Shaughnessy Number: Not available

Date out of EFGWB: _____

(4-24-91)

To: S. Robbins
Product Manager 23
Registration Division (H7505C)

From: Akiva Abramovitch, Section Head
Environmental Fate Review Section #3
Environmental Fate and Ground Water Branch
Environmental Fate and Effects Division (H7507C)

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

Attached, please find the EFGWB review of...

Reg./File #: 100-EUP-92

Chemical Name: 4-(cyclopropyl-α-hydroxy-methylene)-3,5-dioxocyclohexane carboxylic acid ethyl ester

Common Name: CGA-163935

Type Product: growth regulator

Product Name: CGA-163935 Technical and Primo/Vision Turf Growth Regulator

Company Name: Ciba-Geigy

Purpose: EUP -- turf use

Date Received: 9/12/90

Action Code: _____

EFGWB#(s): 90-0879

Total Reviewing Time (decimal days): 6

Deferrals to: ___ Ecological Effects Branch, EFED

___ Science Integration and Policy Staff, EFED

___ Non-Dietary Exposure Branch, HED

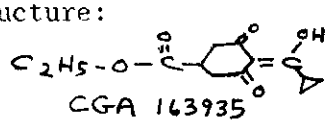
___ Dietary Exposure Branch, HED

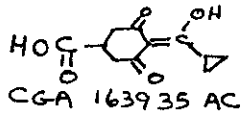
___ Toxicology Branch

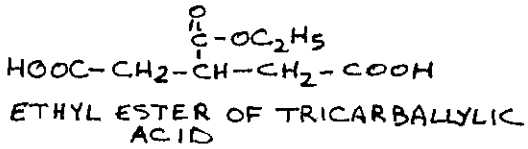
1. CHEMICAL:

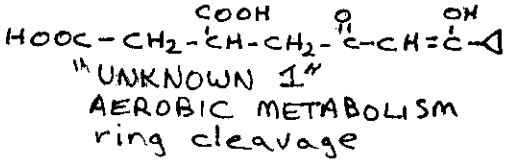
chemical name: 4-(cyclopropyl-α-hydroxy-methylene)-3,5-dioxo cyclohexane carboxylic acid ethyl ester

common name: CGA-163935
trade name: Primo/Vision
structure:


CGA 163935


CGA 163935 ACID


ETHYL ESTER OF TRICARBALLYLIC ACID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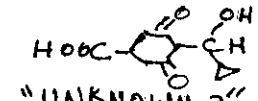
AEROBIC METABOLISM
ring cleavage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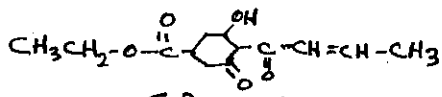
PROPOSED STRUCTURE
ANAEROBIC METABOLISM
double bond reduction


CROTONYL-CGA 163935

CAS #: not given
Shaughnessy #: not assigned

2. TEST MATERIAL: specified in DERs

3. STUDY/ACTION TYPE: submission of environmental fate data

4. STUDY IDENTIFICATION:

Szolics, I.M. **Summary for Environmental Fate Studies for CGA-163935.** performed and submitted by Ciba-Geigy Corp., Greensboro, NC. dated 7/6/90, received EPA 7/13/90 under MRID# 415639-295.

Spare, W.C. **Hydrolysis of ^{14}C-CGA-163935.** performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/21/90, received EPA 7/13/90 under MRID# 415639-30.

Spare, W.C. **Aqueous Photolysis of ^{14}C-CGA-163935.** performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/29/90, received EPA 7/13/90 under MRID# 415639-31.

Spare, W.C. **Soil Photolysis of ^{14}C-CGA-163935.** performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/21/90, received EPA 7/13/90 under MRID# 415639-32.

Spare, W.C. **Aerobic and Anaerobic Soil Metabolism of ^{14}C-CGA-163935.** performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/26/90, received EPA 7/13/90 under MRID# 415639-33.

Spare, W.C. **Leaching Characteristics of ^{14}C-CGA-163935.** performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/21/90, received EPA 7/13/90 under MRID# 415639-34.

Spare, W.C. **Leaching Characteristics of Aged ^{14}C-CGA-163935.** performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/22/90, received EPA 7/13/90 under MRID# 415639-35.

Spare, W.C. Adsorption/Desorption of ^{14}C-CGA-163935. performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 4/5/90, received EPA 7/13/90 under MRID# 415639-36.

Spare, W.C. Adsorption/Desorption of ^{14}C-CGA-163935 Acid. performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/21/90, received EPA 7/13/90 under MRID# 415639-37.

Spare, W.C. Laboratory Soil Volatility of ^{14}C-CGA-163935. performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/21/90, received EPA 7/13/90 under MRID# 415639-38.

Fackler, P.H. Bioconcentration and Elimination of ^{14}C-Residues by Bluegill (*Lepomis macrochirus*) Exposed to CGA-163935. performed by Springborn Laboratories, Inc., Wareham, MA. submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/29/90, received EPA 7/13/90 under MRID# 416042-07.

5. REVIEWED BY:

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

E.B. Conerly 4/4/91

6. APPROVED BY:

Typed Name: Akiva Abramovitch
Title: Section Head, Review Section 3
Organization: EFGWB/EFED/OPP

Akiva Abramovitch APR 24 1991

7. CONCLUSIONS:

1) Hydrolysis, aerobic and anaerobic soil metabolism, and leaching/adsorption/desorption data requirements are fully satisfied by these submissions.

2) Aqueous and soil photolysis, laboratory volatility, and fish bioaccumulation studies provide supplementary information, but do not fully satisfy guidelines requirements. In the case of the laboratory volatility and fish bioaccumulation studies, acceptable additional information, together with the present studies, could fully satisfy the requirements. The aqueous photolysis and soil photolysis studies cannot be salvaged, and new studies are required.

3) Fully acceptable data indicate that CGA-163935 hydrolyzes under basic conditions ($t_{\frac{1}{2}}$ ca. 8 days), but is stable under acid or neutral conditions. CGA-163935 is labile to aerobic metabolism ($t_{\frac{1}{2}}$ 8 hrs, in sandy loam). It is metabolized slowly under anaerobic conditions ($t_{\frac{1}{2}}$ 25 days). It is mobile in sand, loam, and sandy loam (k_{ads} 1.50, 0.67, 0.66, respectively). In clay, it is relatively immobile (k_{ads} 17.71). Supplemental information indicates rapid photolysis in water and soil and negligible volatilization; bioaccumulation in fish is minimal.

These data indicate that CGA-163935 itself would not ordinarily persist, but might do so in anaerobic conditions in acid or neutral water -- i.e. ground water -- if it reached such an area within a day or two of application.

However, its degradates have the potential for persistence. CGA-163935 would not likely persist in surface water, although it could reach these bodies.

