DATA EVALUATION RECORD

STUDY 7

CHEM 128847 Difenoconozole §162-1 and §162-2
CAS No. 119446-68-3
FORMULATION--00-ACTIVE INGREDIENT

STUDY ID 42245133
Spare, W. C. 1992. Soil metabolism of CGA-169374 under aerobic, aerobic/anaerobic, and sterile conditions. Agrisearch Project No.: 1294. Unpublished study performed by Agrisearch Incorporated, Frederick, MD; and submitted by CIBA-GEIGY Corporation, Greensboro, NC.

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REVIEWED BY:	M. K. Mahoney, M.S.	Signature: MKMahoney
TITLE:	Scientist	Date: 4/26/00
EDITED BY:	B. S. Perkovich, M.E.M.	Signature: Brenda Perkovich
TITLE:	Scientist	Date: 4/25/00
APPROVED BY:	P. H. Howard, Ph.D.	Signature: C.A. Sutton for P.A. Howard
TITLE:	Project Manager	Date: 4/25/00
ORG:	Syracuse Research Corp. Arlington, VA 22202	
TEL:	703/413-9369	

APPROVED BY:	James A. Hetrick
TITLE:	Chemist
ORG:	ERB I/EFED/OPP
TEL:	703/305-5237

SIGNATURE:

(1)

CONCLUSIONS

Metabolism - Aerobic and Anaerobic Soil

1. Both the aerobic and anaerobic soil metabolism studies are scientifically valid and provides useful information on the soil metabolism of difenoconozole in sandy loam soil.

2. The anaerobic soil metabolism study does not meet Subdivision N Guidelines for the fulfillment of EPA data requirements for the following reasons:

   (i) the test water was not characterized; and

   (ii) redox potential, pH, and dissolved oxygen content data were not reported.

   The aerobic soil metabolism study meets Subdivision N Guidelines for the fulfillment of EPA data requirements.

3. In the aerobic soil metabolism study, triazole ring-labeled [3,5-^{14}C]difenoconozole, at a nominal application rate of 10 ppm, was relatively stable (registrant-calculated half-life of 679 days; $r^2 = 0.17$) in aerobic sandy loam soil that was incubated in darkness at 23.5-26.0°C for up to 365 days. All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application. Data are reviewer-calculated means of two replicates, each of which were analyzed by two different TLC systems (unless otherwise noted). Concentration data (in ppm) were reviewer-calculated based on the percentage of the applied radioactivity and the nominal application rate. The parent compound was initially 95.6% (9.6 ppm) of the applied radioactivity, was 82.2-83.0% (8.2-8.3 ppm) at 14-91days, and was 69.1% (6.9 ppm) at 365 days posttreatment. The minor degradate CGA-205374 (chemical name not reported) was initially (time 0) 0.9% (0.09 ppm) of the applied radioactivity and was 3.6% (0.36 ppm) at 365 days posttreatment (detected by only one TLC system). The minor degradate CGA 205375 was initially (time 0) 0.73% (0.073 ppm) of the applied radioactivity, was a maximum of 2.7% (0.27 ppm) at 181 days, and was 2.0% (0.2 ppm) at 365 days posttreatment. Nonextractable [^{14}C]residues were initially (time 0) 1.6% (0.16 ppm) of the applied radioactivity, increased to 6.0% (0.6 ppm) by 30 days and a maximum of 8.7% (0.87 ppm) by 181 days, and were 5.5% (0.55 ppm) at 272-365 days posttreatment. Total [^{14}C]volatiles were ≤0.9% (0.09 ppm) of the applied radioactivity throughout the incubation period.

   In aerobic sterile control samples, triazole ring-labeled [3,5-^{14}C]difenoconozole, at a nominal application rate of 10 ppm, was relatively stable in sterile, aerobic sandy loam soil that was incubated in darkness at 23.5-26.0°C for up to 181 days. All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application Data are reviewer-calculated means of two replicates, each of which were

analyzed by two different TLC systems. Concentration data (in ppm) were reviewer-calculated based on the percentage of the applied radioactivity and the nominal application rate. The parent compound was initially 95.6% (9.6 ppm) of the applied radioactivity and was 88.7% (8.9 ppm) at 181 days posttreatment. The minor degradate CGA-205374 was present at 0.35-0.95% (0.035-0.1 ppm) of the applied radioactivity at 30-181 days posttreatment (detected by only one TLC system). The minor degradate CGA-205375 was present at 0.60-1.7% (0.060-0.71 ppm) of the applied radioactivity at 30-181 days posttreatment. Nonextractable [^{14}C]residues were 2.1-3.8% (0.21-0.38 ppm) of the applied radioactivity at 30-181 days posttreatment. Total [^{14}C]volatiles were ≤0.1% (0.01 ppm) of the applied radioactivity.

