151 OPP#34134 27pp

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUN 24 1994

PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Fenamiphos. **Addendum to the Product and Residue Chemistry Chapters for the RED: Confined and Limited Field Rotational Crop Studies.**
Reregistration Case No. 0333; Chemical No. 100601.
DP BARCODE D194664; MRIDs 41659301 and 42043601.

FROM: Paula A. Deschamp, Section Head
Reregistration Section I
Chemistry Branch II: Reregistration Support
Health Effects Division (7509C)

THRU: Edward Zager, Chief
Chemistry Branch II: Reregistration Support
Health Effects Division (7509C)

TO: Lois Rossi, Chief
Reregistration Branch
Special Review and Reregistration Division (7508W)

Attached is a review of confined and limited field rotational crop data submitted by Miles, Inc. (formerly Mobay Corporation) in response to the 1987 Guidance Document. This information was reviewed by Dynamac Corporation under supervision of CBRS, HED. The data assessment has undergone secondary review in CBRS and has been revised to reflect Branch policies.

GLN 165-1: Confined Rotational Study.
The submitted confined rotational crop study is adequate to satisfy the 165-1 guideline requirements for purposes of reregistration. The study indicates that ^{14}C-residues (expressed as fenamiphos equivalents) accumulated at levels >0.01 ppm in/on all commodities of beets, Swiss chard, and wheat that were planted 30, 120, and 269 days after ring-labeled [1-^{13}C/^{14}C]fenamiphos was applied to sandy loam soil at 1.1x the maximum registered rate for annual food/feed crops. Fenamiphos sulfone and fenamiphos sulfoxide, the two metabolites of concern (in addition to the parent), were the principal organosoluble residues identified from the 30-day rotations, and collectively accounted for 12-49% of the radioactivity; the proportion of these two residues declined at subsequent intervals. The parent, fenamiphos, was a minor (<1% of TRR) residue at all intervals.

GLN 165-2: Limited field rotational study

The limited field rotational study indicates that fenamiphos residues of concern were detected at levels >0.01 ppm in/on spinach leaves (0.03 ppm), and sorghum forage (0.44 ppm) and straw (0.02 ppm) from the 4-month rotation grown in test plots treated at 1x the maximum seasonal rate for annual crops.

In order to assure that illegal residues are not found in rotational crops, and to facilitate inclusion of rotational crop residues in dietary risk assessment, the registrant should either (1) amend product labels to include an 8-month plantback interval so that residues of fenamiphos and its regulated metabolites will not be found in rotational crops, or (2) based on the limited field trial data, propose rotational crop tolerances for crops which are specified on product labels. If the registrant elects the later, extensive field rotational crop studies will be required; these field trial data will be considered confirmatory.

Attachment 1: Fenamiphos DP BARCODE D194664. Registrant's Response to Residue Chemistry Data Requirements.

cc: PADeschamp (CBRS), Circulate, Fenamiphos RegStd File, SF, Dynamac, Flora Chow/John Redden (CCB)
cc: RF (Without attachment)

7509C:CBRS:PDeschamp:CM#2:Rm804A:703-305-6227:06/16/94
RDI: MMetzger:06/17/94 EZager:06/22/94

Deschamp
6/24/94

DP BARCODE: D194664 REREG CASE # 0333

CASE: 819346 DATA PACKAGE RECORD DATE: 09/02/93
SUBMISSION: S447126 BEAN SHEET Page 1 of 1

* * * CASE/SUBMISSION INFORMATION * * *

CASE TYPE: REREGISTRATION ACTION: 627 GENERIC DATA SUBMISSION
CHEMICALS: 100601 Fenamiphos %

ID#: 100601-
COMPANY:
PRODUCT MANAGER: 72 LARRY SCHNAUBELT 703-308-8058 ROOM: CS1 3C3
PM TEAM REVIEWER: IRWIN HORNSTEIN 703-308-8042 ROOM: CS1 3RD FL
RECEIVED DATE: 10/29/90 DUE OUT DATE: 01/27/91

* * * DATA PACKAGE INFORMATION * * *

DP BARCODE: 194664 EXPEDITE: N DATE SENT: 09/02/93 DATE RET.: / /
CHEMICAL: 100601 Fenamiphos
DP TYPE: 001 Submission Related Data Package
CSF: N LABEL: N

ASSIGNED TO	DATE IN	DATE OUT
DIV : HED	/ /	/ /
BRAN: RSCB	/ /	/ /
SECT: IO	/ /	/ /
REVR :	/ /	/ /
CONTR:	/ /	/ /

ADMIN DUE DATE: 12/01/93
NEGOT DATE: 12/01/93
PROJ DATE: / /

* * * DATA REVIEW INSTRUCTIONS * * *

FOR CHRIS OLINGER: REQUEST REVIEWS OF MRID 41659301 THAT ADDRESSES GL 165-1 AND MRID 42043601 THAT ADDRESSES GL -165-2.

* * * DATA PACKAGE EVALUATION * * *

No evaluation is written for this data package.

* * * ADDITIONAL DATA PACKAGES FOR THIS SUBMISSION * * *

DP BC	BRANCH/SECTION	DATE OUT	DUE BACK	INS	CSF	LABEL

Dynamac 120 GE tech hours
sent 9/24/93; due 11/24/93

(3)

Rotational Crop Studies

DYNAMAC CORPORATION
Environmental Services

Final Report

FENAMIPHOS
Shaughnessy No. 100601; Case No. 0333 (DP Barcode D194664)

TASK 4
Registrant's Response to Residue Chemistry Data Requirements

November 23, 1993

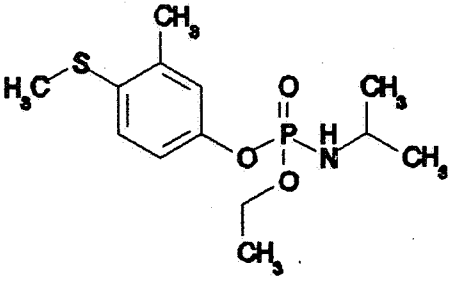
Contract No. 68-D2-0053

Submitted to:
U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:
Dynamac Corporation
The Dynamac Building
2275 Research Boulevard
Rockville, MD 20850-3268

(4)

FENAMIPHOS



Shaughnessy No. 100601; Case No. 0333

(DP Barcode D194664)

Task 4

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

BACKGROUND

Miles Inc. (formerly Mobay Corporation) has submitted a confined rotational crop study (1989; MRID 41659301) and a limited field rotational crop study (1991; MRID 42043601) in response to the Fenamiphos Reregistration Standard Guidance Document dated 6/87. These studies are evaluated in this document for adequacy in fulfilling the reregistration requirements for Guideline Nos. 165-1 and 165-2.