8. RECOMMENDATIONS:

1) The applicant should be informed that three of the four requirements for the EUP, hydrolysis, aerobic soil metabolism, and leaching/adsorption/desorption data, have been fully satisfied. In addition, a satisfactory fish bioaccumulation study is required **for the EUP**. Available data from a study classified as supplemental indicate that CGA-163935 will not bioaccumulate in fish.

2) The applicant should provide additional information/explanation to complete requirements for laboratory volatility and fish bioaccumulation data.

3) The applicant should initiate aqueous and soil photolysis studies as soon as feasible, with attention to specific comments below and in the DERs. The applicant should use somewhat less intense light, and continue the incubation for long enough to establish the pattern of decline of the major degradates.

9. BACKGROUND:

CGA-163935 is a turf growth regulator. The applicant proposes a testing program which will encompass 3840 acres over a 2-year period, and require a total of 7680 pounds of active ingredient (2 lb/A). The applicant states that it is for non-food use, and grazing will not be allowed on the treated area (presumably this applies to the experimental plots, and is not intended to be a permanent prohibition).

All studies listed below are reviewed in this document. The status of data requirements is as follows:

hydrolysis -- MRID# 415639-30 -- **required for EUP** -- satisfied -- CGA-163935 loses the ethyl ester group with a $t_{\frac{1}{2}}$ of 8.1 days at pH 9, and is stable for thirty days at pH 5 and 7 (extrapolated $t_{\frac{1}{2}}$s of 228 and 455 days)

photolysis in water -- MRID# 415639-31 -- supplemental -- a new study is required. The persistence of the major degradates (the ethyl ester of tricarballylic acid and crotonyl CGA-163935) was not elucidated.

The study provides supplemental information that under experimental conditions, CGA-163935 degrades at pH 5 with a $t_{\frac{1}{2}}$ of ca. 8 hours, and at pH 7 with a $t_{\frac{1}{2}}$ of 14 - 16 hours. Photolysis was not tested at pH 9.

soil photodegradation -- MRID# 415639-32 -- supplemental -- A new study is required. Patterns of formation and decline of major degradates were not established. The current study is not useful for defining a photolysis half-life, but it does appear to indicate that photodegradation of CGA is rapid. However, since aerobic metabolism has a $t_{\frac{1}{2}}$ of only 4 hours under these conditions, that mechanism is likely to predominate.

aerobic soil metabolism -- MRID# 415639-33 -- **required for EUP** -- satisfied -- In sandy loam soil, CGA-163935 will undergo rapid metabolism and mineralization under aerobic conditions with a $t_{\frac{1}{2}}$ of ca. 8 hrs for the first step, release of CGA-163935 free acid.

anaerobic soil metabolism -- MRID# 415639-33 -- satisfied -- Anaerobic metabolism is considerably slower than aerobic, with a $t_{\frac{1}{2}}$ of 25 days for release of CGA-163935 free acid. The next step under anaerobic conditions is the saturation of the double bond adjacent to the cyclopropyl moiety.

leaching/adsorption/desorption

MRID# 415639-34, MRID# 415639-35 -- leaching -- **required for EUP** -- -- satisfied for unaged and aged CGA-163935. The compound is mobile in three of four soils tested. Estimated k_{ads} (Freundlich constants) calculated from these leaching results are 1.56 for sand, 0.11 for loam, 60.2 for clay, and 0.76 for sandy loam. For CGA-163935 aged on sandy loam, results are similar to that from unaged, with a calculated k_{ads} of 0.89, and a slightly higher proportion of CGA-163935 acid.

MRID# 415639-36, MRID# 415639-37 -- satisfied for CGA-163935 and CGA-163935 acid -- batch equilibrium. In three of four soils tested, CGA-163935 is highly mobile (k_{ads} 1.50 for sand, 0.67 for loam, 0.66 for sandy loam). In clay, it is relatively immobile (k_{ads} 17.77). These values are in general agreement with those from the leaching study. CGA-163935 acid yielded k_{ads} values of 3.22 for sand, 1.54 for loam, 16.4 for clay, 1.61 for sandy loam; desorption constants ranged between 3.55 and 21.5.

laboratory volatility -- MRID# 415639-38 -- supplemental -- will be satisfied if the applicant provides acceptable data summaries and raw data to confirm application rate and recoveries from soil combustion at various stages. At this time, it provides the supplemental information that CGA-163935 appears not to volatilize.

terrestrial field dissipation -- NOT SATISFIED -- no data reviewed -- for permanent registration, a turf dissipation study will be required

confined accumulation on rotational crops -- NOT SATISFIED -- no data reviewed -- no data are required as long as the use is limited to turf

fish bioaccumulation -- MRID# 416042-07 -- **required for EUP** -- supplemental -- may become fully satisfactory if the applicant provides acceptable supplemental information on the following:

1) whether the fish are age-matched, or randomly selected;
2) why they were fasted before sampling.

Based on this study, CGA-163935 will not tend to accumulate in fish.

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES: See individual DERs.

11. COMPLETION OF ONE-LINER: attached

12. CBI APPENDIX: attached to individual DERs

DATA EVALUATION REVIEW 1

I. Study Type: Environmental Fate Summary

II. Citation:

Szolics, I.M. **Summary for Environmental Fate Studies for CGA-163935.** performed and submitted by Ciba-Geigy Corp., Greensboro, NC. dated 7/6/90, received EPA 7/13/90 under MRID# 415639-29

III. Reviewer:

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

E.B. Conerly 4/4/91

IV. Conclusions:

This is not a study, but summarizes the environmental fate data reported in other documents discussed in this review. The submitter describes the results as follows:

hydrolysis -- hydrolyzes in basic solution (88% free acid after 30 days), stable in neutral or acidic solutions (>90% parent after 30 days)

photolysis -- soil and water -- rapid

metabolism in soil -- aerobic $t_{\frac{1}{2}}$ 3 - 6 hours; anaerobic $t_{\frac{1}{2}}$ 10 - 25 days

leaching -- low tendency to bind

volatility -- not volatile

fish bioaccumulation -- low uptake (BCFs 2.5 to 11); rapid depuration (no quantifiable residues after 3 days depuration)

V. Materials and Methods: n.a.

VI. Study Author's Results and/or Conclusions: described above

VII. Reviewer's Comments:

These results indicate a compound which is mobile but degrades rapidly, and does not bioaccumulate in fish.

VIII. CBI Information Addendum: n.a.

6

DATA EVALUATION REVIEW 2

I. Study Type: hydrolysis

II. Citation:

Spare, W.C. **Hydrolysis of ^{14}C-CGA-163935.** performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/21/90, received EPA 7/13/90 under MRID# 415639-30.

III. Reviewer:

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

E. B. Conerly 12/21/90

IV. Conclusions:

The study is acceptable to fulfill the requirement for hydrolysis data at pH 5, 7, and 9. CGA-163935 loses the ethyl ester group with a $t_{\frac{1}{2}}$ of 8.1 days at pH 9, and is stable for 30 days at pH 5 and 7 ($t_{\frac{1}{2}}$s of 228 and 455 days).

