DP Barcode: D166142
Shaughnessy No.: 129081
Date Out of EFGWB:
OCT 28 1991

TO: Joanne Miller
Product Manager # 23
Special Review & Reregistration Division (H7508W)

FROM: Emil Regelman
Supervisory Chemist, Review Section #2
OPP/EFED/EFGWB (H7507C)

THROUGH: Henry Jacoby, Chief
OPP/EFED/EFGWB (H7507C)

Attached, please find the EFGWB review of:

Reg./File #(s) : 000279-EUP-REO

Common Name : F6285

Chemical Name : 1-(2,4-dichloro-5-methylsulfonylaminophenyl)-4-difluoromethyl-4,5-dihydro-3-methyl-1,2,4-triazole-5(1H)-one

Product Type : Herbicide

Product Name : Not applicable

Company Name : FMC Corporation

Purpose : Request for EUP

Date Received: 07/11/91 **EFGWB #(s):** 91-0741

Action Code: 700 **Total Reviewing time(decimal days):** 10

Deferrals to:

_____Ecological Effects Branch/EFED
_____Science Integration & Policy Staff/EFED
_____Occupational and Residential Exposure Branch/HED
_____Dietary Exposure Branch/HED
_____Toxicology Branch I, II/HED

1. CHEMICAL: Common name:

F6285.

Chemical name:

1-(2,4-dichloro-5-methylsulfonylaminophenyl)-4-difluoromethyl-4,5-dihydro-3-methyl-1,2,4-triazol-5(1H)-one.

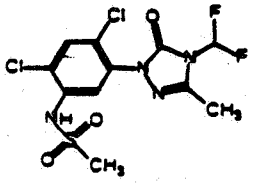
Chemical Abstracts Registry #:

122836-35-5

Trade name(s):

Not applicable.

Structure:



Formulations:

39.6 % ai by weight or 4 lbs/gallon

Physical/Chemical properties:

Molecular formula: $C_{11}H_{10}Cl_2F_2N_4O_3S$.
Molecular weight: 387.19.
Color: Tan
Physical State: Solid
Odor: Faint sulfur-like odor
Melting Point : 126.5 °C
Absolute Density: 1.66 g/cm^3 at 25 °C
Bulk Density: 0.53 g/cm^3 at 25 °C
Water Solubility: 4.0×10^2 ug/g at 25 °C
4.9×10^2 ug/g (PH 6)
1.8×10^3 ug/g (PH 7)
2.0×10^3 ug/g (PH 7.5)
Vapor Pressure : 8×10^{-10} mm Hg at 25 °C
Octanol Water Partition Coefficient (K_{ow}): 31.1 (PH 5)
9.8 (PH 7)
0.27 (PH 9)
Dissociation Constant (PKa): 6.56
Henry's Constant: 1×10^{-12} atm m^3 mol^{-1}
PH (1 % suspension): 4.78

2

2. TEST MATERIAL:

Studies 1-3: Active ingredient ^{14}C-[phenyl (U)]F6285 & ^{14}C-[carbonyl]F6285

3. STUDY/ACTION TYPE:

Review of Hydrolysis, Aerobic Soil Metabolism, and Leaching/Adsorp/Desorp studies submitted for EUP for experimental use on Soybeans.

4. STUDY IDENTIFICATION:

Dykes, J. 1990. Soil adsorption/desorption with ^{14}C-F6285. ABC Laboratory Project ID: ABC Final Report No. 383611; FMC Study No. 162E3289E1; FMC Report No. PC-0138. Unpublished study performed by Analytical Bio-Chemistry Laboratories, Inc., Columbia, MO, and submitted by FMC Corporation, Princeton, NJ. (41911604)

Kabler, K. and K. Williamson; 1991. Hydrolysis as a function of pH at 25 C of ^{14}C-F6285. ABC Final Report No. 38404. FMC Report No. PC-0151. Unpublished study performed by Analytical Bio-Chemistry Laboratories, Inc., Columbia, MO, and submitted by FMC Corporation, Princeton, NJ. (41928202)

Singer, S.S. and M.J. Schocken; 1991. Degradation studies: Aerobic soil metabolism of F6285, a new herbicide. Laboratory Project ID: 162E21RF1. Unpublished study performed and submitted by FMC Corporation, Princeton, NJ. (41928203)

5. REVIEWED BY:

Mah Shamim
Chemist
EFGWB/EFED/OPP
Review Section #2

Signature: M Shamim

Date: OCT 28 1991

6. APPROVED BY:

Emil Regelman
Supervisory Chemist
EFGWB/EFED/OPP
Review Section #2

Signature: E Regelman

Date: OCT 28 1991

7. CONCLUSION:

The registrant, FMC corporation, has submitted studies on Hydrolysis, Aerobic Soil Metabolism, and Leaching/Adsorp/Desorp to support the experimental use of F6285 as a herbicide on soybeans.

161-1 HYDROLYSIS (MRID #41928202)

This study is unacceptable and cannot be used to fulfill the Hydrolysis data requirement for the following reasons:

> the mass spectra of the test substance in the 30-day hydrolysis sample and reference standard revealed a significant difference in fragmentation pattern although their retention times and Rf values appeared to be the same in HPLC and TLC, respectively. It could not be determined if these differences in the mass spectra of hydrolysis product and reference standard were due to the formation of an isomeric product which remained unresolved on HPLC and TLC or the result of impurities which co-eluted with the sample and therefore were not detected by HPLC;
>
> there were unexplained fluctuations in the concentration of total radioactivity recovered from the test solutions during the study.

In order for this study to fulfill the hydrolysis data requirements, the registrant must provide an explanation for the differences in the fragmentation pattern in the mass spectra of test substance and that of the F6285 reference standard; if possible provide GC-MS rather then mass spectrum by solid probe since that would eliminate the possibility of impurities causing additional fragment ions in the mass spectrum of the hydrolysis product; if the hydrolysis product appears to be different from the parent, characterize it by other analytical methods such as NMR or IR; address what factors may have caused the decreases and increases in total radioactivity recovered from the test solutions.