The qualitative nature of the residue in plants is adequately understood. The residues of concern in plant commodities are fenamiphos and its two metabolites, fenamiphos sulfoxide and fenamiphos sulfone. The qualitative nature of the residue in ruminants is adequately understood. The residues of concern in ruminants are fenamiphos, fenamiphos sulfoxide, fenamiphos sulfone, des-isopropyl fenamiphos, des-isopropyl fenamiphos sulfoxide, and des-isopropyl fenamiphos sulfone. Adequate enforcement methods are available for the determination of residues of fenamiphos and its cholinesterase-inhibiting metabolites in/on plant and animal commodities.

Tolerances for residues of fenamiphos in/on raw and in processed plant commodities are currently expressed in terms of the combined residues of fenamiphos [ethyl 3-methyl-4-(methylthio)phenyl (1-methylethyl)phosphoramidate] and its cholinesterase-inhibiting metabolites, fenamiphos sulfoxide and fenamiphos sulfone [40 CFR §180.349(a) and (c), 185.2950, and 186.2950]. Tolerances for residues in/on animal commodities are expressed in terms of the combined residues of fenamiphos and its cholinesterase-inhibiting metabolites fenamiphos sulfoxide, fenamiphos sulfone, des-isopropyl fenamiphos, des-isopropyl fenamiphos sulfoxide, and des-isopropyl fenamiphos sulfone [40 CFR §180.349(b)]. The Pesticide Analytical Manual (PAM) Vol. II lists two GLC methods, each with thermionic detection (TD) and a limit of detection of 0.01 ppm. Method I is available for the determination of the combined residues of fenamiphos and its sulfoxide and sulfone metabolites, measured as fenamiphos sulfone, in/on plant commodities, and Method II is available for the determination of the combined residues of fenamiphos, its sulfoxide and sulfone metabolites, des-isopropyl fenamiphos, des-isopropyl fenamiphos sulfoxide, and des-isopropyl fenamiphos sulfone in animal tissues and milk.

The residue definition for Codex MRLs is the sum of fenamiphos, its sulfoxide and sulfone, expressed as fenamiphos. CBRS has made specific recommendations (See the Residue Chemistry Considerations for Fenamiphos RED, DP Barcode D187029, CBRS No. 11213) regarding efforts to harmonize the Codex MRLs with U.S. tolerances.

CONCLUSIONS AND RECOMMENDATIONS

Confined rotational study

1. The submitted confined rotational crop study is adequate to satisfy the 165-1 guideline requirements for purposes of reregistration. The molecular structures of fenamiphos and its metabolites that were identified in/on crop commodities from this confined rotational crop study are presented in Table 1.

2. The study indicates that ^{14}C-residues (expressed as fenamiphos equivalents) accumulated at levels >0.01 ppm in/on all commodities of beets, Swiss chard, and wheat that were planted 30, 120, and 269 days after ring-labeled [1-^{13}C/^{14}C]fenamiphos was applied to sandy loam soil at 1.1x the maximum registered rate for annual food/feed crops. Accumulation was highest in the 30-day rotation and declined thereafter. The ranges of total radioactive residues (TRR) accumulation were: garden beet roots (0.10-4.62 ppm), garden beet tops (0.36-7.31 ppm), Swiss chard (0.57-8.71 ppm),wheat forage (2.36-17.30 ppm), wheat straw (4.78-46.43 ppm), and wheat grain (0.20-0.98 ppm).

3. The majority of the total radioactive residues (TRR) in/on the matrices of rotated crops were adequately characterized and identified, except for garden beet roots and wheat grain from the 269-DAT rotation interval. The ranges of characterized and identified radioactivity in/on rotated commodities were: garden beet tops (83-98% of TRR), garden beet roots (54-80% of TRR), Swiss chard (89-99% of TRR), wheat forage (91-97% of TRR), wheat straw (79-90% of TRR), and wheat grain (21-76%).

4. No further analytical work is required on the following fractions from the 269-day rotation because adequate data from primary plant metabolism studies, including those from root and tuber vegetables and cereal grains, are available: (i) bound residues (45.9% of TRR, 0.05 ppm) in/on garden beet roots; and (ii) unidentified wheat grain bound residues (79% of TRR, 0.16 ppm).

5. Fenamiphos sulfone and fenamiphos sulfoxide, the two metabolites of concern (in addition to the parent), were the principal organosoluble residues identified from the 30-day rotations, and collectively accounted for 12-49% of the radioactivity; the proportion of these two residues declined at subsequent intervals. The parent, fenamiphos, was a minor (<1% of TRR) residue at all intervals.

6. The principal aqueous-soluble residues identified were phenol sulfone conjugate (maximum of 25% TRR in Swiss chard), des-amino fenamiphos sulfoxide (maximum of 37% TRR in Swiss chard), and phenol sulfone derivatives (maximum of 35% TRR in wheat straw). Other organosoluble- and aqueous-soluble metabolites present at various levels were phenol sulfoxide, phenol sulfone, hydroxymethyl-phenol sulfone, phenol sulfoxide glucoside, and phenol sulfone glucoside.

7. The metabolism of fenamiphos in primary crops is consistent with metabolism in rotational crops. Except for the identification of des-amino fenamiphos sulfoxide in the present study, the metabolites identified were similar. The metabolism of fenamiphos in primary crops and in rotational crops involves the oxidation of fenamiphos to fenamiphos sulfoxide and/or fenamiphos sulfone, subsequent hydrolysis to fenamiphos sulfoxide phenol and fenamiphos sulfone phenol, and the formation of glucosides or other conjugates.

Limited field rotational study

8. The limited field rotational study indicates that residues of fenamiphos and its metabolites, fenamiphos sulfoxide and fenamiphos sulfone, expressed as fenamiphos equivalents, were detected at levels >0.01 ppm in/on several commodities from the 4-month rotation grown in test plots that had been broadcast-treated with the 3 lb/gal EC formulation at 1x the maximum seasonal rate for annual crops. The maximum combined residues from the 4-month rotation, which represents the registrant's established plantback interval, were found in/on spinach leaves (0.03 ppm), and sorghum forage (0.44 ppm) and straw (0.02 ppm).

