sonicated, centrifuged, and the supernatant was decanted; aliquots were analyzed by LSC. The extraction was repeated and the extracts were combined, concentrated by rotary evaporation and by nitrogen, and analyzed by one-dimensional TLC as described previously, except developed with chloroform:methanol (9:1, v:v). Post-extracted soil samples were air dried and analyzed for total radioactivity by LSC following combustion; combustion efficiency was >95% (Appendix A6, pp. 133-143).

To confirm compound identities, [^{14}C]residues isolated by two-dimensional TLC were scraped from the plates, dissolved in methanol, centrifuged, and concentrated under nitrogen (p. 27); aliquots were analyzed by HPLC (Supelco C-18 column) using water:acetonitrile (50:50 to 25:75, v:v) with UV light (254 nm; p. 27). Samples were co-chromatographed with nonradiolabeled reference standards of the parent and the potential degradates CGA-189138 and CGA-205375. Eluent fractions were collected (intervals not specified) and analyzed by LSC. To confirm the identity of the potential degradates CGA-190978 and CGA-205374, methanol:water extracts were analyzed by one-dimensional TLC plates as described previously, except developed twice with 100% acetonitrile (p. 33). Samples were co-chromatographed with nonradiolabeled reference standards of CGA-190978 and CGA-205374.

Triplicate aliquots of leachate at each interval were analyzed for total radioactivity by LSC (p. 25).

DATA SUMMARY

Uniformly phenyl ring-labeled [^{14}C]difenoconazole (CGA-169374; radiochemical purity ≥98.2%), applied at a nominal application rate of 51.8 g a.i./A (0.41 mg/lysimeter) to lysimeter-enclosed bareground plots of loamy sand soil in Reedley, California, dissipated with a registrant-calculated half-life of 252 days (r^2 = 0.91; p. 30; Figure 10, p. 91); however, the observed first half-life occurred between 93 and 182 days posttreatment. The half-life was determined from the parent compound detected in the 0- to 3-inch depth rather than the top 6 inches (see Comment #5). Data are reported as percentages of the nominal application; data are reviewer-calculated means of methanol:water plus oxalic acid:DMF extractions (see Comment #10). Residue data were only reported for the 0- to 3-inch depth. The parent compound was initially present in the 0- to 3-inch depth at 82.4% (0.1 ppm) of the applied radioactivity, decreased to 49.7% (0.073 ppm) of the applied radioactivity by 93 days posttreatment, and was 25.7% (0.03 ppm) of the applied at 363 days posttreatment (Tables XIA-XII, pp. 54-60). Degradate data are reported in parent equivalents. The minor degradate CGA-190978 was a maximum of 1.3% (0.001 ppm; methanol:water extraction only) of the applied radioactivity at 61 days posttreatment and was 0.59% (0.001 ppm) of the applied at 363 days posttreatment. The minor degradate CGA-189138 was a maximum of 2.7% (0.003 ppm) of the applied radioactivity at 61 days posttreatment and was 1.7% (0.002 ppm) of the applied at 363 days posttreatment. The minor degradate CGA-205374 was a maximum of 3.3% (0.003 ppm; methanol:water extraction only) of the applied radioactivity at time 0 and was 1.2% (0.001 ppm) of the applied at 363 days posttreatment. The minor degradate CGA-205375 was a maximum of 6.9% (0.009 ppm) of the applied radioactivity at 182 days posttreatment and was 6.6% (0.008 ppm) of the applied at 363 days posttreatment. Uncharacterized radioactivity (designated "unknowns") was a maximum of 8.5% (0.008 ppm) of the applied radioactivity at 14 days posttreatment and was 4.1% (0.006 ppm) of the applied at 363 days posttreatment. Uncharacterized origin material was a maximum of 7.8% (0.009 ppm) of the applied radioactivity at 61 days posttreatment and was 7.0% (0.008 ppm) of the applied at 363 days posttreatment. [^{14}C]Residues were not characterized below the 0- to 3-inch depth.

In the 3- to 6-inch depth, total [^{14}C]residues were initially present at 0.56% (0.001 ppm) of the applied radioactivity at 7 days posttreatment, increased to a maximum of 5.1% (0.005 ppm) of the applied by 272 days posttreatment, and were 2.5% (0.003 ppm) of the applied at 363 days posttreatment (Table V, p. 48). In the 6- to 9-inch depth, total [^{14}C]residues were ≤0.94% (0.001 ppm) of the applied radioactivity from 14 to 363 days posttreatment. In the 9- to 12-inch depth, total [^{14}C]residues were 0.26-0.47% (0.0003-0.0004 ppm) of the applied radioactivity from 182 to 363 days posttreatment. In the 12- to 18-inch depth, total [^{14}C]residues were 0.30-1.3% (0.0001-0.0006 ppm) of the applied radioactivity from 182 to 363 days posttreatment.