The registrant reported no significant degradation of uniformly phenyl-ring labeled [^{14}C]F6285 (radiochemical purity 98.5%) when it was incubated in the dark at 25 °C for 30 days in sterile buffer solutions (PH 5, 7 & 9) at a nominal test concentration of 8.60-11.02 ug/ml. This was supported by the registrant calculated half lives of 143 days, 207-375 days and 348 days at PH 5, 7 & 9 respectively. However, the analytical data provided by the registrant did not support their claim that F6285 is stable to hydrolysis; it appears that under hydrolysis conditions, F6285 undergoes some kind of rearrangement to form an isomer which is not resolved on HPLC and TLC and, therefore, remains unidentified. At 30 days post treatment, the hydrolysis product comprised 80.2%, 86.0% & 89.7% of initial parent recovered at PH 5, 7, & 9 respectively. At any sampling interval, aqueous soluble radioactivity was ≤1.6% of the initial radioactivity in the test solutions. Approximately 6-15% of organosoluble radioactivity was unaccounted for. Material balances ranged from 86.6% to 107% of the initial radioactivity.

162-1 Aerobic Soil Metabolism (MRID #41928203)

This study is unacceptable and cannot be used to fulfill Aerobic Soil Metabolism data requirement due to the following reasons:

4

the study was not conducted beyond 195-days post-treatment or until the pattern of decline of parent, and formation and decline of metabolites was established.

initial identification of metabolites was based on the comparison of their retention times in HPLC and Rf values in TLC with that of reference standards; mass spectrometry was used to confirm the identity of these metabolites; however the chemical identity of these metabolites could not be established due to major discrepancies in the fragmentation pattern of their mass spectra and those of the reference standards.

In order for this study to fulfill the aerobic soil metabolism data requirements, the registrant must conduct the study for a year or until the pattern of decline of parent, and formation and decline of metabolites has been established; address the differences in the fragmentation pattern in the mass spectra of standards and isolated samples; and as noted earlier provide GC-MS rather then solid probe to avoid possible contamination by impurities.

Uniformly phenyl ring-labeled [^{14}C]F6285 and carbonyl-labeled [^{14}C]F6285 (radiochemical purity >95%) at a nominal concentration of 3.3 ug/ml degraded with registrant calculated half-lives of 122 and 114 days respectively following incubation in sandy loam in the dark at 24 ± 1 °C for 195 days. Parent [^{14}C]F6285 appeared to decline from 97.2% to 31.9% of the total radioactivity for the carbonyl label and 94.4% to 28.9% of the total radioactivity for the phenyl label. Five degradates were isolated from the soil. Two major metabolites #1 and #2 were identified as F6285 3-carboxylic acid and F6285 3-hydroxymethyl. Metabolites #3, #4 & #5 were tentatively identified as F6285 3-desmethyl, F6285 free amine and F6285 3-aldehyde. For both labels bound residues increased to 39.6-42.6% of the total recovered radioactivity at 195 days post treatment. Mineralization of both phenyl and carbonyl labeled molecules to $^{14}CO_2$ remained minimal (0.8%-3.9% of the total recovered radioactivity) throughout the course of the study. Material balances ranged from 86.1 to 105.3% of the applied radioactivity.

163-1 LEACHING/ADSORP/DESORP (MRID #41911604)

This study, while scientifically sound, cannot be used to fulfill the Leaching/Adsorp/Desorp data requirement at this time due to the following reasons:

the test soils were not completely characterized; data on cation exchange capacity (CEC) and field moisture capacity was not provided.

In order for this study to fulfill the data requirements for mobility of unaged F6285 in soil, the registrant must provide field moisture capacity and CEC values of the soils.

This study provides supplemental information on the mobility (batch equilibrium) of unaged phenyl-labeled [^{14}C]F6285 (radiochemical purity 100 %) in sandy loam, silt loam, silty clay loam and sand soil. [^{14}C]F6285 appeared to be highly mobile in all four soils with Freundlich K_{ads} values of 0.551 for the sandy loam soil, 0.767 for the silty loam soil, 0.773 for the silty clay loam soil, and 0.153 for the sand soil; respective K_{oc} values were 29, 26, 40, and 77. K_{des} values ranged from 1.23-1.44 for the four soils.

ENVIRONMENTAL FATE ASSESSMENT

Since the reviewed studies are inconclusive complete environmental fate assessment of F6285 cannot be made at this time. Based on the supplemental information derived from these studies it appears that F6285 is relatively stable to hydrolysis (half-lives of 143 days at PH 5, 207-375 days at PH 7, and 348 days at PH 9 at 25 °C) and apparently is the only compound identified at all sampling intervals; it degrads slowly under aerobic conditions (half lives of 114-122 days in sandy loam soil) and forms few nonvolatile degradates; it is very mobile in sandy loam, silt loam, silty clay loam, and sand soils with respective K^{ads} values of 0.511, 0767, 0.773 & 0.153. If the above information is assumed to be correct and is confirmed by provision of additional data it would indicate that the chemical is fairly persistent, is highly mobile, is moderately soluble in water (400 ppm) and therefore has a potential to leach into ground water.

If satisfactory answers are provided by the registrant for the scientific deficiencies in the submitted data, EFGWB would concur with the EUP request for F6285 since the chemical is used at a relatively low rate (0.5 lb ai/A), on a limited scale and for a short time duration; however, due to concerns about ground water contamination by the chemical, EFGWB would be very hesitant to concur for the renewal of EUP for a second year. In case the registrant decides to pursue the registration of this product, the registrant should conduct a definitive Field Dissipation study with sampling done to a sufficient depth (90 cm) to define leaching at all sampling intervals. The study should also provide a soil profile, report the depth to the water table and track any vertical movement associated with rainfall. If the Field Dissipation study also alerts to potential ground water contamination problems, ground water studies would also be required.