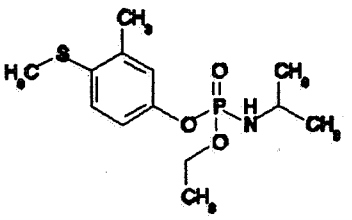
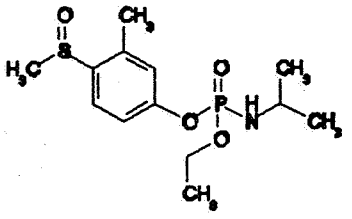
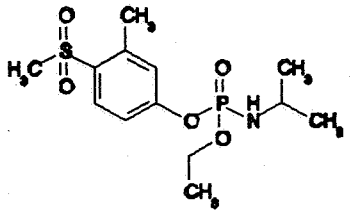
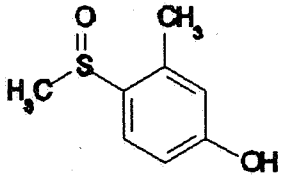
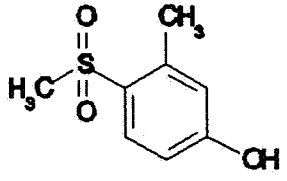
9. Although additional data are required to support rotational crop tolerances, sufficient data are presently available to conclude that residues may be found in rotational crops at levels which will require rotational crop tolerances at plantback intervals of less than 8 months.

10. In order to assure that illegal residues are not found in rotational crops, and to facilitate inclusion of rotational crop residues in dietary risk assessment, the registrant should either amend product labels to include an 8-month plantback interval so that residues of fenamiphos and its regulated metabolites will not be found in rotational crops, or (2) based on the limited field trial data, propose rotational crop tolerances for crops which are specified on product labels.

11. If the registrant wishes to propose rotational crops tolerances, then extensive field rotational crop studies will be required. The requirement for number of trials would be the same as that to establish primary tolerances on all crops (or crop groups) which the registrant intends to have as rotational crops. If the registrant desires to allow the "universe" of crop groups to be rotated, then magnitude of the residue data will be required on representative crops [see 40 CFR §180.34 (f)] for all crop groups which could be planted in a typical crop rotation sequence.

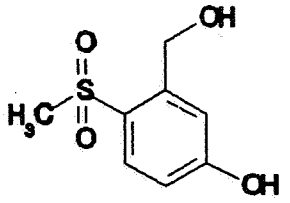
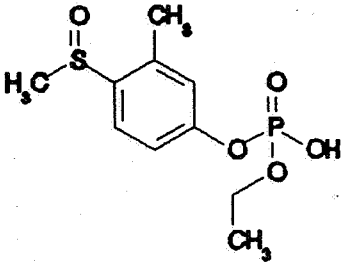
(7)

Table 1. Fenamiphos and its metabolites in rotational crops (MRID 41659301).

Common Name Chemical Name	Structure	Substrate
Fenamiphos Ethyl 3-methyl-4-(methylthio)phenyl (1-methylethyl)phosphoramidate		garden beet roots and tops, Swiss chard, wheat forage, straw, and grain
Fenamiphos sulfoxide Ethyl 3-methyl-4-(methylsulfinyl)phenyl (1-methylethyl)phosphoramidate		garden beet roots and tops, Swiss chard, wheat forage, straw, and grain
Fenamiphos sulfone Ethyl 3-methyl-4-(methylsulfonyl)phenyl (1-methylethyl)phosphoramidate		garden beet roots and tops, Swiss chard, wheat forage, straw, and grain
Phenol sulfoxide 3-Methyl-4-(methylsulfinyl)phenol		garden beet roots and tops, Swiss chard, wheat forage, straw, and grain
Phenol sulfone 3-Methyl-4-(methylsulfonyl)phenol		garden beet roots and tops, Swiss chard, wheat forage, straw, and grain

(continued)

Table 1 *(continued)*.

Common Name Chemical Name	Structure	Substrate
Hydroxymethylphenol sulfone 3-Hydroxymethyl-4-(methylsulfonyl)phenol		garden beet roots and tops, Swiss chard, wheat forage, straw, and grain
Des-amino fenamiphos sulfoxide Ethyl 3-methyl-4-(methylsulfinyl)phenyl phosphate		garden beet tops, Swiss chard, wheat forage, and grain

DETAILED CONSIDERATIONS

Directions for use

Two end-use products (EPs) of fenamiphos are presently registered to Miles Inc. (formerly Mobay Corporation) for use on food/feed crops grown in the U.S.: the 15% granular (G; Nemacur®15%; EPA Reg. No. 3125-236) and the 3 lb/gal emulsifiable concentrate (EC; Nemacur®3; EPA Reg. No. 3125-283). These formulations are registered on the following food/feed crops that can be rotated: asparagus, beets, bok choy (Chinese cabbage), Brussels sprouts, cabbage, cotton, eggplant, garlic, okra, peanuts, peppers, strawberries, and tobacco. Applications may be made preplant, preemergence, at-planting, or postharvest via soil (in band, furrow, broadcast, or through irrigation system) with and without incorporation. A post-plant drench application is also registered for cabbage. Depending on the timing and mode of applications, the recommended single application rates range from 2 to 6 lb ai/A, with a maximum seasonal rate of 6 lb ai/A. The established plantback interval for both formulations is 120 days. These use directions were obtained from registered EP labels.

GLN 165-1: Confined Rotational Crop Study (MRID 41659301)

In-life phase

Ring-labeled [1-^{13}/C^{14}C]fenamiphos (radiochemical purity >99%, specific activity 18.9 Ci/mole) was formulated with unlabeled fenamiphos as the 3 lb/gal EC. The final specific activity of the formulated test substance was 2.17 Ci/mole. The formulated test substance was applied at a field rate of 6.8 lb ai/A (1.1x the maximum registered rate for annual crops) to the surface of sandy loam soil (56.4% sand, 28.2% silt, 15.4% clay, 1.4% organic matter, pH 4.73, cation exchange capacity of 7.5 mval/100 g) in containers having a surface area of 0.98 m^2 (dimensions were not provided). The bottom of the container was covered with a 10-cm layer of gravel and then filled with a 50-cm layer of the test soil. The test substance was suspended in water and uniformly applied to the soil surface with a plot sprayer. During treatment, and for a few hours following treatment, the test containers were covered with a plastic tent. Radioactive aerosols were removed slowly with suction. After removal of the tent, the test substance was incorporated into the soil by sprinkler irrigation over a 5-hour period. Soybeans were planted as a cover crop one day prior to treatment, but no samples were collected for determination of ^{14}C-residue accumulation because of poor seed germination. At 30, 120, and 269 days after treatment (DAT), the containers were planted with garden beets, Swiss chard, and wheat. Prior to each rotational crop planting, the soil was tilled to a depth of 15 cm. For the first four months, the test containers were located outdoors and protected from rainfall. The test containers were then transferred to a greenhouse for the remainder of the study and maintained at day/night temperatures of 20/16 C. The crops were fertilized, watered, and treated with pesticides as necessary. Information pertaining to the maintenance schedule was provided.