V. Materials and Methods:

test compound -- pure active ingredient 1,2,6-^{14}C-labelled CGA-163935, (radioactive purity 99.28%, sp. act. 30.0 µCi/mg)

test solution -- test compound (water solubility given as 2.7 g/100 ml) was dissolved in acetonitrile [10 µg/µl(10 µg/mg or 1 ppt)]

test protocol -- 450 µl aliquots were dissolved in 450 ml filter sterilized buffer, for a theoretical concentration of 10 ppm. The solutions were incubated in the dark (covered with foil) at 25 ± 1°C for 30 days.

sampling protocol -- sampled at 0, 3, and 6 hours, 1, 3, 7, 14, and 30 days

analytical methods

product identification

preparative -- immediately after sampling, solutions were subjected to TLC in two different solvents.[1] Plates were quantified using a Berthold TLC Linear Analyzer. Results demonstrated that ^{14}C-CGA-163935 was hydrolyzed at pH 9 with a calculated $t_{\frac{1}{2}}$ of 8.1 days. In pH 5 and 7 buffers, the $t_{\frac{1}{2}}$ was much longer than 30 days[2].

[1] For preparative work, silica gel plates were developed in one of two solvent systems:

1) toluene/dioxane/methanol/ammonium hydroxide (4:4:3:1)
2) toluene/acetone/formic acid 75:25:1 twice

[2] The extrapolated figures are 228 days for pH 5 and 456 days for pH 7. Since these intervals are well beyond the scope of the experiment, they are probably not too reliable.

7

confirmatory -- analyses on CGA-163935 and its free acid were performed using two 2-dimensional TLC systems[3] and HPLC.

quantification of radioactivity -- LSC

VI. Study Author's Results and/or Conclusions:

1) CGA-163935 is hydrolyzed in basic solutions, and hydrolysis may be a major degradative pathway in the environment in basic media.

2) Hydrolysis of CGA-163935 is substantially slower in neutral and acid environments.

VII. Reviewer's Comments:

1) The first reaction in hydrolysis of CGA-163935 in basic solution is nothing more than removal of the ethyl moiety, producing the free acid. This alteration of the molecule may not greatly change the pesticidal or toxicological characteristics of the compound.

2) Overall recoveries of labelled material were not explicitly given, but in the case of pH 5 and 7, more than 90% of the radioactivity added was recovered as parent compound. At pH 9, recoveries of parent compound and free acid totaled more than 90% at all but two time points, which were 86 and 89% respectively. This is acceptable.

2) The half-life calculations appear to be accurate. The extrapolated $t_{\frac{1}{2}}$s for pH 5 and 7 are well beyond the experimental period, and are probably inaccurate, although they may approximately indicate the magnitude of the half lives.

3) Although a small amount of organic solvent is permitted to be used in studies of this type, the water solubility of CGA-163935 is certainly sufficient that this was not necessary. EFGWB would appreciate an explanation for the record.

VIII. CBI Information Addendum: attached

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[3] For confirmation of products, 2-dimensional systems were used:

1) solvent 1 -- toluene/dioxane/methanol/ammonium hydroxide 4:4:3:1
solvent 2 -- butanol/water/acetic acid 4:1:5

2) solvent 1 -- 100% acetonitrile
solvent 2 -- toluene/dioxane/methanol/ammonium hydroxide 4:4:3:1

8

Page ___ is not included in this copy.

Pages 9 through 30 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 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.

✓ 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.

DATA EVALUATION REVIEW 3

I. Study Type: aqueous photolysis

II. Citation:

Spare, W.C. Aqueous Photolysis of ^{14}C-CGA-163935. performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/29/90, received EPA 7/13/90 under MRID# 415639-31.

III. Reviewer:

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

E. B Conerly 4/23/91

IV. Conclusions:

The study is scientifically sound, but does not fully satisfy the requirement because the persistence of one of the major degradates, ethyl ester of tricarballylic acid, was not elucidated. At 72 hours at pH 7, it represented approximately 82% of the applied dose. The photolytic half-life of this degradate has not been established. A new study is required, using somewhat less intense light, and continuing the incubation until the pattern of formation and decline of the degradate is established.

It provides the supplemental information that, under experimental conditions, CGA-163935 degrades at pH 5 with a $t_{\frac{1}{2}}$ of ca. 8 hours, and at pH 7 with a $t_{\frac{1}{2}}$ of 14 - 16 hours.

V. Materials and Methods:

test compound -- pure active ingredient 1,2,6-^{14}C-labelled CGA-163935, (radioactive purity >99%, sp. act. 20.7 µCi/mg)

stock solution -- test compound (water solubility = 2.7 g/100 ml at pH 5 and 0.5 gm/100 ml at pH 7) was dissolved in acetonitrile [10 mg/ml (1 ppt)]

test solutions
- kinetic exposure at pH 7 -- stock solution diluted to 10 µg/ml with buffer (3.5 µl/3.5 ml)
- kinetic exposure at pH 5 -- diluted as for pH 7
- bulk exposure at pHs 5 and 7 -- diluted as for the kinetic exposure but 100µl/100 ml

test protocol -- aliquots were incubated under artificial light (xenon arc lamp) for up to 72 hrs at 24.9 $\pm$ 1½ °C. The light source provided 3.7 x 10^{-5} to 4 x 10^{-5} W/cm^2, vs natural sunlight (clear sunny afternoon in Frederick, MD) which provided 2.0 to 2.6 x 10^{-5} W/cm^2.

sampling protocol
- pH 5 -- sampled at 0, 1, 2, 4, 6, 8, 12, 16, and 21 hours
- pH 7 -- sampled at 0, 0.5, 1, 2, 4, 8, 24, 48, and 72 hours
- pH 9 -- not done, *since rapid degradation by hydrolysis had been demonstrated*, per the applicant.

analytical methods

product identification

preparative -- immediately after sampling, solutions were subjected to TLC in one of two different solvents[1]. Plates were scanned using an Ambis Radioanalytical Imaging system.

confirmatory -- analyses on degradates were performed using two different 2-dimensional TLC systems[2], HPLC, and MS.

quantification of radioactivity -- LSC

VI. Study Author's Results and/or Conclusions:

1) CGA-163935 degraded on exposure to xenon arc light.

2) The calculated $t_{\frac{1}{2}}$ for pH 5 was ca. 8 hrs; for pH 7, it was 14 - 16 hrs.

3) Major photoproducts included crotonyl CGA-163935 and the ethyl ester of tricarballylic acid. [Results are summarized in attached data.]

VII. Reviewer's Comments:

1) The major degradate, ethyl ester of tricarballylic acid, was still increasing when the experiment was discontinued. This is a matter of concern depending on the toxicity and actual longevity of this compound.

2) The artificial light source is probably not equivalent to natural light, since it provides approximately double the light energy of a sunny summer day, which represents the most intense natural light. This tends to give a rate of photodegradation much higher than would occur ordinarily, causing $t_{\frac{1}{2}}$ to be underestimated.