8. RECOMMENDATIONS :

The studies that must be conducted to fulfil the outstanding data requirements for experimental use of F6285 on soybeans (terrestrial food crop use) are summarized below:

161-1 HYDROLYSIS
162-1 AEROBIC SOIL METABOLISM
163-1 LEACHING/ADSORPTION/DESORPTION
165-1 CONFINED ROTATIONAL CROP
165-4 BIOACCUMULATION IN FISH

The studies on Hydrolysis, Aerobic Soil Metabolism and Leaching/Adsorp/Desorp have been reviewed and are found unacceptable due to the deficiencies noted in the CONCLUSIONS section. No other environmental fate data has been satisfied.

The data requirement for Rotational Crop could be waived if the label shows a rotational crop restriction which clearly indicates a rotational crop destruct after use of the herbicide. EFGWB would also concur with a waiver request for Fish Accumulation data requirement if octanol/water partition coefficient data (K = 31.1, 9.8 & 0.27 at PH 5, 7 & 9 respectively) is validated and a copy of the validated data is submitted to EFGWB.

9. BACKGROUND:

A. Introduction

F6285, 1-(2,4-dichloro-5-methylsulfonylaminophenyl)-4-difluoromethyl-4,5-dihydro-3-methyl-1,2,4-triazol-5(1H)-one, is a herbicide currently being developed by FMC Corporation for control of annual grass and broadleaf weeds on soybeans.

B. Directions for Use

The proposed treatment of soybeans involves a single application of 0.25 to 0.5 lbs of active ingredient per acre of F6285 4F herbicide as a preemergence surface applied treatment or as a soil incorporated treatment at planting. F6285 could be applied, using commercial ground equipment, alone or tank mixed with other herbicides; water or liquid fertilizer may be used as a carrier. If treatments are to be incorporated, incorporate at a depth to a depth of 1 to 3 inches. No cover crop should be planted with in 4 months of application of F6285.

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

A. Refer to attached reviews.

B. Proposed Experimental Program (Summary)

Label (copy attached)

Trade Name: F6285
Target Crop: Soybeans
Target Pest: Annual Grass and Broadleaf Weeds
Maximum single application rate: 0.5 lb ai/acre
Total acreage: 220
Total gallons product: 27.5
Total lbs. active ingredient (2 lb ai/gallon): 110

states: AL, AR, DE, FL, GA, IL, IN, IA, KS, KY, LA, MD, MI, MN, MS, MO, NE, NJ, NC, OH, OK, PA, SC, SD, TN, TX, VA, & WI
Trial Time: 1 year

11. COMPLETION OF ONE-LINER:

EFGWB one-liner was updated on 10/22/91

12. CBI APPENDIX:

All data reviewed here are considered "company confidential" by the registrant and must be treated as such.

DYNAMAC
CORPORATION

F6285: EUP

TASK 1: REVIEW AND EVALUATION OF INDIVIDUAL STUDIES

September 9, 1991

Initial Draft Report

Contract No. 68D90058

Submitted to:
Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
2275 Research Boulevard
Rockville, MD 20850-3262

F6285

Table of Contents

INTRODUCTION

F6285, 1-(2,4-dichloro-5-methylsulfonylaminophenyl)-4-difluoromethyl-4,5-dihydro-3-methyl-1,2,4-triazol-5(1H)-one, is a herbicide currently being developed by FMC Corporation for use at a maximum label rate of 0.5 lb ai/A. The registrant is applying for an EUP.

DATA EVALUATION RECORD

STUDY 1

CHEM 129081 F6285 §161-1

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 41928202
Kabler, K. and K. Williamson. 1991. Hydrolysis as a function of pH at 25 C of ^{14}C-F6285. ABC Final Report No. 38404. FMC Report No. PC-0151. Unpublished study performed by Analytical Bio-Chemistry Laboratories, Inc., Columbia, MO, and submitted by FMC Corporation, Princeton, NJ.

DIRECT REVIEW TIME = 6

REVIEWED BY: L. Binari TITLE: Staff Scientist

EDITED BY: C. Cooke TITLE: Staff Scientist
W. Martin Staff Scientist

APPROVED BY: W. Spangler TITLE: Project Manager

ORG: Dynamac Corporation
Rockville, MD
TEL: 301-417-9800

APPROVED BY: Mah Shamim
TITLE: Chemist
ORG: EFGWB/EFED/OPP
TEL: 703-557-2025

SIGNATURE:

CONCLUSIONS:

Degradation - Hydrolysis

1. This study is unacceptable and cannot be used to fulfill data requirements at this time.

2. F6285 was reported to be relatively stable to hydrolysis with half-lives of 143 days at pH 5, 207-375 days at pH 7, and 348 days at pH 9 in sterile aqueous buffered solutions that were incubated at 25 C in the dark for 30 days. Identification of the only compound, present in the buffer solutions at all sampling intervals, as parent F6285 was based on TLC and HPLC analysis.

3. This study does not meet Subdivision N guidelines for the following reasons:

the mass spectrum of test substance in 30-day, PH 7 hydrolysis sample and F6285 reference standard appeared to be different; the base peak in the mass spectrum of F6285 reference was m/z 307 compared to m/z 129 in the test substance; also the fragment ions observed in the mass spectrum of reference standard were not present in the mass spectrum of test substance making the chemical identity of hydrolysis product questionable;

recoveries of initial (time 0) radioactivity in all test solutions steadily decreased from the 0- to 7-day samples, then increased in the 14-day samples to an equal or greater concentration of that detected in the 0-day samples, and again steadily decreased from the 14- to 30-day samples.