Total [^{14}C]residues detected in the leachate were 0.36% of the applied radioactivity throughout the study period (Table VIII, p. 51).

Material balances (based on LSC analysis) were 96.1-97.8% of the applied radioactivity from 0 to 14 days posttreatment, with the exception of 82.8% of the applied at 7 days posttreatment; were 75.6-81.6% of the applied at 31-93 days posttreatment; and were 59.2% of the applied at 363 days posttreatment (Table IX, p. 52).

COMMENTS

1. Replicate soil columns were not utilized. Instead, single lysimeters were removed for analysis at each sampling interval. Generally, a minimum of duplicate samples (lysimeters) is necessary for a valid determination of a half-life.

2. Frozen storage stability data were inadequate. The study author stated that "analysis of the day 0 soil sample performed after approximately 30 months of storage of the original soil sample shows that 85% of the total radiocarbon is CGA-169374" (p. 33; Figure 6A, p. 71; Appendix A9, p. 147). Storage stability studies should be conducted using samples collected from the test site which are fortified separately with the parent and degradates, and stored for a length of time equal to the longest interval utilized for the test samples.

3. The study was not representative of actual field-use conditions as generally used for a terrestrial field dissipation study. Data from the study may be considered supplemental data which provide some useful information on the mobility of the compound in the field.

4. Material balances generally decreased from 97.8% of the applied radioactivity to 59.2% of the applied from 0 to 363 days posttreatment (Table IX, p. 52). Material balances were ≤82.8% of the applied radioactivity from 7 to 363 days posttreatment with the exception of 14 days (96.1%). The study author stated that volatilization may have contributed to the observed pattern of loss (p. 32). However, the reviewer noted that in the aerobic soil metabolism study (MRID 42245131), evolved $^{14}CO_2$ accounted for ≤5.0% of the applied radioactivity following 120 days of incubation. Generally, material balance data are not reported for a field dissipation study.

5. The registrant-calculated half-life was based on data from the 0- to 3-inch soil depth, rather than the 0- to 6-inch depth. However, the reviewer noted that 89.9-100% of the recovered radioactivity was present in the 0- to 3-inch soil depth (Table IV, p. 49).

6. Natural vegetation (grasses and weeds) growing inside the lysimeter-enclosed plots was not analyzed for the parent or its degradates. It is necessary that total residues in the vegetation be monitored in order to accurately determine the routes of dissipation of the test material.

7. The parent compound may have been applied at an exaggerated rate (51.8 g a.i./A). The study author stated on page 31 that the proposed maximum use rate was 30 g a.i./A. However, the study author stated in the protocol (Appendix A1, p. 95) that the nominal application rate utilized (50 g a.i./A) represents the crop (unspecified) use rate.

8. Nonextractable [^{14}C]residues increased throughout the study to 11.8% (0.0098 ppm; single replicate) of the applied radioactivity by 182 days posttreatment, and were a maximum of 13.5% (0.0086 ppm) of the applied at 363 days posttreatment (Table X, p. 53). Subdivision N Guidelines require the identification of residues present at levels ≥10% of the applied radioactivity. However, a reasonable attempt was made to extract [^{14}C]residues; soil samples were extracted three times with methanol:water (9:1, v:v) followed by two extractions with 0.1 *N* oxalic acid:DMF (1:1, v:v; p. 25).

9. The limits of detection and quantitation were not reported for TLC and HPLC analyses, and the limit of quantitation was not reported for LSC analysis. It is necessary that both limits of detection and quantitation be reported to allow the reviewer to evaluate the adequacy of the method for the determination of the test compound and its degradates.

10. The reviewer-calculated concentration data and the "percentages of the applied radioactivity present as parent and degradates" data represent the sum of the methanol:water and oxalic acid:DMF extractions analyzed by TLC (Tables XIA, XIB, pp. 54-59).

11. The parent compound contained addition ring structures that were not radiolabeled.

12. The soil series name was not reported.

13. The reviewer noted that concurrent recovery data were not reported. Generally, concurrent recovery data are reported to demonstrate the adequacy of the method.