In the anaerobic soil metabolism study, triazole ring-labeled [3,5-^{14}C]difenoconozole, at a nominal application rate of 10 ppm, was relatively stable in flooded sandy loam soil that was incubated anaerobically (nitrogen) in darkness at 23.5-26.0°C for up to 61 days following a 30-day aerobic incubation period. All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application Data are reviewer-calculated means of two replicates, each of which were analyzed by two different TLC systems. Data were not reported in units of concentration. Time-0 data were determined prior to flooding (following 30 days of aerobic incubation). Sampling intervals are reported as days following the initiation of the anaerobic phase of the study. In the total soil/water system, the parent compound was initially present at 82.6% of the applied radioactivity and was 75.7-79.7% at 29-61 days following the initiation of anaerobic conditions. In the soil phase, the parent compound was initially present at 82.6% of the applied radioactivity and was 73.1-77.2% at 29-61 days. The minor degradate CGA-205374 was initially (time 0) 1.9% of the applied radioactivity and was 3.6% at 61 days following the initiation of anaerobic conditions (detected by only one TLC system). The minor degradate CGA-205375 was initially (time 0) 1.1% of the applied radioactivity (three of four replicates) and increased to 2.5% by 61 days following the initiation of anaerobic conditions. Nonextractable [^{14}C]residues were initially (time 0) 6.0% of the applied radioactivity, were 6.2% at 29 days, and were 4.3% at 61 days following the initiation of anaerobic conditions. In the water phase, the parent compound was present at 2.5-2.7% of the applied radioactivity at 29-61 days following the initiation of anaerobic conditions. The minor degradate CGA-205374 was 0.7-0.9% of the applied radioactivity at 29-61 days following the initiation of anaerobic conditions (detected by only one TLC system). The minor degradate CGA-205375 was 0.45-1.1% of the applied radioactivity at 29-61 days following the initiation of anaerobic conditions. [^{14}C]Volatiles were not measured.

METHODOLOGY

Two bulk samples (305 g) of sieved (2 mm) Hesperia sandy loam soil (from Kerman, CA; 67% sand, 27% silt, 6% clay, 1.0% organic matter, pH 8.5, CEC 10.4 meq/100 g; p.

16) were each weighed into amber borosilicate glass bottles and treated with triazole ring-labeled [3,5-^{14}C]difenoconozole (CGA-169374; 1-[[2-[2-chloro-4-(4-chloro-phenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]-methyl]-1H-1,2,4-triazole; radiochemical purity 96.7%, specific activity 22.2 μCi/mg; p. 15; Figure 1, p. 42), dissolved in acetonitrile, at a nominal application rate of 10 ppm (p. 17). The bottles were roller-mixed for one hour prior to incubation to evenly distribute the compound. Subsamples (25 g) of the treated, mixed soil were weighed into Erlenmeyer flasks, wrapped in foil, adjusted to 75% of 0.33 bar moisture content, and aerobically incubated in darkness at 23.5-26.0°C for up to 365 days (Table II, p. 26); the flasks were sealed with polyurethane foam plugs. Sterile (autoclaved) soil samples were prepared and incubated under similar conditions. The soil moisture content was monitored periodically and water was added as needed (Table III, pp. 27-29). Moist, room-temperature air was pumped through the samples for eight hours each weekday (see Comment #10). To capture volatiles, selected samples (aerobic 12 months; sterile 6 months) were connected to an ethylene glycol trap, 1 *N* H_2SO_4 trap, and two 1 *N* NaOH traps (diagram presented in Figure 4, p. 45). Duplicate soil samples were removed for analysis at 0, 1, 3, 7, 14, 30, 91, 181, 272, and 365 days posttreatment during the aerobic phase (p. 14). Sterile soil samples were removed for analysis at 30 and 181 days posttreatment. Volatile trapping solutions were replaced at each sampling interval (p. 19).