4. In order for this study to be used to fulfill the hydrolysis data requirement, the registrant must address the differences in the mass spectra of F6285 reference and test substance in the 30-day, PH 7 hydrolysis sample; provide mass spectra of test substance for 0-day and 30-day, PH 5, 7, and 9 hydrolysis samples; provide mass spectral analysis of hydrolysis samples by GC-MS rather then direct probe and if the samples are not positively identified by mass spectrometry, employ other analytical methods such as NMR or IR to characterize the hydrolysis product.

The registrant must address what factors may have caused the decreases and increases in total radioactivity recovered from the test solutions during the study.

METHODOLOGY:

Uniformly phenyl ring-labeled [^{14}C]F6285 (radiochemical purity 98.5%, specific activity 20.1 mCi/mMol, FMC Corporation), plus unlabeled F6285 (purity 99.8%, FMC), dissolved in methanol, were added to four flasks and the methanol was evaporated under nitrogen. The test substance was redissolved using sonication in filter-sterilized (0.22 u) aqueous buffered solutions adjusted to pH 5 (acetate), pH 7 (one each of TRIS and HEPES), and pH 9 (borate); the nominal concentration of [^{14}C]F6285 in solution was 10 ppm. Aliquots of the test solutions were transferred to autoclaved amber borosilicate glass culture tubes, the tubes were sealed with Teflon-lined caps, and the samples were incubated in the dark in an environmental chamber maintained at 25 $\pm$ 1 C. Duplicate tubes of each solution were removed for analysis at 0, 3.1, 5.1, 7, 14, 21, and 30 days posttreatment.

Duplicate aliquots (100 uL) of each test solution were analyzed for total radioactivity using LSC. The remaining portion of each sample was partitioned three times with ethyl acetate; the pH 9 test

TRIS - Hydroxymethyl aminomethane,
HEPES - N-2-Hydroxyethylpiperazine - N'-2-ethanesulfonic acid

solutions were neutralized with 1 N hydrochloric acid prior to partitioning. The organic phases were combined, and aliquots of the organic and aqueous phases were analyzed for radioactivity using LSC. Aliquots of the pooled organic phase were also analyzed using one-dimensional TLC on silica gel plates developed with methylene chloride:methanol:concentrated ammonium hydroxide (85:15:1, v:v:v). Radioactive areas were detected using radioscanning and autoradiography. The radioactive areas were identified by comparison with a reference standard of [^{14}C]F6285 cochromatographed with the samples. The radioactive areas on the plates from the 0- and 30-day samples were quantified by scraping the plates, eluting the residues in methanol, and analyzing the eluate by LSC. Additional aliquots of the 30-day samples were analyzed using HPLC on an ODS-2 column with water:acetonitrile (65:35, v:v) as the mobile phase and UV detection (220 nm). Fractions were collected from the column at 1-minute intervals and analyzed for radioactivity using LSC. Identification of the peaks was made by comparison with an unlabeled reference standard of F6285 cochromatographed with the samples. The identity of parent F6285 was confirmed in samples of 30-day pH 7 (TRIS) test solution using MS.

DATA SUMMARY:

Uniformly phenyl-ring labeled [^{14}C]F6285 (radiochemical purity 98.5%), at 8.60-11.02 ppm, degraded with registrant-calculated half-lives of 143 days at pH 5, 207 and 375 days at pH 7, and 348 days at pH 9 in sterile aqueous buffered solutions that were incubated in the dark at 25 $\pm$ 1 C for 30 days (Tables II-V). [^{14}C]F6285 was the only compound identified in the buffered solutions at all sampling intervals. At 30 days posttreatment, [^{14}C]F6285 comprised 80.2% of the initial (time 0) parent recovered (73.2% of the initial radioactivity) from the pH 5 solution, 86.0% of initial parent recovered (79.4% of initial radioactivity) from the pH 7 HEPES-buffered solution, 89.7% of initial parent recovered (82.1% of initial radioactivity) from the pH 7 TRIS-buffered solution, and 89.3% of initial parent recovered (83.8% of initial radioactivity) from the pH 9 solution (Tables II-V). Following TLC analysis of organic extracts from the test solutions, approximately 6-15% of the organosoluble radioactivity was unaccounted for. Aqueous soluble radioactivity was $\leq$1.6% of the initial radioactivity (0.02-0.18 ppm) in the test solutions at any sampling interval. During the study, material balances prior to TLC analysis of organic phases ranged from 86.6% to 107% of the initial radioactivity (Tables VI-IX); following TLC, material balances ranged from 73.4% to 96.6% of the initial radioactivity.

At the final sampling interval (30 days posttreatment), the pH of the test solutions were 5.20-5.47, 7.06-7.10 (HEPES buffer), 7.28-7.29 (TRIS buffer), and 8.81-8.85 (Table X).

COMMENTS:

1. EFGWB prefers that [^{14}C]residues in samples be separated by chromatographic methods (such as TLC, HPLC, or GC) with at least three solvent systems of different polarity, and that specific compounds isolated by chromatography be identified using a confirmatory methods such as MS in addition to comparison with the R_f of reference standards.

   In this study the [^{14}C]residues in hydrolysis samples were identified as parent F6285 by one dimensional TLC and reverse phase HPLC. Mass spectra of the F6285 reference and test substance in the 30-day, PH 7 hydrolysis sample were also provided to confirm the structure of the hydrolysis product. Although the two samples cochromatographed on TLC and HPLC their mass spectral distribution appeared to be different; the base peak in the mass spectrum of F6285 reference was m/z 307 compared to m/z 129 in the test substance; also the fragment ions observed in the mass spectrum of F6285 reference were not present in the mass spectrum of test substance. This indicates that the hydrolysis product is not identical to the parent F6285 but may be closely related in structure and, therefore, remained unresolved on HPLC or TLC. On the other hand additional fragment ions that appeared in the mass spectrum of test substance could be the result of impurities; if this is the case mass spectral analysis of the samples by GC/MS instead of solid probe would prove helpful in resolving this problem.