3) Although the use of a small amount of organic solvent (less than 1%) is permitted, it seems unnecessary in this case given the water solubility of CGA-163935.

4) Based on submitted data (attached), there was little, if any, volatile material produced during the incubation.

VIII. CBI Information Addendum: attached

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[1]For preparative work, silica gel plates were developed in one of two solvent systems:

1) toluene/dioxane/methanol/ammonium hydroxide (4:4:3:1)
2) toluene/acetone/formic acid 75:25:1 twice

[2]For confirmation of products, two 2-dimensional systems were used:

1) solvent 1 -- toluene/acetone/formic acid 75:25:1
solvent 2 -- toluene/dioxane/methanol/ammonium hydroxide 4:4:3:1

2) solvent 1 -- toluene/acetone/formic acid 75:25:1
solvent 2 -- chloroform/methanol/formic acid/water 75:20:4:2

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Pages 33 through 66 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 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.

✓ 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.

DATA EVALUATION REVIEW 4

I. Study Type: soil photolysis

II. Citation:

Spare, W.C. Soil Photolysis of ^{14}C-CGA-163935. performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/21/90, received EPA 7/13/90 under MRID# 415639-32.

III. Reviewer:

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

E. B. Conerly 4/23/91

IV. Conclusions:

The study does not fully satisfy the requirement for soil photolysis data, and cannot be made acceptable by submission of additional information. A new study is required. The study does not establish a reliable half-life for CGA-163935 because the light source was approximately twice the intensity of a sunny summer day (*per the applicant*). The half-lives of major degradates were not established. It does provide supplemental information that photolysis of CGA-163935 on soil, a combination of metabolism and photodegradation, can be expected to be rapid, with metabolism as the probable rate-limiting process. The data specifically suggest that the light inhibited metabolism, since the light-exposed sample yielded a half-life twice as long as the comparable dark control.

V. Materials and Methods:

test compound -- pure active ingredient 1,2,6-^{14}C-labelled CGA-163935, (radioactive purity >99%, sp. act. 20.7 µCi/mg)

stock solutions -- test compound (water solubility 2.7 g/100 ml at pH 5 and 0.5 gm/100 ml at pH 7) was dissolved in acetonitrile [10 mg/ml (1 ppt)]. This solution was further diluted with acetonitrile to 2 µg/ml (2 ppm).

test soil -- Maryland sandy loam

test protocol

exposure 1 -- 1/17/90 through 2/16/90 -- 200 ppm CGA-163935 applied to air-dried soil films on glass slides; sampled at 2, 4, 6, 12, 24, 36, 72, 180, and 360 hrs. Temperature was 24.9 ± 1.0 °C.

exposure 2 -- 2/20-21/90 -- CGA-163935 applied at 10 ppm to active moist soil in test tubes; sampled at 1, 2, 3, 4, 6, 8, and 16 hrs. Temperature was 24.9 ± 1.0 °C.

exposure 3 -- 4/4 - 5/4/90 -- CGA-163935 was applied at 200 ppm to sterile (Γ-ray) air-dry soil on glass slides; sampled at 24, 60, 108, 204, 252, and 360 hrs. Temperature was 24.5 ± 1.1 °C.

analytical methods

soil extraction

1) sonication 30 - 60" with MeOH/H_2O/formic acid 90:10:2
2) refluxing 30 - 60" with MeOH/H_2O/formic acid 90:10:2
3) sonication 30 - 60" with MeOH/H_2O/formic acid 50:50:2
4) refluxing 30 - 60" with MeOH/H_2O/formic acid 50:50:2

(5)

5) sonication 30" with 0.1N oxalic acid/ dimethylformamide 1:1

6) refluxing 30" with 0.1N oxalic acid/ dimethylformamide 1:1

product identification

preparative

immediately after sampling, solutions were subjected to TLC in one of two different solvents[1].

confirmatory

analyses on degradates were performed using two different 2-dimensional TLC systems[2], HPLC, and MS.

quantification of radioactivity -- LSC

VI. Study Author's Results and/or Conclusions:

1) CGA-163935 on soil films and soil surfaces degraded on exposure to xenon arc light.

2) The calculated $t_{\frac{1}{2}}$ was ca. 24 days (288 hours of 12 hour days) for the dry soil film, and ca. 8 hrs on active moist soil. The half-life was 10 days (125 hours of 12 hour days) for sterilized soil.

3) A dark control for active moist soil yielded a $t_{\frac{1}{2}}$ of 4 hrs, showing a reaction more rapid than the light-exposed samples. This indicates that exposure to light slows metabolic degradation.

4) Average extractable radiocarbon was 99.3% of dose on exposed dry soil film and 94.1% on moist active soils. 108.7% was extractable on dry soil kept in the dark, and 93.9% from moist active soil dark controls. Combustion was therefore not performed on these soils. Average recovery from exposed sterile soil film was 83.5% of dose, and from the dark sterile controls was 102.7%. These soils were combusted, but the additional radioactivity was not recovered. No further effort was made with these samples.

4) Major products included crotonyl CGA-163935; the ethyl ester of tricarballylic acid; and CGA-163935 free acid. [Results are summarized in attached data.]

VII. Reviewer's Comments:

1) It is difficult to determine whether degradates have peaked or reached a plateau at the termination of the experiment. This is a matter of concern depending on their toxicities and actual half-lives.

---

[1]For preparative work, silica gel plates were developed in one of two solvent systems:

1) toluene/dioxane/methanol/ammonium hydroxide (4:4:3:1)
2) toluene/acetone/formic acid 75:25:1 twice

[2]For confirmation of products, one of two 2-dimensional systems was used:

1) solvent 1 -- toluene/acetone/formic acid 75:25:1 twice
solvent 2 -- toluene/dioxane/methanol/ammonium hydroxide 4:4:3:1

2) solvent 1 -- toluene/acetone/formic acid 75:25:1
solvent 2 -- chloroform/methanol/formic acid/water 75:20:4:2

2) This reviewer does not agree with the applicant's assertion that the artificial light source is equivalent to natural light. The light intensity was measured at 3.7×10^{-5} W/cm^2. As a comparison, in another study the applicant reported that natural sunlight on a clear sunny afternoon in Frederick, MD) provided 2.0 to 2.6×10^{-5} W/cm^2. A sunny summer day represents the most intense natural light, and the artificial source provides approximately double that. In most cases, this tends to give a estimated rate of light-mediated decomposition much higher than would occur under ordinary natural conditions, and also affect the microbial metabolism which is occurring simultaneously. The data in this study indicate that the light severely inhibited metabolism, which is the major mode of degradation in this case. The moist dark control showed a twofold **faster** degradation than did the moist light exposed sample, half-lives of 4 hours versus 8 hours. Exposure of sterile and dry films yielded half-lives of 10 and 24 days (12 hour days) respectively.

3) Except possibly in the sterilized soil, there was little, if any, volatile material produced during the incubation.

4) The reviewer's task is made simpler, and indeed, a better review results, when data are summarized concisely and in tabular form. Unfortunately this was not done in this case.