Following 30 days of aerobic incubation, anaerobic conditions were induced in four samples by flooding with distilled water and pumping nitrogen gas through the flasks (p. 18); the flasks were sealed with Teflon-coated rubber stoppers (with septa) prior to nitrogen purging. The flasks were anaerobically incubated in darkness at 23.5-26.0°C (Table II, p. 26) for up to 2 months; dextrose (0.25 g) was added to each flask after two weeks of anaerobic incubation (p. 18). Duplicate soil samples were removed for analysis 1 and 2 months after anaerobic conditions were induced.

At each sampling interval, duplicate subsamples of each soil sample were analyzed for total radioactivity by LSC following combustion (p. 19). Soil samples were extracted twice by sonication with methanol:water (90:10, v:v), and the extracts were filtered. Samples collected at 91, 181, 272, and 365 days posttreatment were refluxed with methanol:water (90:10, v:v). Samples collected at 272 and 365 days posttreatment were further extracted by sonicating twice with 0.1 *N* oxalic acid:dimethyformamide (1:1, v:v) followed by refluxing with 0.1 *N* oxalic acid:dimethyformamide (1:1, v:v). The extracts were analyzed for total radioactivity by LSC. The methanol extracts were also analyzed by TLC on silica gel plates developed with acetonitrile (twice) OR chloroform:methanol: formic acid:water (75:20:4:2, v:v:v:v; p. 20). Samples were co-chromatographed with nonradiolabeled reference standards of the parent and potential degradates which were visualized with UV (254 nm) light (see Comment #8). Areas of radioactivity on the plates were quantified using radioimage scanning. Selected samples (12 months) were further analyzed by two-dimensional TLC on a silica gel plate developed in chloroform:methanol (9:1, v:v) followed by chloroform:methanol:formic acid:water

(75:20:4:2, v:v:v:v). The plates were exposed to x-ray film, and areas of radioactivity were scraped from the plates and analyzed by LSC. Duplicate subsamples of the post-extracted soil were analyzed by LSC following combustion (p. 19).

To confirm compound identities and isolate the parent, selected sample extracts (methanol:water) were analyzed by two-dimensional TLC on silica gel plates developed in chloroform:methanol (9:1, v:v) followed by toluene:ethyl formate:formic acid (5:7:1, v:v:v) OR developed in acetonitrile (twice) followed by toluene:acetone (3:1, v:v) and acetonitrile:ammonium hydroxide:water (6:1:1, v:v:v; p. 21). Samples were analyzed after two years of frozen storage (see Comment #3). Samples were co-chromatographed with nonradiolabeled reference standards which were visualized with UV (254 nm) light or Dragendorff's reagent spray followed by exposure to iodine vapors (see Comment #8). Areas of radioactivity on the plates were quantified by radioimage scanning.

At each sampling interval (29 and 61 days following the induction of anaerobic conditions), duplicate aliquots of the water layer from the anaerobic phase were analyzed for total radioactivity by LSC (p. 20). Aliquots of the water phase were analyzed by TLC (method not specified; p. 20).

At each sampling interval, duplicate aliquots of the volatile trapping solutions were analyzed for total radioactivity by LSC (p. 19).

To determine soil viability prior to treatment, at 6 and 12 months posttreatment, and at 1 month following the induction of anaerobic conditions, soil samples were analyzed by plating on plate count (bacteria), rose bengal (fungi), actinomycetes isolation (actinomycetes), and thioglycollate (anaerobes) agars (p. 16); results indicated that the soils were viable (Table IV, p. 30).

Sample extracts were stored frozen for more than two years at approximately -20°C prior to reanalysis by two-dimensional TLC (p. 21). To address frozen storage stability, the extracts analyzed for total radioactivity by LSC; losses of radioactivity during the storage period were not observed. Also, parent stability during storage was confirmed by TLC (method not specified; data not reported; see Comment #3).

DATA SUMMARY

Aerobic Soil Metabolism

Triazole ring-labeled [3,5-^{14}C]difenoconozole (radiochemical purity 96.7%), at a nominal application rate of 10 ppm, was relatively stable (registrant-calculated half-life of 679 days; $r^2 = 0.17$) in aerobic sandy loam soil that was incubated in darkness at 23.5-26.0°C for up to 365 days (Tables VIII, IX; pp. 34, 35; see Comments #4 and #5). All data,

reported as percentages of the applied radioactivity, represent percentages of the nominal application. Data are reviewer-calculated means of two replicates, each of which were analyzed by two different TLC systems (unless otherwise noted). Concentration data (in ppm) were reviewer-calculated based on the percentage of the applied radioactivity and the nominal application rate.