2. In all four test solutions, recovery of initial radioactivity steadily decreased from the 0- to 7-day samples. However, in the 14-day samples, the concentration of recovered radioactivity abruptly increased to an equal or greater concentration than that of the 0-day samples, then recoveries again steadily decreased from the 14- to 30-day samples. This anomaly was not addressed by the study authors.

3. The study authors reported that HPLC analysis of 30-day samples of the test solutions found parent F6285 comprised 99-108% of the initial dose (Table XI). It could not be determined if this meant percent of the initial (time 0) radioactivity detected in each test solution, the percent of initial parent F6285 detected in each test solution, or the percent of radioactivity applied to the HPLC. If the results are expressed as percent of initial radioactivity, the study authors need to address the discrepancy between the concentrations of F6285 detected using HPLC as compared to TLC; using TLC, F6285 comprised 87-95% of the initial (time 0) radioactivity in the 30-day ethyl acetate fractions.

4. Three preliminary studies were conducted using pH 5, 7 (TRIS and HEPES buffers), and 9 buffer solutions containing 10 ppm [^{14}C]F6285. A preliminary 7-day hydrolysis study was conducted at 25 C to estimate rate constants and half-lives; at 7 days posttreatment, parent F6285 comprised 90.7-93.4% the total radioactivity (Figure 3). A second study determined that F6285 did not adsorb to nonsilanized

glassware during a 7-day incubation (Table I). A stability study was conducted at 4 C and -20 C and samples of the test solutions were collected after 0, 3, and 7 days of storage. It was reported that total radioactivity in the test solutions remained "relatively unchanged" at both temperatures, but the data were not provided for review. It could not readily be determined from the raw data how long the test solutions were stored prior to LSC analysis and extraction, or how long extracts were stored prior to LSC and TLC analysis.

5. The statistical estimations of the hydrolytic half-lives of F6285 in the pH 5, 7, and 9 test solutions that were reported are of limited value because the calculations involve extrapolation beyond the experimental time limits of the study. Data are often incapable of accurately predicting trends outside of their range because small differences are magnified and reactions which appear to be linear may, in fact, be curvilinear.

Substance Derived

Page _____ is not included in this copy.

Pages 17 through 33 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 RECORD

STUDY 2

CHEM 129081 F6285 §162-1

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 41928203
Singer, S.S. and M.J. Schocken. 1991. Degradation studies: Aerobic soil metabolism of F6285, a new herbicide. Laboratory Project ID: 162E21RF1. Unpublished study performed and submitted by FMC Corporation, Princeton, NJ.

DIRECT REVIEW TIME = 8

REVIEWED BY: L. Binari TITLE: Staff Scientist

EDITED BY: C. Cooke TITLE: Staff Scientist
W. Martin Staff Scientist

APPROVED BY: W. Spangler TITLE: Project Manager

ORG: Dynamac Corporation
Rockville, MD
TEL: 301-417-9800

APPROVED BY: Mah Shamim
TITLE: Chemist
ORG: EFGWB/EFED/OPP
TEL: 703-557-2025

SIGNATURE:

CONCLUSIONS:

Metabolism - Aerobic Soil

1. This study cannot be used to fulfill data requirements at this time.

2. F6285 degraded with half-lives of 114-122 days in sandy loam soil that was incubated in the dark at 24 C and 75-80% of 0.33 bar moisture. Nonvolatile degradates identified were F6285 3-carboxylic acid and F6285 3-hydroxymethyl; tentatively identified minor degradates included F6285 3-desmethyl, F6285 free amine, and F6285 3-aldehyde.

3. This study does not meet Subdivision N guidelines for the following reasons:

34

at final sampling interval (195-days posttreatment), the concentration of parent was still declining while that of the metabolites was increasing. According to the subdivision N guidelines, the study must be conducted for one year or until the pattern of decline of parent or pattern of formation and decline of all degradates in the soil are established;

major discrepancies in the mass spectra of standards and isolated samples (parent, metabolites) were not adequately addressed.

4. In order for this study to fulfill the aerobic soil metabolism data requirement, the registrant must provide additional information on the formation and decline of parent and metabolites beyond the 195-day sampling interval. The study should be conducted for a longer time period or up to a year if necessary.

The registrant must address the discrepancies in the mass spectra of standards and isolated samples (parent and metabolites); additional fragment ions that appear in the mass spectra of metabolites could be the result of impurities (isomers and other metabolites) that probably remained unresolved on TLC and HPLC and perhaps could be eliminated by use of GC/MS rather than solid probe.

METHODOLOGY:

Samples of sieved (2 mm) sandy loam soil (68% sand, 13% silt, 19% clay, 1.1% organic matter, pH 7.1, CEC 6.8 meq/100 g) were weighed (50 g) into biometer flasks and treated with either uniformly phenyl ring-labeled [^{14}C]F6285 or carbonyl-labeled [5-^{14}C]F6285 (radiochemical purities >95%; specific activities 20.1 and 24.0 mCi/mMol, respectively; New England Nuclear) dissolved in ethanol, at a nominal concentration of 3.3 ppm. The soil samples were adjusted to 75-80% of 0.33 bar moisture and the side well of each biometer flask was filled with a 0.1 M potassium hydroxide trapping solution. The flasks were incubated in the dark at 24 $\pm$ 1 C. Duplicate flasks of soil and the corresponding trapping solutions were sampled at 0, 7, 33, 61, 90, 141, and 195 days posttreatment.