5) Although the use of a small amount of organic solvent (less than 1%) is permitted to be used, it seems unnecessary in this case given the water solubility of CGA-163935. However, this is not likely to have influenced the results of the study.

VIII. CBI Information Addendum: attached

Page ___ is not included in this copy.

Pages 70 through 99 are not included in this copy.

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_____ 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.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

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DATA EVALUATION REVIEW 5

I. Study Type: aerobic and anaerobic soil metabolism

II. Citation:

Spare, W.C. Aerobic and Anaerobic Soil Metabolism of ^{14}C-CGA-163935. performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/26/90, received EPA 7/13/90 under MRID# 415639-33.

III. Reviewer:

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

E.B. Conerly 4/23/91

IV. Conclusions:

The study is acceptable to fulfill the requirement for data on aerobic and anaerobic soil metabolism.

1) In sandy loam soil, CGA-163935 will metabolize and mineralize rapidly under aerobic conditions with a $t_{\frac{1}{2}}$ of ca. 8 hrs for the first step, release of CGA-163935 free acid ($t_{\frac{1}{2}}$ ca. 20 hrs.).

2) Anaerobic metabolism has a $t_{\frac{1}{2}}$ of 25 days for release of CGA-163935 free acid. The next *proposed* step under anaerobic conditions is the saturation of the exocyclic double bond of the cyclopropyl moiety (structure proposed, could not be confirmed). These compounds will probably persist, and could contaminate ground water.

V. Materials and Methods:

test compounds
ring-labelled ^{14}C-CGA-163935 -- sp. act. 20.7 µCi/mg, radiopurity 98.3% -- dissolved in acetonitrile at 10 mg/ml (= 10 ppt)
carbonyl-labelled ^{14}C-CGA-163935 -- sp. act. 22.1 µCi/mg, radiopurity 99.5%

test soil -- Maryland sandy loam (characteristics attached), sieved (2 mm mesh) before use.

test protocol -- test compound, ring or carbonyl labelled CGA-163935 applied at 10 ppm [0.25 mg to 25 gm] into soil. Shorter-term samples were dosed individually and roller-mixed during the incubation or up to 6 hrs. For all incubations longer than 24 hours, soil was dosed in bulk at 20 ppm and roller-mixed for 6 hrs. Zero-time analysis was performed immediately after dosing, with no roller-mixing. To each flask 25 gm (dry weight) of dosed sandy loam soil was added randomly from the bulk dosed soil. For sterile incubations, 25 gm of sterile (autoclaved or Γ-irradiated) soil was dosed individually at 10 ppm and hand mixed.

100

aerobic incubation -- fourteen 25 gm samples were dosed with either ring or carbonyl labelled CGA-163935, sealed with screw caps and roller-mixed up to 6 hrs. 8 and 18 hr samples were roller-mixed for 6 hrs, then placed in a laboratory incubator at 25 $\pm$ 1 ^{0}C for the remaining time. Eighteen soil samples were similarly prepared, dosed, and connected to the metabolism apparatus (figure 2 attached).

anaerobic incubation -- after 6 hrs aerobic incubation during roller-mixing, samples of 25 gm each of dosed soil was placed into flasks,flooded with 50 ml distilled water, foil wrapped, and sealed. Each chamber was flushed for 30 minutes with compressed N_2 gas at ca. 40 - 60 ml/minute. All flasks were incubated at 25 $\pm$ 1 ^{0}C. Flasks intended for sampling after 60 days anaerobic incubation were connected to the metabolism apparatus and flushed with N_2 under positive pressure at 40 - 60 ml/min for 60 minutes. After 2 wks incubation, 0.25 gm dextrose was added to each anaerobic chamber to encourage utilization of all available oxygen and thus aid conversion to anaerobic conditions. All anaerobic chambers were again flushed with N_2 under positive pressure at 40 - 60 ml/min for 60 minutes and returned to the incubator. Anaerobic chambers were periodically flushed with nitrogen during incubation. Later, after 6 hrs aerobic incubation, four additional samples were prepared with ring labelled CGA-163935 and treated as above, except that no volatile traps were used.

sterile incubation -- four individual flasks were treated with each of the two labelled compounds.

sampling protocol

aerobic flasks were sampled at designated times
anaerobic flasks were sampled at 1 and 2 months
sterile flasks were sampled at 30 days and 3 months
trapping solutions were analyzed at each soil sampling period after one day, or weekly, whichever was more frequent

soil extraction

For anaerobic samples, water was decanted from the flasks and centrifuged to pellet the soil, which was added to the soil remaining in the flask. Soils were extracted with MeOH/H_2O/formic acid 90:10:2 by sonication 2 x for 30 min. Solvent was removed by vacuum filtration or centrifugation, with the soil cake subsequently refluxed with MeOH/H_2O/formic acid 50:50:2. Solutions were again removed by filtration or centrifugation. Filtered soils were allowed to air dry, while centrifuged samples remained moist. The extraction solution was further analyzed for total radioactivity and product identification.

Residues not extracted by the above procedure were quantified by combustion of the soil and determination of the total radioactivity released. Further extraction was performed in an

effort to characterize the bound residues. Soil samples were sonicated (2 x for 30 min) followed by a 2 hr reflux with 0.1 N oxalic acid/dimethylformamide 1:1. The volume of each extract was measured and [the amount of radioactivity released into the extract] quantified by LSC. The extract was partitioned 3 x with chloroform/ethyl acetate 1:1. After each partition the organic phase was collected through anhydrous sodium sulfate, combined and quantitated. The combined organic phase was concentrated and analyzed. Residues not extracted by these two procedures were quantified by combustion of the soil and determination of the total radioactivity released.

analytical methods

LSC -- total radioactivity

degradate identification

1) preparative TLC -- in one of the two following systems
   SS1 -- toluene/acetone/formic acid 75:25:1 twice
   SS2 -- toluene/dioxane/methanol/ammonium hydroxide 4:4:3:1
2) confirmatory TLC
   1-dimensional in solvent system 1 (SS1) below
   2-dimensional
   SS1 - toluene/acetone/formic acid (90%) 150:50:2
   SS2 - chloroform/methanol/formic acid (90%)/H_2O 150:40:8:4
3) HPLC in an acetonitrile/0.1 M phosphoric acid system
4) biphasic partition -- samples were adjusted to pH 5 with 90% formic acid and partitioned 2 x with 50 ml $MeCl_2$. The two $MeCl_2$ fractions were combined and passed through sodium sulfate to remove any remaining water, and concentrated by rotary evaporation.
5) base hydrolysis
6) GC/MS

VI. Study Author's Results and/or Conclusions:

1) CGA-163935 was rapidly metabolized under aerobic conditions in Maryland sandy loam soil to CGA-163935 with a 3 to 6 hour half-life. Continued incubation resulted in loss of CGA-163935 acid with copious production of CO_2, up to 56% of applied radiocarbon by 90 days. Ring cleavage at the carbonyl group resulted in the other isolated degradate with further oxidation to a series of easily oxidized two-carbon units with a cyclopropyl group.