Rotational crops were harvested at the following postplant intervals: 120-392 days for garden beets, 99-335 days for Swiss chard, 49-289 days for wheat forage, and 120-392 days for wheat grain and straw. Except for wheat forage, rotational crops were harvested at maturity for each sampling interval. In the 30-day rotation, wheat forage was harvested 49 days posttreatment, and mature beets, Swiss chard, and wheat were harvested at 120 days (beets and wheat) and 99 days (Swiss chard) posttreatment. In the 120-day rotation, wheat forage was harvested 134 days posttreatment, and mature beets, Swiss chard, and wheat were harvested 233, 203, and 251 days, respectively. In the 269-day rotation, wheat forage was harvested 289 days posttreatment, and mature beets, Swiss chard, and wheat were harvested 392 (beets and wheat) and 335 (Swiss chard) posttreatment. Mature beets were separated into roots and tops, and mature wheat plants were separated into grain and straw. The harvested plant samples were homogenized in liquid

nitrogen and stored frozen at -18 C until analyzed by Bayer AG (Leverkusen-Bayerwerk, Federal Republic of Germany). The intervals between sampling, storage, extraction, and analysis were not specified.

Total radioactive residues (TRR)

Subsamples of garden beet roots and tops, Swiss chard, and wheat forage, grain, and straw were analyzed in triplicate for total radioactive residues (TRR) by liquid scintillation spectrometry (LSS) following combustion. The LSS limit of detection was 0.01 ppm. The TRR in/on plant commodities are listed in Table 2.

Table 2. Total radioactive residues (TRR) found in/on rotational crops.

Substrate	TRR (ppm)		
	30 DAT •	120 DAT	269 DAT
Garden beet roots	4.62	0.48	0.10
Garden beet tops	7.31	2.83	0.36
Swiss chard	8.71	1.25	0.57
Wheat forage	17.30	15.17	2.36
Wheat straw	46.43	19.79	4.78
Wheat grain	0.98	0.73	0.20

• DAT = days after soil treatment.

The data in Table 2 indicate that total ^{14}C-residues exceeded 0.01 ppm in/on the commodities of all tested crops that were planted 30, 120, and 269 days after ring-labeled [1-^{13}C/^{14}C]fenamiphos was applied to sandy loam soil at 6.8 lb ai/A (≈ 1x the maximum registered single application rate). Accumulation was greatest in the 30-day rotational crops, with ^{14}C-residues ranging from 0.98 to 46.43 ppm; accumulation in the 120-day rotation was 0.48-19.79 ppm and in the 269-day rotation was 0.10-4.78 ppm. The greatest accumulation in each rotation was in wheat straw, declining from 46.43 ppm at the 30-day rotation to 4.78 pm at the 269-day rotation. ^{14}C-Residues accumulated least in wheat grain (0.98 ppm declining to 0.20 ppm) and beet roots (4.62 ppm declining to 0.10 ppm). [*Note: the present submission also contains data (TRR, fractionation characterization, identification, and storage stability) on soils as a result of application of the test substance. These soil data are not addressed herein*].

Extraction and hydrolysis of ^{14}C-residues in/on plant commodities

The registrant provided descriptions and a general flow chart of the fractionation scheme for all commodities. The registrant indicated that aliquots or subsamples were analyzed by LSS or combustion/LSS at each step of the extraction and partitioning procedures. Fractionation data were presented for radioactivity detected in organosoluble, aqueous-soluble, and non-extractable fractions. The amounts of radioactivity released by hydrolysis (except for wheat grain) and/or recovered after purification and derivatization procedures were not reported, but were included in the total values reported for organosoluble and aqueous extracts.

Subsamples of crop tissues were extracted sequentially with acetone, acetone:water (6:4; v:v), and methanol:water (6:4; v:v). After each extraction, the homogenates were filtered and the filtrates combined. The combined filtrates were concentrated by rotary evaporation at 40 C until only the aqueous phase remained. The aqueous extracts were then partitioned with dichloromethane. If precipitates formed, they were removed by centrifugation and analyzed by LSS/combustion; results were combined with those of the non-extractable residues. The amounts of radioactive residues recovered in/on plant matrices following extraction, partitioning, and concentration were: garden beet roots (90-98%), garden beet tops (92-115%), Swiss chard (90-95%), wheat forage (93-102%), wheat straw (89-95%), and wheat grain (94-97%). Radioactivity in extracts and in non-extractable residues were normalized to 100% total recovery by the registrant; non-normalized data were not presented. Aqueous extracts were analyzed by thin-layer chromatography (TLC), and organosoluble residues were analyzed by TLC and HPLC.

Due to the presence of interfering substances in some of the aqueous phases, some of the aqueous extracts required additional purification prior to TLC analysis. Aqueous extracts from Swiss chard and wheat grain (at all rotation intervals) were applied to an RP-18 column, and aqueous extracts from garden beet roots and tops (120- and 269-day rotations) were applied to cation exchange columns. The columns were sequentially eluted with water and methanol. Aqueous eluates from 269-DAT garden beet roots and tops were further purified on an anion exchange column sequentially eluted with water, methanol, and methanol:ammonia (methanol and methanol:ammonia eluates were combined). The purified eluates were then analyzed by TLC. Data depicting the recovery of radioactivity in each eluate were not provided.

Aqueous-soluble residues from 30-DAT Swiss chard and wheat straw were subjected to fractionation by enzyme hydrolysis. Aliquots of the aqueous extracts were concentrated to dryness under a stream of nitrogen, redissolved in phosphate-citrate buffer (pH 5.5) and hydrolyzed with β-glucosidase at 30 C for 5 and 22 hours, respectively. In a second hydrolysis procedure, separate aliquots of the aqueous extracts were mixed with 100 mM acetate buffer (pH 6.2) and hydrolyzed with aryl sulfatase at 37 C for 20 hours. An aliquot of the Swiss chard aqueous extract was concentrated, dissolved in phosphate buffer (pH 7.0), and hydrolyzed with carboxyesterase at 30 C for 5 hours. The carboxyesterase hydrolysate was then adjusted to pH 5.5 with 10 N acetic acid and hydrolyzed with β-glucosidase for an additional 5 hours at 30 C. All of the resulting hydrolysates were analyzed by TLC. Aliquots of the 30-DAT Swiss chard and wheat straw aqueous extracts were also derivatized with diazomethane prior to analysis by GC/MS.