The soil samples were extracted twice with acetonitrile:water (70:30, v:v) at "room temperature" using a magnetic stirrer followed by vacuum filtration and a 1-hour reflux in the acetonitrile:water solution. Extracts were filtered, combined, and concentrated by rotary evaporation (<35 C). The concentrated extracts were partitioned three times with ethyl acetate. Aliquots of the organic and aqueous phases were analyzed for radioactivity using LSC. Aqueous phases from the 33- to 195-day soil samples were acidified to pH 1, then repartitioned three times with ethyl acetate. All organic phases were combined, dried over anhydrous sodium sulfate, and concentrated by rotary evaporation (temperature not specified). The concentrated extracts were analyzed using one-dimensional TLC on

silica gel plates developed with methylene chloride:methanol:ammonium hydroxide (75:25:1, v:v:v or 85:15:1, v:v:v). Radioactive areas were detected using autoradiography; the radioactive areas were scraped from the plates, eluted with methanol and quantified by LSC. Unlabeled reference standards of F6285 and possible degradates were detected under UV light; it could not be determined if the reference standards were cochromatographed with the samples. Selected organic phases were also analyzed by reverse HPLC with UV (280 nm) detection using Zorbax ODS or Zorbax C-8 columns eluted with acetonitrile:water:acetic acid gradients. Identities of degradates were confirmed using electron impact MS and chemical ionization MS. The extracted soil was analyzed by LSC following combustion. The potassium hydroxide trapping solutions were analyzed for total radioactivity using LSC.

In order to characterize unextractable [^{14}C]residues, the previously extracted 141-day soil samples treated with phenyl ring-labeled [^{14}C]F6285 were further extracted with hexane and methylene chloride, then fractionated into humin, humic acid, and fulvic acid (Figure 4). Subsamples of the extracted soil were air-dried, refluxed with 0.25 N hydrochloric acid for 1 hour, then centrifuged. The supernatant was partitioned three times with ethyl acetate; the organic and aqueous phases were analyzed by LSC. The remaining soil pellet was stirred with 0.5 N sodium hydroxide for 24 hours and the extract was decanted. Soil solids (humin fraction) were air-dried and analyzed for radioactivity by LSC following combustion. The extract was analyzed for radioactivity by LSC, acidified to pH 1 with concentrated hydrochloric acid to precipitate the humic acid fraction, and centrifuged. The supernatant (fulvic acid fraction) was analyzed by LSC, and the precipitate (humic acid fraction) was redissolved in 0.5 N sodium hydroxide for LSC analysis.

Four additional flasks of soil were autoclaved on three consecutive days (121 C for 1 hour) prior to treatment with phenyl ring-labeled [^{14}C]F6285 and incubated as described above. Duplicate flasks of the sterile soil were sampled at 67 and 170 days posttreatment and analyzed as previously described.

DATA SUMMARY:

Uniformly phenyl ring-labeled [^{14}C]F6285 and carbonyl-labeled [5-^{14}C]F6285 (radiochemical purities >95%), at 3.3 ppm, degraded with calculated half-lives of 122 and 114 days, respectively, in sandy loam soil that was incubated in the dark at 24 $\pm$ 1 C and 75-80% of 0.33 bar moisture for up to 195 days. For both label positions, nonvolatile degradates included F6285 3-carboxylic acid and F6285 3-hydroxymethyl; three additional degradates, F6285 3-desmethyl, F6285 free amine, and F6285 3-aldehyde, were tentatively identified.

For both label positions, [^{14}C]F6285 decreased from 94.4-97.2% of the recovered radioactivity at day 0 to 38.7-48.5% at 90 days and 28.9-

31.9% at 195 days (Tables 1 and 2). Five degradates were isolated from the soil:

F6285 3-carboxylic acid (metabolite #1),

at a maximum 11.8-23.9% of the recovered at 90 days;

F6285 3-hydroxymethyl (metabolite #2),

at a maximum 2.3% at 61 days for the carbonyl-label and 6.3% at 33 days for the phenyl ring-label;

F6285 3-desmethyl (metabolite #3),

at a maximum 2.0% at 195 days for the carbonyl-label and 2.7% at 7 days for the phenyl ring-label;

F6285 free amine (metabolite #4),

at a maximum 4.5-4.8% at 195 days; and

F6285 3-aldehyde (metabolite #5),

at a maximum 3.2% at 7 days for the carbonyl-label and 2.4% at 141 and 195 days for the phenyl ring-label.

At 195 days posttreatment, unextracted [^{14}C]residues had increased to 39.6-42.6% of the recovered radioactivity and evolved $^{14}CO_2$ totaled <5% of the recovered.

Analysis of the [^{14}C]residues from the extracted 141-day soil samples treated with phenyl ring-labeled [^{14}C]F6285 determined that 3.7% of the recovered radioactivity was associated with the humin fraction, 12.8% with the humic acid fraction, and 5.7% with the fulvic acid fraction (Table 5).

In sterilized sandy loam soil treated with phenyl ring-labeled [^{14}C]F6285, F6285 comprised 92.1 and 89.5% of the recovered radioactivity at 67 and 170 days posttreatment, respectively (Table 4).

Material balances ranged from 86.1 to 105.3% of the applied radioactivity.

COMMENTS:

1. At 195 days posttreatment (final sampling interval), the concentrations of metabolite #3 (tentatively identified as F6285 3-desmethyl) in soil treated with carbonyl-labeled [^{14}C]F6285 and metabolite #4 (tentatively identified as F6285 free amine) in soil treated with both labels were still increasing. Subdivision N

guidelines specify that the study must be conducted either until the pattern of degradation of the parent and the patterns of formation and decline of all degradates in the soil are established or for 1 year, whichever comes first. Additional information concerning the patterns of formation and decline of metabolites #3 and #4 beyond the 195-day sampling interval is required; the registrant should submit the results from the analysis of soil beyond the 195-day sampling period and up to a year if necessary.

2. EFGWB prefers that [^{14}C]residues in samples be separated by chromatographic methods (such as TLC, HPLC, or GC) with at least three solvent systems of different polarity, and that specific compounds isolated by chromatography be identified using a confirmatory methods such as MS in addition to comparison with the R_f of reference standards.

   In this study, the organic extracts were analyzed using one-dimensional TLC with one solvent system; it could not be determined which reference standards other than parent F6285 were cochromatographed with the samples. It was also reported that selected organic phases were analyzed using reverse HPLC; however, it was not specified which samples were analyzed by HPLC, no quantitative data were provided, and only one chromatogram tracing was provided (Appendix B10).