2) The estimated half-life of CGA-163935 under anaerobic conditions (10-25 days) was determined using specified sampling intervals of 1 month and 2 months. The major products of anaerobic metabolism were the CGA-163935 acid and the reduced exocyclic double bond from the CGA-163935 acid.

3) Radiocarbon balance averaged 104, 97, and 103% of dose for aerobic, anaerobic, and sterile incubations respectively.

VII. Reviewer's Comments:

1) The initial step in the metabolism, the removal of the ethyl ester, is a relatively minor change in the molecule, and may not result in greatly altered toxicological or pesticidal properties. The $t_{\frac{1}{2}}$ of the free acid is ca. 20 days, which is considered moderately short. There would likely not be a problem of persistence under aerobic conditions.

2) The $t_{\frac{1}{2}}$ for production of the free acid under anaerobic conditions appears to be 25 - 30 days based on figure 41. The submitter states that mineralization does not take place under these conditions -- this is to be expected. The first and second degradates have the potential to persist and accumulate where CGA-163935 is used if anaerobiasis prevails, e.g. ground water.

3) EFGWB notes the efforts made to confirm the structure of "unknown 3", and accepts as "proposed" the structure given.

VIII. CBI Information Addendum: attached

Page ___ is not included in this copy.

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_____ 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.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

✓ FIFRA registration data.

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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.

DATA EVALUATION REVIEW 6

I. Study Type: aged and unaged leaching

II. Citation:

Spare, W.C. Leaching Characteristics of ^{14}C-CGA-163935. performed by Agrisearch Inc., Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/21/90; rec'd EPA 7/13/90, MRID# 415639-34.

Spare, W.C. Leaching Characteristics of Aged ^{14}C-CGA-163935. performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/22/90; rec'd EPA 7/13/90, MRID# 415639-35.

III. Reviewer:

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

E.B. Conerly 4/23/91

IV. Conclusions:

The study, together with the study discussed in DER 7, is acceptable to fulfill the requirement for mobility of unaged CGA-163935. The compound is mobile in three of four soils tested. Approximate estimated k_{ads} (Freundlich constants) calculated from these leaching results are 1.56 for sand, 0.11 for loam, 60.2 for clay, and 0.76 for sandy loam. CGA-163935 aged on sandy loam yields a calculated k_{ads} of 0.89, which is similar to that from unaged; the leachate contains a slightly higher proportion of CGA-163935 acid. Additional mobility data, batch adsorption/desorption studies, were also submitted, and are discussed in DER 7.

V. Materials and Methods:

test soils -- sand, sandy loam, loam, clay (details attached) air-dried and sieved (2 mm mesh) before use

test compound -- ^{14}C-CGA-163935, spec. act. 30 µCi/mg, radiopurity > 99% (unaged) and 98.7 (aged)

stock solution -- 10 mg/ml in acetonitrile

test solution -- 50 µl stock + 500 µl acetonitrile placed directly in borosilicate bottles

application method -- after the solvent had evaporated from the test solutions, 50 gm soil was added to the bottles and the contents were roller-mixed for 2 hrs at 125 rpm. Homogeneity and applied concentration (nominal 10 ppm) were checked by combustion of 3 to 6 random aliquots for each type of soil.

test protocol -- 10 gm of dosed soil was applied as a top layer over a prepared column (3" diameter, 12" long) of soil. For the aged study the soil was aged for 5 hours (1 $t_{\frac{1}{2}}$ per the applicant) before application to the column, and only sandy loam was tested. The columns were leached with the equivalent of 20 inches of water at the rate of 1"/hr. Following this procedure the total leachate from the column was measured and each column divided into 1" sections. Soil and leachate were quantified for radioactivity.

156

soil extraction

unaged -- no extractions were performed on the unaged soils

aged -- 50 gm soil samples were sonicated 2 x for 30 min with 75 ml MeOH/H_2O/formic acid 9:1:0.2, then refluxed 2 hrs with 75 ml MeOH/H_2O/formic acid 5:5:0.2. Another sonication followed in 0.1 M oxalic acid/DMF 1:1. Extracted soil was then refluxed for 2 hrs with 0.1M oxalic acid/DMF 1:1. The two oxalic acid fractions were combined and partitioned 3 x with chloroform/ethyl acetate 1:1. The organic fraction was rotary evaporated for TLC analysis. The methanol/H_2O/formic acid fractions were combined and concentrated directly by rotary evaporation for TLC.

analytical methods

LSC -- total radioactivity of liquid samples and combusted soils

TLC -- identity of compounds in the leachates was established by chromatography in two systems previously described.

unaged -- 1-dimensional in either SS1 or SS2

SS1 - toluene/dioxane/methanol/ammonium hydroxide 4:4:3:1

SS2 - toluene/acetone/formic acid 75:25:1 twice

aged

1-dimensional in either SS1 or SS2

SS1 - toluene/dioxane/methanol/ammonium hydroxide 4:4:3:1

SS2 - toluene/acetone/formic acid 75:25:1 twice

2-dimensional in the system below

a) SS2 above

b) chloroform/methanol/formic acid/H_2O 80:15:4:2

VI. Study Author's Results and/or Conclusions:

Unaged:

1) Results demonstrated that parent CGA-163935 would leach in sand, sandy loam, and loam soils. Clay showed little leaching.

2) The material balance for the clay was poor, indicating loss of ^{14}C, probably due to metabolic mineralization during the 17 - 20 day leaching period. Material balances for the other three soils ranged from 80 to 101%.

3) For sand, 35.1% of the applied dose was in the leachate, of which 81% was parent and 11% was CGA-163935 acid.

4) For sandy loam, 45.4% of the applied dose was in the leachate, of which 94% [*42.7% of applied*] was CGA-163935 acid and 2% [*1.9% of applied*] was parent.

5) For loam, 87% of the applied dose was in the leachate, of which 38% was parent and 56% was CGA-163935 acid.

6) Approximate k_{ads} (Freundlich constants) calculated from these results are 1.56 for sand, 0.11 for loam, 60.2 for clay, and 0.76 for sandy loam.

Aged:

1) The approximate k_{ads} of the sandy loam was 0.89. Approximately 62% of the applied dose was found in the leachate (57% CGA-163935 acid, 2% parent, and 3% polar metabolites).

VII. Reviewer's Comments:

1) Column leaching is an acceptable method for determining mobility. Although it is not an "official" policy, EFGWB tends to prefer batch equilibrium data, since this is most easily comparable among different chemicals, and will provide Freundlich constants by the most direct method. A batch study has been submitted and is discussed in DER 7.

2) The method of application, i.e., ablation of the dried compound from the vessel walls by roller mixing with soil, is certainly unusual [at least in this reviewer's experience], but appears to have given good results.

2) Product identification by TLC alone is not considered definitive in most cases. However, these products have been confirmed by MS and HPLC in other studies in this submission. For the aged soil in this study two different solvent systems were used, as well as co-chromatographed standards. Approximately the same patterns should exist with the unaged soil, since the metabolic half-life is short, and the leaching period is long relative to it.