An aliquot of the aqueous extract from 120-DAT wheat grain was mixed with 6 N HCl, layered with toluene, and hydrolyzed at 100 C for 8 hours. After cooling, the hydrolysate was extracted three times with toluene, and the toluene extracts were combined. The combined toluene extracts were concentrated and then analyzed by TLC. The acidic aqueous phase was applied to a C-18 column to remove HCl, and was eluted sequentially with water and methanol; the methanol eluate was analyzed by TLC.

Non-extractable residues of 120-DAT wheat grain only (67.7% TRR), were subjected to additional fractionation by reverse-isotope dilution following derivatization with phenylhydrazine. The non-extractable residues were refluxed in 4% HCl for 2.5 hours, then filtered. The filtrate was cleaned up on an anion-exchange column, and the radioactivity was eluted with water, concentrated, and combined with glucose, acetic acid, and ethylene glycol monomethyl ether. The mixture was heated to 80 C, then derivatized with phenylhydrazine at 80 C for 1 hour. The resulting precipitate was analyzed by LSS following combustion.

Metabolite characterization and identification in/on plant commodities

The %TRR data for all characterized/identified metabolites were normalized to 100% recovery for each matrix; non-normalized data were not presented. The methods used to detect, identify, and quantify fenamiphos and its metabolites in rotational crop matrices are described below.

One-dimensional TLC analyses were conducted on silica gel using the following solvent systems: ethyl acetate:cyclohexane:methanol (6:4:1; v:v:v; LM 1), diethyl ether:diisopropyl ether:acetone (2:2:1; v:v:v; LM 2), acetone:toluene (3:1; v:v; LM 3), ethyl acetate:isopropanol:water (5:3:1; v:v:v; LM 4), chloroform:methanol (9:1; v:v; LM 4), and butanol:acetic acid:water (8:2:1; v:v:v; LM 6). Metabolites were tentatively identified by comparison to the TLC R_f values of the following non-labeled reference standards: fenamiphos, fenamiphos sulfoxide, fenamiphos sulfone, phenol, phenol sulfoxide, phenol sulfone, des-ethyl fenamiphos, des-ethyl fenamiphos sulfoxide, des-ethyl fenamiphos sulfone, des-isopropyl fenamiphos, des-isopropyl fenamiphos sulfoxide, des-isopropyl fenamiphos sulfone, phenol sulfone-methyl ester, hydroxymethylphenol sulfone, des-amino fenamiphos sulfoxide, and des-amino fenamiphos sulfone. Radioactive metabolites were visualized by linear analyzer scan and autoradiography. Non-labeled reference standards were detected by UV-induced fluorescence at 254 nm. Representative radiochromatograms were presented.

Micropreparative and analytical HPLC analyses of organosoluble extracts were conducted on a Superspher 100 RP 18 column (250 mm x 4 mm I.D. x 4 μm) equipped with a Superspher RP 18 guard column and using a mobile phase of 5% acetonitrile (in pH 4 citrate-HCl buffer) changing to 100% acetonitrile in a series of linear gradients over a period of 45 minutes (designated as Method M1). Analyses using a second micropreparative HPLC method (designated as M2) were conducted on a LiChrospher RP 8 column (250 mm x 4 mm x 5 μm) equipped with a Licrospher RP 8 guard column and using the mobile phase described above, over a period of 50 minutes. For both HPLC methods, radioactive metabolites were identified by comparison of retention times with the retention times of the non-labeled reference standards listed above. Radioactive metabolites were detected using a flow-through radiodetector, and quantified by LSS fraction analysis; non-labeled reference standards were detected by UV at 254 nm. Representative chromatograms were presented.

Confirmatory analyses were conducted for metabolites in selected matrices (see below) in derivatized aqueous and organic fractions by GC/MS analyses. GC/MS analyses were conducted on a DB-5 column operated in the electron impact (EI) or chemical ionization (CI) mode. Representative mass spectra were presented. Additional confirmatory analyses were conducted by nuclear magnetic resonance (NMR) spectroscopy of ring-labeled [1-^{13}C/^{14}C]-residues.

Prior to confirmatory analyses by GC/MS and NMR, phenol sulfone, phenol sulfoxide, phenol sulfone conjugate, and des-amino fenamiphos sulfoxide, isolated from 30-DAT Swiss chard aqueous extracts, were purified by a combination of semi-preparative HPLC, preparative TLC, and preparative automatic multiple development (AMD) TLC procedures. Briefly, semi-preparative HPLC was conducted on a LiChrosorb RP8 SNC column using a mobile phase consisting of 100% water (containing 1% acetic acid) changing to 100% acetonitrile in a series of step and linear gradients over a period of 270 minutes (Method M3) or over a period of 315 minutes (Method M4). Metabolites were detected as previously described. Preparative TLC was conducted on silica gel, and residues were separated using dichloromethane:methanol (1:1; v:v; system LM7). The AMD-TLC analyses were conducted on silica gel using solvent gradients consisting of 100% methanol changing to 100% dichloromethane over an unspecified time interval.

Organosoluble metabolites: Organosoluble metabolites were identified in wheat straw or garden beet top samples from each rotational interval by analysis on TLC systems LM 1, 2, 3, and 5 and/or by HPLC method M1. In addition, the structures of fenamiphos sulfoxide and fenamiphos sulfone extracted from Swiss chard were confirmed by NMR and GC/MS. The registrant assumed

that organosoluble metabolites identified in wheat straw and garden beet samples were the same as organosoluble metabolites identified in other crop matrices. Therefore, organosoluble residues from other matrices were analyzed only by TLC system LM1 or HPLC system M1. Radioactive residues that co-chromatographed with reference standards or with metabolites previously identified by TLC or HPLC, were assumed to be identical.

Aqueous-soluble metabolites: Aqueous-soluble metabolites were identified by analysis on TLC systems LM 1-4 and HPLC system M2, in Swiss chard, wheat forage, and/or wheat straw samples harvested at the 30-DAT sampling interval. Phenol sulfoxide and phenol sulfone from wheat forage and straw were confirmed by GC/MS and NMR. GC/MS and NMR were also used to confirm the structures of these two metabolites, along with a phenol sulfone conjugate (apparently a glycoside) and des-amino fenamiphos sulfoxide (a metabolite which had not been reported in primary crops) in 30-DAT Swiss chard following purification procedures, and the phenol sulfone conjugate, two acidic phenol sulfone derivatives, and des-amino fenamiphos in 30-DAT Swiss chard and wheat straw following hydrolysis and derivatization with diazomethane. Glucosides of phenol sulfone and phenol sulfoxide were identified by TLC in wheat straw extracts, following glucosidase hydrolysis. The aqueous phases described above were co-chromatographed with the aqueous phases from all other rotational crop matrices to confirm the identity of metabolites identified in those matrices. Generally, TLC systems LM 4 and LM 6 were used for these confirmatory analyses. The registrant assumed that radiolabeled metabolites from different matrices with the same TLC R_f values were identical.