   Mass Spectrometry was used to confirm the identities of isolated parent F6285, metabolite #1 (F6285 3-carboxylic acid), and metabolite #2 (F6285 3-hydroxymethyl). Metabolites #3, 4, and 5 were only tentatively identified as F6285 3-desmethyl, F6285 free amine, and F6285 3-aldehyde, respectively. Mass spectra of most of these metabolites seemed to have a high background level which could be due to the presence of impurities that probably remained unresolved by TLC and HPLC. Use of GC/MS instead of solid probe is highly recommended; however, if the mass spectrum of the GC trace still showed these additional fragment ions it would either mean that the isolated peak does not have the same identity as that of the standard or is a mixture of isomers or other metabolites that are not resolved by GC.

3. It was reported that the treated soils were aerobically incubated, but it was not specified how the biometer flasks were sealed after the soil was treated and the trapping solution was placed in the side arm. It was not specified if the moisture content of the soil samples was monitored or maintained during the study.

4. The description of additional extractions of the previously extracted 141-day phenyl ring-labeled [^{14}C]F6285-treated soil samples provided in the methodology section of the study (V. TEST METHOD/C. Analysis of Bound Residues) was not consistent with the fractionation scheme provided in Figure 4 and the results provided in Table 5. Since the fractionation scheme provided in Figure 4 and the data in Table 5

appeared to coincide, the fractionation scheme in Figure 4 was summarized in this review.

5. Results were presented in terms of percent of recovered radioactivity. Results from TLC analysis of ethyl acetate extracts were normalized to 100%. Recoveries of radioactivity applied to the TLC plates were only reported for two replicate samples of 195-day carbonyl-labeled [^{14}C]F6285-treated sandy loam soil and were approximately 101% of the applied; TLC plate recoveries were not reported for any other samples.

6. In an additional experiment, samples of silt loam and silty clay loam soil were treated with phenyl ring-labeled [^{14}C]F6285 and incubated as described above; soil subsamples were collected at 77, 103, and 145 days posttreatment. At the first sampling interval (77 days posttreatment), F6285 comprised 66.6% and 73.6% of the recovered radioactivity in the silt loam and silty clay loam soils, respectively (Table 3). Results from these experiments were not reviewed; the first sampling interval occurred too late after treatment to confirm the application rate. The study authors did not explain the purpose of conducting these soil incubations with the limited number of sampling intervals. These experiments provide supplemental data and are not needed to fulfill the data requirements.

7. It was reported that bulk soil incubations were conducted to generate additional material for degradate identification. Samples of soil (50 g) were treated with phenyl ring-labeled [^{14}C]F6285 and incubated as described above; samples were collected at 62, 74, 111, and 133 days posttreatment. Soil samples were extracted and the extracts were analyzed by preparative TLC or preparative HPLC. The soil used was not described (sandy loam, silt loam, or silty clay loam), and the preparative TLC and HPLC techniques were not described.

Subsequence Denied

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DATA EVALUATION RECORD

STUDY 3

CHEM 129081 F6285 §163-1

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 41911604
Dykes, J. 1990. Soil adsorption/desorption with ^{14}C-F6285. ABC Laboratory Project ID: ABC Final Report No. 383611; FMC Study No. 162E3289E1; FMC Report No. PC-0138. Unpublished study performed by Analytical Bio-Chemistry Laboratories, Inc., Columbia, MO, and submitted by FMC Corporation, Princeton, NJ.

DIRECT REVIEW TIME = 4

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SIGNATURE:

CONCLUSIONS:

Mobility - Leaching and Adsorption/Desorption

1. This study cannot be used to fulfill data requirements at this time.

2. F6285 is very mobile in sodium azide-sterilized sandy loam, silt loam, silty clay loam, and sand soils. Adsorption increased with increasing soil organic matter content and clay content.

3. This study is scientifically sound, but does not meet Subdivision N guidelines for the following reason:

complete characterization of the test soils was not carried out; data on cation exchange capacity (CEC) and field moisture capacity was missing.

4. In order for this study to fulfill the data requirements for mobility of unaged F6285 in soil, the registrant must completely characterize the soils with information on field moisture capacity and cation exchange capacity.

METHODOLOGY:

Sandy loam, silt loam, silty clay loam, and sand soils (Table I) were air-dried, sieved (2 mm), and sterilized with the addition of 1% sodium azide (w:w). Filter-sterilized (0.22 u) deionized water was used to prepare the 0.01 M calcium chloride solution. Based on preliminary experiments to define test parameters, an equilibration time of 24 hours and a 1:5 soil:solution ratio were selected for the definitive experiment.

For the adsorption studies, 1 g samples of soil and 5 mL of a 0.01 M calcium chloride solution containing 0.1, 2, 5, 7, or 10 ppm of uniformly phenyl-labeled [^{14}C]F6285 (radiochemical purity 100%, specific activity 20.1 mCi/mMol, FMC) were transferred to sterilized (autoclaved) culture tubes. The tubes were sealed with Teflon-lined caps, wrapped in foil, and the soil:solutions slurries were shaken in the dark at 25 ± 1 C for 24 hours. After shaking, the slurries were centrifuged and the supernatant was decanted. Aliquots of the supernatants were analyzed using LSC.

Desorption of F6285 was determined by replacing the supernatant removed from the soil after adsorption with an equal volume of pesticide-free calcium chloride solution. The soil:solution slurries were shaken in darkness at 25 ± 1 C for 24 hours. After shaking, the slurries were centrifuged and supernatants were analyzed by LSC. The [^{14}C]F6285 remaining adsorbed to the soil after desorption was determined by LSC following combustion.