3) Aging the treated soil for five hours before applying it to the column will have little effect since the 2-day leaching period was considerably longer than the metabolic half-life of the compound. As is to be expected, results from the aged leaching study agree well with those from the unaged study.

VIII. CBI Information Addendum: attached

Page ___ is not included in this copy.

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_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

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_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

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DATA EVALUATION REVIEW 7

I. Study Type: adsorption/desorption

II. Citation:

Spare, W.C. **Adsorption/Desorption of ^{14}C-CGA-163935**. performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 4/5/90; rec'd EPA 7/13/90, MRID# 415639-36.

Spare, W.C. **Adsorption/Desorption of ^{14}C-CGA-163935 Acid**. performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/21/90; rec'd EPA 7/13/90, MRID# 415639-37.

III. Reviewer:

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

E. B. Conerly 12/21/90

IV. Conclusions:

The studies are acceptable to fulfill the requirement for mobility (leaching adsorption/desorption) data. In three of four soils tested, CGA-163935 is highly mobile. The adsorption constants were 1.50 for sand, 0.67 for loam, and 0.66 for sandy loam. In clay, it was relatively immobile (k_{ads} 17.77).

CGA-163935 acid was somewhat less mobile in the same soils (k_{ads} were 3.22 for sand, 1.54 for loam, 1.61 for sandy loam). In clay, it was relatively immobile (k_{ads} 16.4). The approximate k_{ads} (Freundlich constant) *calculated from the leaching results* is 0.89 for sandy loam.

These data indicate a potential for ground and surface water contamination from parent and major degradate in some circumstances.

V. Materials and Methods:

test soils -- clay, sand, sandy loam, and loam (details attached)

CGA-163935

test compound -- ^{14}C-CGA-163935, spec. act. 30 µCi/mg, radiopurity 97.9%

stock solution -- 10 mg/ml in acetonitrile

test solutions -- 0.2 ml of stock solution was further diluted in 0.01 calcium acetate solution. This was used at 10 µg/ml = 10 ppm (undiluted test solution), 5 µg/ml, 1 µg/ml, 0.5 µg/ml, 0.2 µg/ml, and, as a control, 0.0 µg/ml (= calcium acetate solution with no added CGA-163935).

test protocol -- following a range-finding study, samples were prepared for each of the four soils and six concentrations listed above at soil/solution ratios of 4 gm/20 ml. These preparations were shaken for 8 hours, and centrifuged. Following centrifugation, soil pellets were desorbed with fresh calcium acetate solutions.

analytical method -- 1-dimensional TLC in two different systems
toluene/dioxane/methanol/ammonium hydroxide 4:4:3:1
toluene/acetone/formic acid 75:25:1 run twice

147

CGA-163935 Acid

test compound -- ^{14}C-CGA-163935 acid, spec. act. 30 µCi/mg, radiopurity >99%

stock solution -- 0.4 mg/ml in acetonitrile

test solutions -- mixed with 10 mg/ml non-labelled solution in acetonitrile to a spec. act of 19.1 µCi/ml, in 0.01 calcium acetate solution. Dilutions were as described above

test protocol -- as above except that these preparations were shaken for 4 hours, and centrifuged.

analytical method -- TLC in two dimensions using two different solvents
1) toluene/acetone/formic acid 150:50:2
2) chloroform/methanol/formic acid/H_2O 150:40:8:4

VI. Study Author's Results and/or Conclusions:

CGA-163935

1) Results demonstrated that the Freundlich isotherm was applicable to analysis of adsorption and desorption of CGA-163935. Logarithmic plots were a straight line for all soils tested for both adsorption and for desorption except in the case of sandy loam. Adsorption constants were 1.50 for sand, 0.67 for loam, 17.77 for clay, 0.66 for sandy loam; and the desorptions constants were between 3.23 and 22.10. K_{oc} values were 283 for sand, 143 for loam, 635 for clay, and 60 for sandy loam. 1/n-values ranged between 0.99 and 1.09.
2) Only parent compound was detected in the liquid phases, analyzed by TLC in two different solvent systems.

CGA-163935 ACID

1) Results demonstrated that the Freundlich isotherm was applicable to analysis of adsorption and desorption of CGA-163935. Logarithmic plots were a straight line for all soils tested for both adsorption and desorption. Adsorption constants were 3.22 for sand, 1.54 for loam, 16.4 for clay, 1.61 for sandy loam; desorption constants ranged between 3.55 and 21.5. K_{oc} values were 609 for sand, 328 for loam, 581 for clay, and 144 for sandy loam. 1/n-values ranged between 0.96 and 1.08.
2) Only CGA-163935-acid was present in the liquid phases, analyzed by both 1- and 2-dimensional TLC.

VII. Reviewer's Comments:

Although the compounds in this study were identified by TLC alone, the two entities in question are clearly well separated by the solvent systems used, and more elaborate techniques appear to be unnecessary in this case.

CGA-163935

1) Approximate k_{ads} (Freundlich constants) *calculated from the leaching results* are 1.56 for sand, 0.11 for loam, 60.2 for clay, and 0.76 for sandy loam (unaged). These results are in general agreement with the batch equilibrium study reported here.

CGA-163935 ACID

1) The approximate k_{ads} (Freundlich constant) *from the leaching results* is 0.89 for sandy loam. The material in the leachate was more than 90% CGA-163935-acid. This supports the batch equilibrium study reported here, indicating a high degree of mobility for CGA-163935-acid.

VIII. CBI Information Addendum: attached

198

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_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

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_____ FIFRA registration data.

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DATA EVALUATION REVIEW 8

I. Study Type: soil volatility

II. Citation:

Spare, W.C. Laboratory Soil Volatility of ^{14}C-CGA-163935. performed by Agrisearch Incorporated, Frederick, MD, submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/21/90; rec'd EPA 7/13/90, MRID# 415639-38.

III. Reviewer:

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

E.B. Conerly 12/21/90

IV. Conclusions:

The study will be acceptable to fulfill data requirements if the applicant submits acceptable data summaries and raw data to confirm application rate and recoveries from soil combustion at various stages. At this time, it provides the supplemental information that CGA-163935 appears not to volatilize.