Non-extractable residues: Derivatization of 120-DAT wheat grain with phenylhydrazine released 72% of the bound radioactivity. The registrant indicated that phenylglucosazone contained 15% of the bound radioactivity. Three subsequent recrystallizations did not change the specific activity of phenylglucosazone, although some of the TRR were lost. According to the registrant these data indicate that at least 10.2% of 120-DAT wheat grain TRR was present as glucose. The registrant further concluded that other unspecified natural plant products also were radiolabeled. The presence of [^{14}C]glucose and other bound radioactive residues in wheat grain was attributed to the assimilation of $^{14}CO_2$ produced by the oxidation of [^{14}C]fenamiphos in the soil, and its subsequent uptake by the test plants. Non-extractable residues in all other rotational crop matrices, accounting for up to 78.6% of the TRR, were not further fractionated or analyzed.

In addition to the metabolites identified above, five additional metabolites, for which no structures were proposed, were characterized in rotational crop matrices: Metabolites 6, 13, and 16a and b, and Metabolite Group 10.

The quantitative results of the extraction and characterization procedures in garden beet roots and tops, Swiss chard, and wheat forage, straw, and grain resulting from soil treatment with ring-labeled [1-^{13}C/^{14}C]fenamiphos are presented in Tables 3 (garden beets), 4 (Swiss chard), and 5 (wheat). A summary of the metabolites characterized/identified in/on rotational crops is presented in Table 6.

Table 3. Distribution of total radioactive residues (TRR) in garden beets grown in aged sandy loam soil treated with ring-labeled [1-^{13}C/^{14}C]fenamiphos at 1.1x.

Fraction	% TRR	ppm	Characterization/Identification
30-DAT garden beet roots (4.62 ppm)			
Organosoluble	29	1.34	Phenol sulfone (7.1% TRR, 0.33 ppm), fenamiphos sulfone (7.3% TRR, 0.33 ppm), phenol sulfoxide (1.6% TRR, 0.07 ppm), fenamiphos sulfoxide (12.4% TRR, 0.57 ppm), and TLC origin (0.3% TRR, 0.01 ppm).
Aqueous-soluble	51	2.36	Hydroxymethylphenol sulfone and phenol sulfone (2.1% TRR, 0.10 ppm), phenol sulfoxide (3.0% TRR, 0.14 ppm), phenol sulfone glucoside (4.1% TRR, 0.19 ppm), Metabolite Group 10 and phenol sulfoxide glucoside (11.0% TRR, 0.51 ppm), phenol sulfone conjugate (7.0% TRR, 0.32 ppm), Metabolite 13 (3.3% TRR, 0.14 ppm), phenol sulfone derivatives (6.6% TRR, 0.30 ppm), and TLC origin (14.1% TRR, 0.65 ppm).
Non-extractable	20	0.94	Not further analyzed (NA).
120-DAT garden beet roots (0.48 ppm)			
Organosoluble	10	0.05	Phenol sulfone (2.6% TRR, 0.01 ppm), fenamiphos sulfone (3.6% TRR, 0.02 ppm), phenol sulfoxide (0.4% TRR, <0.01 ppm), fenamiphos sulfoxide (3.1% TRR, 0.01 ppm).
Aqueous-soluble	61	0.29	Hydroxymethylphenol sulfone and phenol sulfone (9.2% TRR, 0.04 ppm), Metabolite Group 10 and phenol sulfoxide glucoside (17.5% TRR, 0.08 ppm), phenol sulfone conjugate (3.8% TRR, 0.02 ppm), Metabolite 13 (2.4% TRR, 0.01 ppm), and TLC origin (27.7% TRR, 0.13 ppm).
Non-extractable	30	0.14	NA.
269-DAT garden beet roots (0.10 ppm)			
Organosoluble	5	<0.01	Phenol sulfone (0.9% TRR, <0.01 ppm), fenamiphos sulfone (2.1% TRR, <0.01 ppm), fenamiphos sulfoxide (1.7% TRR, <0.01 ppm), and TLC origin (0.1% TRR, <0.01 ppm).
Aqueous-soluble	49	0.05	Hydroxymethylphenol sulfone and phenol sulfone (2.8% TRR, <0.01 ppm), phenol sulfone glucoside (2.8% TRR, <0.01 ppm), Metabolite Group 10 and phenol sulfoxide glucoside (20.9% TRR, 0.02 ppm), phenol sulfone conjugate (7.9% TRR, 0.01 ppm), and TLC origin (14.9% TRR, 0.01 ppm).
Non-extractable	46	0.05	NA.
30-DAT garden beet tops (7.31 ppm)			
Organosoluble	36	2.63	Fenamiphos (0.4% TRR, 0.03 ppm), phenol sulfone (3.2% TRR, 0.23 ppm), fenamiphos sulfone (11.1% TRR, 0.81 ppm), phenol sulfoxide (0.9% TRR, 0.07 ppm), fenamiphos sulfoxide (19.0% TRR, 1.39 ppm), Metabolite 6 (0.4% TRR, 0.03 ppm), and TLC origin (0.7% TRR, 0.05 ppm).
Aqueous-soluble	62	4.53	Hydroxymethylphenol sulfone and phenol sulfone (0.4% TRR, 0.03 ppm), phenol sulfoxide (1.2% TRR, 0.09 ppm), phenol sulfone glucoside (3.7% TRR, 0.27 ppm), Metabolite Group 10 (4.3% TRR, 0.31 ppm), phenol sulfoxide glucoside (4.1% TRR, 0.30 ppm), phenol sulfone conjugate (18.0% TRR, 1.32 ppm), Metabolite 13 (4.3% TRR, 0.31 ppm), phenol sulfone derivatives (7.5% TRR, 0.55 ppm), des-amino fenamiphos sulfoxide (13.2% TRR, 0.96 ppm), and TLC origin (5.2% TRR, 0.38 ppm).

(continued)

Table 3 (*continued*).