DATA SUMMARY:

Based on batch equilibrium studies, uniformly phenyl-labeled [^{14}C]F6285 (radiochemical purity 100%), at 0.1, 2, 5, 7, and 10 ppm, was determined to be very mobile in sodium azide-sterilized sandy loam, silt loam, silty clay loam, and sand soil:calcium chloride solution slurries (1:5) that were equilibrated for 24 hours at 25 ± 1 C. Freundlich K_{ads} values were 0.153 for the sand soil, 0.551 for the sandy loam soil, 0.767 for the silt loam soil, and 0.773 for the silty clay loam soil; respective K_{oc} values were 77, 29, 26, and 40 (Table XVI). Adsorption increased with increasing soil organic matter content and clay content. K_{des} values were 1.23-1.44 for the

four soils. Material balances ranged from 96.6 to 104.7% of the applied radioactivity (Tables XVII-XX).

COMMENTS:

1. The test soils were not completely characterized; data on cation exchange capacity (CEC) and field moisture capacity was not provided for the soils.

2. The soils were sterilized by the addition of 1% sodium azide (w:w). It is suspected that sterilization of soils by sodium azide alters the soil in such a way that it changes the mobility of pesticides in soil. The registrants should address this issue.

3. It was reported that the test substance was determined to be stable under the test conditions used for this study, but quantitative data were not provided for review.

4. The study author reported that a 20-80% adsorption range was not achieved with an initial 1:5 soil:solution ratio; however, the ratio was not changed for the definitive study because the correlation for the K_d determination was high (r^2 >0.98). It was also determined that adsorption of the test substance to glass surfaces was insignificant after 24 hours. Quantitative data from the preliminary experiments performed to determine the equilibration time, soil:solution ratio, and if the test substance adsorbed to glassware were not provided for review.

Withdrawn - Revised

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REFERENCES

The following studies were reviewed:

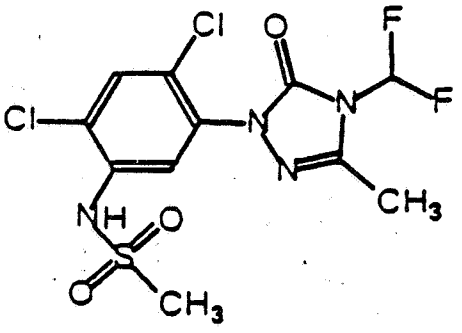
Dykes, J. 1990. Soil adsorption/desorption with "C-F6285. ABC Laboratory Project ID: ABC Final Report No. 383611; FMC Study No. 162E3289E1; FMC Report No. PC-0138. Unpublished study performed by Analytical Bio-Chemistry Laboratories, Inc., Columbia, MO, and submitted by FMC Corporation, Princeton, NJ. (41911604)

Kabler, K. and K. Williamson. 1991. Hydrolysis as a function of pH at 25 C of "C-F6285. ABC Final Report No. 38404. FMC Report No. PC-0151. Unpublished study performed by Analytical Bio-Chemistry Laboratories, Inc., Columbia, MO, and submitted by FMC Corporation, Princeton, NJ. (41928202)

Singer, S.S. and M.J. Schocken. 1991. Degradation studies: Aerobic soil metabolism of F6285, a new herbicide. Laboratory Project ID: 162E21RF1. Unpublished study performed and submitted by FMC Corporation, Princeton, NJ. (41928203)

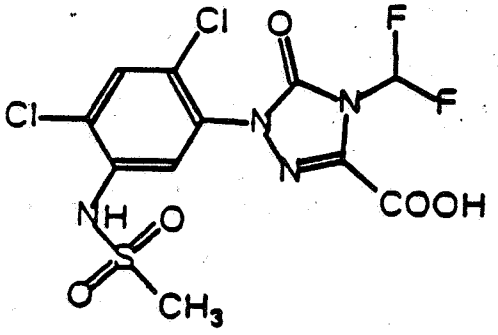
APPENDIX

F6285 AND ITS DEGRADATES

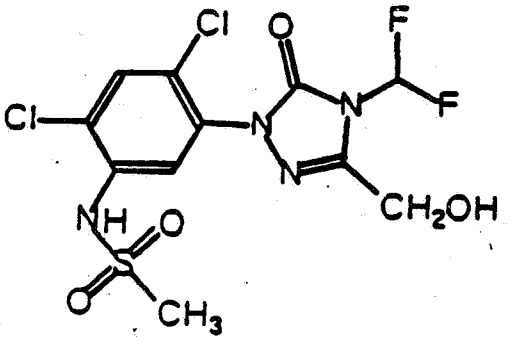


1-(2,4-dichloro-5-methylsulfonylaminophenyl)-4-difluoromethyl-4,5-dihydro-3-methyl-1,2,4-triazol-5(1H)-one

(F6285)



F6285 3-Carboxylic acid (metabolite #1)



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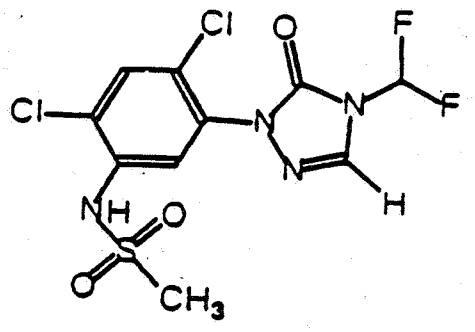
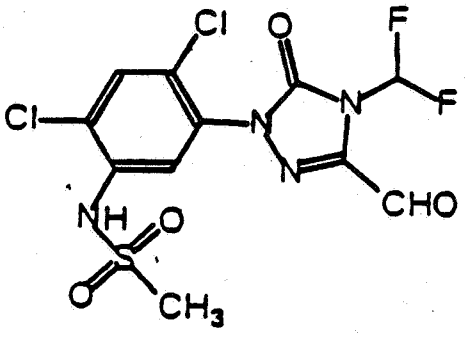


F6285 3-Desmethyl (metabolite #3)



F6285 3-Aldehyde (metabolite #5)

Revised Summary Sheet

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