V. Materials and Methods:

test compound -- 1,2,6 ^{14}C CGA-163935, sp. act. 21.4 µCi/mg, radiopurity >99%

test solution -- the above dissolved in acetonitrile at 10 mg/ml

test soil -- sand -- air-dried and sieved (2 mm mesh), sterilized by autoclaving 2 x at 121 ^{0}C, 15 psig for 60'. Soil was also purged with nitrogen gas to eliminate any aerobic microbial growth which may have metabolized CGA-163935 to CO_2.

test protocol -- 800 µl radioactive stock was mixed with 3 ml of H_2O and coated onto inner walls of a clean amber bottle. 800 gm of sterile sand soil was added, and the preparation roller-mixed for 1 hour. Samples were combusted immediately after mixing to determine homogeneity of application. The dosed sand (ca. 10 ppm) was transferred to gas saturation vessels at 200 gm/vessel. The dosing procedure was performed twice. The first batch was used immediately after dosing, and the second batch was remixed on the roller mill for 1 hr following addition of water to bring the soil to 75% of 1/3 bar. The treated sand was transferred to cylindrical funnels and nitrogen flow initiated. Foam plugs were used to trap the volatile materials (if any).

extraction -- each plug was extracted with 20 ml of MeOH/H_2O/formic acid 90:10:2, sonicated for 15', allowed to equilibrate for 2 hrs -- two subsamples were then counted for total radioactivity. Control plugs were also dosed and extracted with 100 ml of solvent.

analytical procedures
LSC -- for total radioactivity
TLC -- 1-dimensional TLC in two different systems
1) toluene/dioxane/methanol/ammonium hydroxide 4:4:3:1
2) toluene/acetone/formic acid 75:25:1 run twice

231

VI. Study Author's Results and/or Conclusions:

1) No detectable CGA-163935 was found to volatilize from dry or moist soil (sand).

2) The results showed no differences between using 100% and 0% humidity in the purging gas, nor dry or 75% field capacity soil. At nitrogen flow rates of 100 ml/min (0.144 m^3/day) or 300 ml/min.

3) Radiocarbon balance recovery of CGA-163935 ranged from 98.7 to 112.0% using 0% humidity nitrogen, and 102.7 to 109.0% using 100% humidity nitrogen.

4) The correlation between volatilization rates determined in the laboratory and those which can be expected in the field is unknown. However the figures obtained should be viewed as an indication that volatilization may not be important as a mode of movement for CGA-163935 in the environment.

5) Detection limits were 2.2 to 4.6 x 10^{-4} µg/cm/hr

VII. Reviewer's Comments:

1) The applicant did not submit tabular summaries or raw data to support the claims regarding application rate and recoveries from soil combustion at various stages.

2) The vapor pressure is reported to be 1.2 x 10^{-5} Torr at 20 °C.

3) The method of application, i.e., ablation of the dried compound from the vessel walls by roller mixing with soil, is certainly unusual [at least in this reviewer's experience], but appears to have given good results.

4) The use of sterile soil simplifies interpretation of the results. It allows the measurement of actual volatility, unconfounded by the production of degradates due to the high susceptibility of CGA-163935 to metabolism by microorganisms. This does not simulate a field situation, but is acceptable in this case.

VIII. CBI Information Addendum: attached

232

Page ___ is not included in this copy.

Pages 233 through 247 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 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.

✓ FIFRA registration data.

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DATA EVALUATION REVIEW 9

I. Study Type: laboratory fish bioaccumulation

II. Citation:

Fackler, P.H. **Bioconcentration and Elimination of ^{14}C-Residues by Bluegill (*Lepomis macrochirus*) Exposed to CGA-163935.** performed by Springborn Laboratories, Inc., Wareham, MA. submitted by Ciba-Geigy Corp., Greensboro, NC. dated 6/29/90; rec'd EPA 7/13/90, MRID# 416042-07.

III. Reviewer:

Typed Name: E. Brinson Conerly E.B. Conerly 12/21/90
Title: Chemist, Review Section 3
Organization: EFGWB/EFED/OPP

IV. Conclusions:

The study partially satisfies the requirement for fish bioaccumulation data. It may become fully satisfactory if the applicant provides acceptable supplemental information on the following:

1) whether the fish are age-matched, or randomly selected
2) why the fish were fasted before sampling

These data provide the supplemental information that CGA-163935 will not tend to accumulate in fish.

V. Materials and Methods:

test material -- 1, 2, and 6 ^{14}C-CGA-163935 sp. act. 21.4 µCi/mg, radiopurity 96.2%

test fish and regimen -- bluegill, mean wet weight of 1.9 (± 1.0) gm (range 0.76 - 4.9 gm, and a mean total length of 53 (± 9.4) mm (range 41 - 74 mm). All fish were fed a dry pellet food daily *ad libitum* except during the 24 hours prior to each testing period. There was no mortality in the test fish population during the 48 hours prior to testing. Test fish were maintained in the holding tank for 14 days prior to test initiation. These tanks were 761 x 40w x 30h cm and were filled to the 25 cm level -- thus containing 76 l of water (76 kg). Each aquarium was stocked with 176 fish [weighing an average of 1.9 gm for a total of 334.4 gm of fish].

VI. Study Author's Results and/or Conclusions:

1) The concentration of ^{14}C-activity in the exposure solution remained relatively constant throughout the 28-day exposure period at a mean measured concentration of 1.4 (±0.1) mg/L CGA-163935. Concentrations of ^{14}C-activity present in the water of the depuration aquarium remained < 0.15 mg/L (the lod) throughout the 14-day period.

2) The concentration of ^{14}C-residues in the edible tissue of blugill reached steady state by day 3. The mean steady-state bioconcentration factor for CGA-163935 in the edible tissue of bluegill was 2.5X. Model calculations based on the mean measured water and individual edible tissue concentrations estimated a bioconcentration factor of 2.8X.

3) The concentration of ^{14}C-residues in the non-edible tissue of the exposed bluegill reached steady state by day 10. The mean steady-state bioconcentration factor for CGA-163935 in the non-edible tissue of bluegill was 11X. Model calculations based on the mean measured water and individual edible tissue concentrations estimated a bioconcentration factor of 11X.

4) The concentration of ^{14}C-residues calculated for the whole body tissue of bluegill exposed to CGA-163935 reached steady state by day 3. The mean steady-state bioconcentration factor for CGA-163935 in the whole body of bluegill was 6.0X. Model calculations based on the mean measured water and individual edible tissue concentrations estimated a bioconcentration factor of 6.5X.

5) Elimination of ^{14}C-residues from the selected tissue portions of bluegill and consequently on a whole fish basis was observed during the depuration period. Half-life (50% elimination) of the ^{14}C-residues present in the tissue of bluegill on the last day of exposure occurred between the first and third day of depuration in all tissue portions. By day 7 of the depuration period, 100% of the ^{14}C-residues present on the last day of exposure had been eliminated from all tissue portions.

6) Of the accumulated ^{14}C-residues in edible tissue of bluegill exposed to CGA-163935, 6.5% was extractable with a nonpolar solvent (hexane); 45% was extractable with a polar solvent (acetonitrile); and 32% was not extractable with either solvent.

VII. Reviewer's Comments:

1) CGA-163935 would not be expected to bioaccumulate, since it has considerable water solubility.

1) The size (as represented by length and weight) of the fish seems somewhat variable -- the applicant should explain whether they are supposed to be the same age, or a more-or-less random selection?

2) The applicant must explain why the fish were "fasted" for 24 hours before sampling. This practice would seem to bias the results in favor of a lower pesticide content, since fat, and pesticide burden, would be lost if the fish are not feeding.

VIII. CBI Information Addendum: attached

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