The parent compound was initially present in the soil at 95.6% (9.6 ppm) of the applied radioactivity, was 82.2-83.0% (8.2-8.3 ppm) of the applied at 14-91days posttreatment, and was 69.1% (6.9 ppm) of the applied at 365 days posttreatment (Tables VIII, IX; pp. 34, 35). The minor degradate CGA-205374 (chemical name not reported; structure provided in Figure 1, p. 42) was initially (time 0) 0.9% (0.09 ppm) of the applied radioactivity and was 3.6% (0.36 ppm) of the applied at 365 days posttreatment (detected by only one TLC system; Table IX, p. 35). The minor degradate CGA 205375 (chemical name not reported; structure provided in Figure 1, p. 42) was initially (time 0) present at 0.73% (0.073 ppm) of the applied radioactivity, was a maximum of 2.7% (0.27 ppm) of the applied at 181 days posttreatment, and was 2.0% (0.2 ppm) of the applied at 365 days posttreatment (Tables VIII, IX; pp. 34, 35). Seven unidentified minor degradates were each present at ≤3.4% (0.34 ppm) of the applied radioactivity throughout the incubation period (each detected by only one TLC system; see Comment #7). Uncharacterized origin material was initially (time 0) 0.63% (0.063 ppm) of the applied radioactivity and increased to a maximum of 5.4% (0.54 ppm) of the applied. Uncharacterized radioactivity was ≤5.8% (0.58 ppm) of the applied radioactivity (Table VI, p. 32). Nonextractable [^{14}C]residues were initially (time 0) 1.6% (0.16 ppm) of the applied radioactivity, increased to 6.0% (0.6 ppm) by 30 days and a maximum of 8.7% (0.87 ppm) by 181 days, and were 5.5% (0.55 ppm) of the applied at 272-365 days posttreatment. Total [^{14}C]volatiles were ≤0.9% (0.09 ppm) of the applied radioactivity throughout the incubation period.

Material balances (based on LSC analyses of individual replicates) were 90.4-108.7% of the applied radioactivity throughout the aerobic incubation period, with no observed pattern of decline (Table VI, p. 32).

Aerobic Sterile Control Samples

Triazole ring-labeled [3,5-^{14}C]difenoconozole (radiochemical purity 96.7%), at a nominal application rate of 10 ppm, was relatively stable in sterile, aerobic sandy loam soil that was incubated in darkness at 23.5-26.0°C for up to 181 days (Tables VIII, IX, pp. 34, 35; see Comments #4 and #5). All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application Data are reviewer-calculated means of two replicates, each of which were analyzed by two different TLC systems. Concentration data (in ppm) were reviewer-calculated based on the percentage of the applied radioactivity and the nominal application rate.

The parent compound was initially 95.6% (9.6 ppm) of the applied radioactivity and was 88.7% (8.9 ppm) of the applied at 181 days posttreatment (Tables VIII, IX, pp. 34, 35). The minor degradate CGA-205374 (chemical name not reported; structure provided in Figure 1, p. 42) was present at 0.35-0.95% (0.035-0.1 ppm) of the applied radioactivity at 30-181 days posttreatment (detected by only one TLC system; Table IX, p. 35). The minor degradate CGA-205375 was present at 0.60-1.7% (0.060-0.71 ppm) of the applied radioactivity at 30-181 days posttreatment (Tables VIII, IX, pp. 34, 35). Seven unidentified minor degradates were each present at ≤2.1% (0.21 ppm) of the applied radioactivity (each detected by only one TLC system; see Comment #7). Uncharacterized origin material was present at 1.5-1.8% (0.15-0.18 ppm) of the applied radioactivity at 30-181 days posttreatment. Nonextractable [^{14}C]residues were 2.1-3.8% (0.21-0.38 ppm) of the applied radioactivity at 30-181 days posttreatment (Table VII, p. 33). Total [^{14}C]volatiles were ≤0.1% (0.01 ppm) of the applied radioactivity.

Material balances (based on LSC analysis of individual replicates) were 96.7-99.0% of the applied radioactivity at 30 and 181 days posttreatment (Table VII, p. 33).