Methanol/Water Extraction		Day 0	14	31	61	93	182	272	363
Parent	Rep 1	88.33	64.89	54.04	53.23	48.63	30.44	27.72	24.15
	Rep 2	76.40	61.79	56.44	50.30	48.62	33.06	27.85	24.93
	Average	82.37	63.34	55.24	51.77	48.63	31.75	27.79	24.54
CGA-190978	Rep 1	0.89	0.41	0.37	0.70	0.26	0.31	0.16	0.43
	Rep 2	0.71	0.43	0.17	0.89	0.26	0.30	0.24	0.27
	Average	0.80	0.42	0.27	0.80	0.26	0.31	0.20	0.35
CGA-189138	Rep 1	0.64	0.65	1.19	1.59	2.20	0.56	0.71	0.85
	Rep 2	0.67	0.51	1.13	1.72	2.00	0.57	0.82	0.95
	Average	0.66	0.58	1.16	1.66	2.10	0.57	0.77	0.90
CGA-205374	Rep 1	3.17	3.14	0.91	1.15	0.92	1.14	1.20	0.56
	Rep 2	2.08	3.01	1.08	1.20	0.96	1.29	1.21	0.54
	Average	2.63	3.08	1.00	1.18	0.94	1.22	1.21	0.55
CGA-205375	Rep 1	1.40	8.81	4.16	6.05	5.83	6.37	5.74	5.43
	Rep 2	1.21	8.17	4.66	5.91	5.91	6.37	6.03	5.94
	Average	1.31	8.49	4.41	5.98	5.87	6.37	5.89	5.69
Unknowns	Rep 1	0.61	4.67	5.82	1.34	1.75	3.07	2.15	1.68
	Rep 2	ND	4.42	0.97	3.55	2.18	2.60	1.54	1.66
	Average	0.61	4.55	3.40	2.45	1.97	2.84	1.85	1.67
Origin	Rep 1	1.76	1.21	1.26	1.80	0.26	0.52	0.54	0.93
	Rep 2	1.94	0.74	1.82	1.42	0.61	0.48	1.20	2.39
	Average	1.85	0.98	1.54	1.61	0.44	0.50	0.87	1.66

Oxalic acid/DMF Extraction		Day 0	14	31	61	93	182	272	363
Parent	Rep 1	ND	0.95	0.47	0.89	1.00	1.29	1.17	0.88
	Rep 2	ND	0.89	ND	1.88	1.09	1.02	1.24	1.48
	Average		0.92	0.47	1.39	1.05	1.16	1.21	1.18
CGA-190978	Rep 1	ND	0.25	0.02	0.38	0.34	0.09	0.17	0.09
	Rep 2	ND	0.05	ND	0.59	0.17	0.14	0.13	0.38
	Average		0.15	0.02	0.49	0.26	0.12	0.15	0.24
CGA-189138	Rep 1	ND	0.61	0.06	1.11	0.54	0.79	0.90	1.01
	Rep 2	ND	0.39	ND	0.96	0.46	0.57	0.63	0.52
	Average		0.50	0.06	1.04	0.50	0.68	0.77	0.77
CGA-205374	Rep 1	ND	0.26	0.03	0.63	0.35	0.57	0.62	0.67
	Rep 2	ND	0.14	ND	0.49	0.32	0.26	0.57	0.55
	Average		0.20	0.03	0.56	0.34	0.42	0.60	0.61
CGA-205375	Rep 1	ND	0.77	0.05	0.51	0.72	0.72	1.08	0.50
	Rep 2	ND	0.71	ND	0.31	0.57	0.32	0.63	1.24
	Average		0.74	0.05	0.41	0.65	0.52	0.86	0.87
Unknowns	Rep 1	ND	4.47	1.76	6.08	3.51	6.48	4.95	3.34
	Rep 2	ND	3.49	ND	5.89	2.72	3.91	3.82	1.52
	Average		3.98	1.76	5.99	3.12	5.20	4.39	2.43
Origin	Rep 1	ND	3.78	0.41	5.51	1.19	3.44	2.44	5.09
	Rep 2	ND	2.81	ND	6.78	1.62	3.40	4.95	5.56
	Average		3.30	0.41	6.15	1.41	3.42	3.70	5.33

Sum of both extractions		Day 0	14	31	61	93	182	272	363
Parent	Sum	82.4	64.3	55.7	53.2	49.7	32.9	29.0	25.7
CGA-190978	Sum	0.80	0.57	0.29	1.28	0.52	0.42	0.35	0.59
CGA-189138	Sum	0.66	1.08	1.22	2.69	2.60	1.25	1.53	1.67
CGA-205374	Sum	2.63	3.28	1.03	1.74	1.28	1.63	1.80	1.16
CGA-205375	Sum	1.31	9.23	4.46	6.39	6.52	6.89	6.74	6.56
Unknowns	Sum	0.61	8.53	5.16	8.43	5.08	8.03	6.23	4.10
Origins	Sum	1.85	4.27	1.95	7.76	1.84	3.92	4.57	6.99

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