Fraction	% TRR	ppm	Characterization/Identification
30-DAT garden beet tops (continued)			
Non-extractable	3	0.18	NA.
120-DAT garden beet tops (2.83 ppm)			
Organosoluble	17	4.8	Phenol sulfone (3.2% TRR, 0.09 ppm), fenamiphos sulfone (6.1% TRR, 0.17 ppm), phenol sulfoxide (0.2% TRR, 0.01 ppm), and fenamiphos sulfoxide (7.2% TRR, 0.20 ppm).
Aqueous-soluble	73	20.7	Phenol sulfone glucoside (8.6% TRR, 0.24 ppm), Metabolite Group 10 (3.2% TRR, 0.09 ppm), phenol sulfoxide glucoside (10.4% TRR, 0.29 ppm), phenol sulfone conjugate (14.5% TRR, 0.41 ppm), phenol sulfone derivatives (19.2% TRR, 0.54 ppm), des-amino fenamiphos sulfoxide, Metabolites 16 a/b, and TLC origin (16.7% TRR, 0.47 ppm).
Non-extractable	11	3.1	NA.
269-DAT garden beet tops (0.36 ppm)			
Organosoluble	13	0.05	Fenamiphos (0.1% TRR, <0.01 ppm), phenol sulfone (3.0% TRR, 0.01 ppm), fenamiphos sulfone (4.6% TRR, 0.02 ppm), phenol sulfoxide (0.4% TRR, <0.01 ppm), fenamiphos sulfoxide (4.5% TRR, 0.02 ppm), and TLC origin (0.2% TRR, <0.01 ppm).
Aqueous-soluble	71	0.26	Phenol sulfone glucoside (10.9% TRR, 0.04 ppm), phenol sulfoxide glucoside (6.2% TRR, 0.02 ppm), phenol sulfone conjugate (11.5% TRR, 0.04 ppm), Metabolite 13 (11.7% TRR, 0.04 ppm), and TLC origin (30.3% TRR, 0.11 ppm).
Non-extractable	17	0.06	NA.

Table 4. Distribution of total radioactive residues (TRR) in Swiss chard grown in aged sandy loam soil treated with ring-labeled [1-^{13}C/^{14}C]fenamiphos at 1.1x.

Fraction	% TRR	ppm	Characterization/Identification
30-DAT Swiss chard (8.71 ppm)			
Organosoluble	54	4.70	Fenamiphos (0.4% TRR, 0.03 ppm), phenol sulfone (3.7% TRR, 0.32 ppm), fenamiphos sulfone (20.2% TRR, 1.76 ppm), phenol sulfoxide (1.1% TRR, 0.10 ppm), fenamiphos sulfoxide (28.1% TRR, 2.45 ppm), Metabolite 6 (0.3 % TRR, 0.03 ppm), and TLC origin (0.3% TRR, 0.03 ppm).
Aqueous-soluble	45	3.92	Hydroxymethylphenol sulfone and phenol sulfone (2.4% TRR, 0.21 ppm), phenol sulfoxide (2.0% TRR, 0.17 ppm), phenol sulfone glucoside (1.0% TRR, 0.09 ppm), Metabolite Group 10 and phenol sulfoxide glucoside (2.0% TRR, 0.17 ppm), phenol sulfone conjugate (15.7% TRR, 1.37 ppm), Metabolite 13 (2.1% TRR, 0.18 ppm), des-amino fenamiphos sulfoxide (13.9% TRR, 1.21 ppm), Metabolites 16 a/b (4.7% TRR, 0.41 ppm), and TLC origin (1.5% TRR, 0.13 ppm).
Non-extractable	0.5	0.04	NA.
120-DAT Swiss chard (1.25 ppm)			
Organosoluble	9	0.11	Phenol sulfone (5.8% TRR, 0.07 ppm), fenamiphos sulfone (1.8% TRR, 0.02 ppm), phenol sulfoxide (0.3% TRR, <0.01 ppm), fenamiphos sulfoxide (1.4% TRR, 0.02 ppm), and TLC origin (0.1% TRR, <0.01 ppm).
Aqueous-soluble	81	1.01	Hydroxymethylphenol sulfone and phenol sulfone (2.7% TRR, 0.03 ppm), phenol sulfone glucoside (2.5% TRR, 0.03 ppm), phenol sulfone conjugate (24.7% TRR, 0.31 ppm), Metabolite 13 (4.2% TRR, 0.05 ppm), des-amino fenamiphos sulfoxide (37.3% TRR, 0.47 ppm), Metabolites 16 a/b (7.6% TRR, 0.10 ppm), and TLC origin (2.1% TRR, 0.03 ppm).
Non-extractable	10	0.13	NA.
269-DAT Swiss chard (0.57 ppm)			
Organosoluble	15	0.09	Fenamiphos (0.1% TRR, <0.01 ppm), phenol sulfone (4.5% TRR, 0.03 ppm), fenamiphos sulfone (5.8% TRR, 0.03 ppm), phenol sulfoxide (0.5% TRR, <0.01 ppm), fenamiphos sulfoxide (4.1% TRR, 0.02 ppm), and TLC origin (0.2% TRR, <0.01 ppm).
Aqueous-soluble	74	0.42	Phenol sulfone glucoside (2.8% TRR, 0.02 ppm), phenol sulfone conjugate (25.0% TRR, 0.14 ppm), Metabolite 13 (4.3% TRR, 0.02 ppm), des-amino fenamiphos sulfoxide (28.5% TRR, 0.16 ppm), Metabolites 16 a/b (10.5% TRR, 0.06 ppm), and TLC origin (3.0% TRR, 0.02 ppm).
Non-extractable	11	0.06	NA.

Table 5. Distribution of total radioactive residues (TRR) in wheat grown in aged sandy loam soil treated with ring-labeled [1-^{13}C/^{14}C]fenamiphos at 1.1x.