Anaerobic Soil Metabolism

Triazole ring-labeled [3,5-^{14}C]difenoconozole (radiochemical purity 96.7%), at a nominal application rate of 10 ppm, was relatively stable in flooded sandy loam soil that was incubated anaerobically (nitrogen) in darkness at 23.5-26.0°C for up to 61 days following a 30-day aerobic incubation period (Tables VIII, XI, pp. 34, 35; see Comments #4 and #5). All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application Data are reviewer-calculated means of two replicates, each of which were analyzed by two different TLC systems. Data were not reported in units of concentration. Time-0 data were determined prior to flooding (following 30 days of aerobic incubation). Sampling intervals are reported as days following the initiation of the anaerobic phase of the study.

In the total soil/water system, the parent compound was initially present at 82.6% of the applied radioactivity and was 75.7-79.7% of the applied at 29-61 days following the initiation of anaerobic conditions (Tables VIII, IX, pp. 34, 35). In the soil phase, the parent compound was initially present at 82.6% of the applied radioactivity and was 73.1-77.2% of the applied at 29-61 days. The minor degradate CGA-205374 (chemical name not reported; structure provided in Figure 1, p. 42) was initially (time 0) 1.9% of the applied radioactivity and was 3.6% of the applied at 61 days following the initiation of anaerobic conditions (detected by only one TLC system; Table IX, p. 35). The minor degradate CGA-205375 (chemical name not reported; structure provided in Figure 1, p. 42) was initially (time 0) 1.1% of the applied radioactivity (three of four replicates) and increased to 2.5% of the applied by 61 days following the initiation of anaerobic conditions (Tables VIII, IX, pp. 34, 35). Seven unidentified minor degradates were each present at ≤1.6% of the applied radioactivity (each detected by only one TLC system; see

Comment #7). Uncharacterized origin material initially (time 0) accounted for 1.2% of the applied radioactivity (three of four replicates) and was 1.7% of the applied at 61 days following the initiation of anaerobic conditions. Nonextractable [^{14}C]residues were initially (time 0) 6.0% of the applied radioactivity, were 6.2% of the applied at 29 days, and were 4.3% of the applied at 61 days following the initiation of anaerobic conditions (Tables VI, VII, pp. 32, 33). [^{14}C]Volatiles were not measured.

In the water phase, the parent compound was present at 2.5-2.7% of the applied radioactivity at 29-61 days following the initiation of anaerobic conditions (Tables VIII-IX, pp. 34-35). The minor degradate CGA-205374 (chemical name not reported; structure provided in Figure 1, p. 42) was 0.7-0.9% of the applied radioactivity at 29-61 days following the initiation of anaerobic conditions (detected by only one TLC system; Table IX, p. 35). The minor degradate CGA-205375 was 0.45-1.1% of the applied radioactivity at 29-61 days following the initiation of anaerobic conditions (Tables VIII-IX, pp. 34-35). Six unidentified minor degradates were each present at ≤0.8% of the applied radioactivity (each detected by only one TLC system; see Comment #7). Uncharacterized origin material was present at ≤2.6% of the applied radioactivity throughout the incubation period.

Material balances (based on LSC analysis of individual replicates) were 90.4-108.7% and 82.9-98.4% of the applied radioactivity throughout the aerobic and anaerobic incubation periods, respectively; a pattern of loss was not observed (Tables VI, VII, pp. 32, 33).

COMMENTS

1. The test water used to induce anaerobic conditions at 30 days posttreatment was not characterized as required by Subdivision N Guidelines. The study author stated that the test water was distilled (p. 18), but data on the pH and dissolved oxygen content were not provided. The characteristics of the test water are important to define the conditions under which the study was conducted.

2. Redox potential, pH, and dissolved oxygen content data were not reported in the anaerobic metabolism study. Subdivision N Guidelines require that such data be reported to confirm the presence of anaerobic conditions. The reviewer notes that anaerobic conditions in the test systems were induced by flooding with water and pumping nitrogen gas through the samples, and adding dextrose (two weeks after flooding and nitrogen purging) to stimulate oxygen consumption by bacteria. Generally, this is sufficient to produce anaerobic conditions.

3. Frozen storage stability data were inadequate. Sample extracts were stored frozen for more than two years at approximately -20°C prior to reanalysis by two-dimensional TLC (p. 21). To address frozen storage stability, the extracts were analyzed only for total

radioactivity by LSC; losses of radioactivity during the storage were not observed. Also, parent stability was confirmed by TLC (method not specified). The results of the TLC analysis used to confirm storage stability were not reported. Also, the study author did not describe any attempt or provided data to determine the storage stability of the degradate compounds. The reviewer noted that the TLC results for the parent compound prior to and following frozen storage were similar, despite the use of different TLC systems (Tables VIII-XII, pp. 34-38). However, the results for the degradate compounds were different; two additional degradates were identified after frozen storage and several unidentified degradates remained.

4. The reviewer notes that the parent compound was relatively stable in both aerobic and anaerobic sandy loam soil. The registrant-calculated half-lives for the parent in aerobic, anaerobic, and sterile aerobic sandy loam soil systems were 1059 days ($r^2 = 0.69$; Table XIII, p. 39), 679 days ($r^2 = 0.17$; Table XIV, p. 40), and 1811 days ($r^2 = 0.53$; Table XV, p. 41), respectively. At 365 days posttreatment (aerobic phase), the parent compound was still present at 75.6% of the applied radioactivity. Following 61 days of anaerobic incubation, the parent was still present at 78.2% of the applied radioactivity. In the sterile aerobic soil samples, the parent was still present at 89.7% of the applied radioactivity at 181 days posttreatment. The half-lives of the parent compound were estimated assuming the continuation of the apparent degradation pattern beyond the scope of the observed data. However, data which appear linear may become curvilinear with time, and half-life estimations based on extrapolated data may be inaccurate. In addition, only three data points were used to calculate the half-life of the parent under both anaerobic and sterile aerobic conditions. Generally, a minimum of four data points are necessary for the valid calculation of a half-life.

5. As reported in the methodology, the sample extracts were initially analyzed by two one-dimensional TLC systems and a two-dimensional TLC system was used as a confirmatory analysis (p. 20). The extracts were analyzed by two additional two-dimensional TLC systems as a confirmatory analysis following more than two years of frozen storage (p. 21; also see Comment #3). The reviewer notes that the results from the one-dimensional and two-dimensional analyses are not substantially different for the parent compound, but are different for the degradate compounds (Tables VIII-XII, pp. 34-38). The registrant-calculated half-lives (also see Comment #4) were based on the confirmatory TLC performed after frozen storage (Table XIII, XIV, pp. 39, 40); however, the reviewer chose to report the initial one-dimensional TLC results in the data summary of this DER. The initial results were reported because the data were not a confirmatory analysis and the storage stability was not an issue.

6. Residue data were only reported as percentages of the applied radioactivity. In future studies submitted to the EPA, it is necessary that residue data also be reported in units of concentration, such as ppm.

7. In each of the five TLC systems used in this study, unidentified minor degradates were isolated (Tables VIII-XII, pp. 34-38); however, due to the way in which the data were reported, the reviewer was unable to determine if the same unidentified degradates were observed in of the TLC systems. In future studies, it would be useful to designate each isolated area of unidentified radioactivity with a unique identifier based on its relative TLC retention factors (R_f).

8. The study author did not specify which potential degradates were used for co-chromatography. The reviewer notes that a list of analytical standards was provided in Table I (p. 25), and a list of relative TLC retention factors for the parent and possible degradation standards was provided in Table V (p. 31).

9. Method detection limits were not reported. Both limits of detection and quantitation should be reported to allow the reviewer to evaluate the adequacy of the method for the determination of the parent compound and its degradates.

10. It is unclear to the reviewer whether moist, CO_2-free air was pumped through all samples during the aerobic phase of the study or just the samples used to collect volatiles (12 month aerobic; 6 month sterile; p. 17). The reviewer notes that without air circulation, samples can become anaerobic, which would preclude a valid determination of the rate of aerobic metabolism. Clarification by the registrant may be necessary.

11. The study author did not provide the chemical names for the degradates CGA-205374 and CGA-205375. The chemical structures of the degradates were presented in Figure 1 (p. 42). In future studies submitted to the EPA, it is necessary that the chemical names and structures of the parent and its degradates be reported.

12. The aqueous solubility of the parent compound was reported as 20 ppm at 20 °C (unspecified pH; p. 15).

PIN 0509-04

EFED Review for MRID # 422451-33

Page_____ is not included in this copy.

Pages 11 through 33 are not included.

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 quality control procedures.

_____ Identity of the source of product ingredients.

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