Fraction	% TRR	ppm	Characterization/Identification
30-DAT wheat forage (17.30 ppm)			
Organosoluble	67	11.59	Phenol sulfone (10.1% TRR, 1.75 ppm), fenamiphos sulfone (18.0% TRR, 3.11 ppm), phenol sulfoxide (5.7% TRR, 0.99 ppm), fenamiphos sulfoxide (31.3% TRR, 5.41 ppm), Metabolite 6 (1.6% TRR, 0.28 ppm), and TLC origin (0.2% TRR, 0.03 ppm).
Aqueous-soluble	28	4.84	Hydroxymethylphenol sulfone (2.4% TRR, 0.42 ppm), phenol sulfone (0.5% TRR, 0.09 ppm), phenol sulfoxide (6.4% TRR, 1.11 ppm), phenol sulfone glucoside (5.2% TRR, 0.90 ppm), phenol sulfoxide glucoside (3.4% TRR, 0.59 ppm), phenol sulfone conjugate (1.4% TRR, 0.24 ppm), phenol sulfone derivatives (5.5% TRR, 0.95 ppm), des-amino fenamiphos sulfoxide (2.3% TRR, 0.40 ppm), and TLC origin (0.4% TRR, 0.07 ppm).
Non-extractable	6	0.95	NA.
120-DAT wheat forage (15.17 ppm)			
Organosoluble	68	10.32	Phenol sulfone (23.0% TRR, 3.49 ppm), fenamiphos sulfone (18.6% TRR, 2.82 ppm), phenol sulfoxide (6.8% TRR, 1.03 ppm), fenamiphos sulfoxide (19.1% TRR, 2.90 ppm), and Metabolite 6 (0.5% TRR, 0.08 ppm).
Aqueous-soluble	29	4.40	Hydroxymethylphenol sulfone and phenol sulfone (3.1% TRR, 0.47 ppm), phenol sulfoxide (3.5% TRR, 0.53 ppm), phenol sulfone glucoside (2.0% TRR, 0.30 ppm), phenol sulfoxide glucoside (0.9% TRR, 0.14 ppm), phenol sulfone conjugate (1.6% TRR, 0.24 ppm), phenol sulfone derivatives (12.1% TRR, 1.84 ppm), des-amino fenamiphos sulfoxide (3.3% TRR, 0.50 ppm), and TLC origin (2.0% TRR, 0.30 ppm).
Non-extractable	3	0.52	NA.
269-DAT wheat forage (2.36 ppm)			
Organosoluble	75	1.77	Phenol sulfone (16.7% TRR, 0.39 ppm), fenamiphos sulfone (29.1% TRR, 0.69 ppm), phenol sulfoxide (3.2% TRR, 0.08 ppm), fenamiphos sulfoxide (26.1% TRR, 0.62 ppm), and TLC origin (0.4% TRR, 0.01 ppm).
Aqueous-soluble	16	0.38	Hydroxymethylphenol sulfone and phenol sulfone (10.1% TRR, 0.24 ppm), phenol sulfoxide (2.6% TRR, 0.06 ppm), phenol sulfone glucoside (0.5% TRR, 0.01 ppm), phenol sulfoxide glucoside (0.5% TRR, 0.01 ppm), phenol sulfone conjugate (0.3% TRR, 0.01 ppm), and TLC origin (1.6% TRR, 0.04 ppm).
Non-extractable	9	0.21	NA.
30-DAT wheat straw (46.43 ppm)			
Organosoluble	34	15.79	Phenol sulfone (5.3% TRR, 2.46 ppm), fenamiphos sulfone (14.1% TRR, 6.55 ppm), phenol sulfoxide (2.8% TRR, 1.30 ppm), fenamiphos sulfoxide (10.4% TRR, 4.83 ppm), Metabolite 6 (0.9% TRR, 0.42 ppm), and TLC origin (0.8% TRR, 0.37 ppm).

(continued)

Table 5 *(continued)*.

Fraction	% TRR	ppm	Characterization/Identification
30-DAT wheat straw (continued)			
Aqueous-soluble	56	26.00	Hydroxymethylphenol sulfone (0.5% TRR, 0.23 ppm), phenol sulfone (0.6% TRR, 0.28 ppm), phenol sulfoxide (2.8% TRR, 1.30 ppm), phenol sulfone glucoside (13.5% TRR, 6.27 ppm), phenol sulfoxide glucoside (10.3% TRR, 4.78 ppm), phenol sulfone conjugate (1.7% TRR, 0.79 ppm), phenol sulfone derivatives (16.6% TRR, 7.71 ppm), Metabolites 16 a/b (6.4% TRR, 2.97 ppm), and TLC origin (3.5% TRR, 1.63 ppm).
Non-extractable	10	4.60	NA.
120-DAT wheat straw (19.79 ppm)			
Organosoluble	21	4.16	Phenol sulfone (5.8% TRR, 1.15 ppm), fenamiphos sulfone (8.6% TRR, 1.70 ppm), phenol sulfoxide (1.6% TRR, 0.32 ppm), fenamiphos sulfoxide (5.3% TRR, 1.05 ppm), and Metabolite 6 (0.3% TRR, 0.06 ppm).
Aqueous-soluble	67	13.26	Hydroxymethylphenol sulfone and phenol sulfone (0.9% TRR, 0.18 ppm), phenol sulfoxide (1.7% TRR, 0.34 ppm), phenol sulfone glucoside (9.4% TRR, 1.86 ppm), phenol sulfoxide glucoside (8.1% TRR, 1.60 ppm), phenol sulfone conjugate (3.1% TRR, 0.61 ppm), phenol sulfone derivatives (34.3% TRR, 6.79 ppm), and TLC origin (9.3% TRR, 1.84 ppm).
Non-extractable	12	2.32	NA.
269-DAT wheat straw (4.78 ppm)			
Organosoluble	17	0.81	Fenamiphos (<0.1% TRR, <0.01 ppm), phenol sulfone (2.2% TRR, 0.11 ppm), fenamiphos sulfone (8.5% TRR, 0.41 ppm), phenol sulfoxide (1.1% TRR, 0.05 ppm), fenamiphos sulfoxide (4.5% TRR, 0.22 ppm), Metabolite 6 (0.2% TRR, 0.01 ppm), and TLC origin (0.5% TRR, 0.02 ppm).
Aqueous-soluble	62	2.96	Phenol sulfone glucoside (11.6% TRR, 0.55 ppm), phenol sulfoxide glucoside (6.4% TRR, 0.31 ppm), phenol sulfone conjugate (3.1% TRR, 0.15 ppm), phenol sulfone derivatives (35.4% TRR, 1.69 ppm), and TLC origin (5.7% TRR, 0.27 ppm).
Non-extractable	21	0.98	NA.
30-DAT wheat grain (0.98 ppm)			
Organosoluble	17	0.17	Phenol sulfone (3.9% TRR, 0.04 ppm), fenamiphos sulfone (7.8% TRR, 0.08 ppm), phenol sulfoxide (0.7% TRR, 0.01 ppm), fenamiphos sulfoxide (4.0% TRR, 0.04 ppm), and TLC origin (0.4% TRR, <0.01 ppm).
Aqueous-soluble	59	0.58	Hydroxymethylphenol sulfone and phenol sulfone (22.4% TRR, 0.22 ppm), phenol sulfoxide (3.1% TRR, 0.03 ppm), phenol sulfone glucoside (15.9% TRR, 0.16 ppm), phenol sulfoxide glucoside (9.4% TRR, 0.09 ppm), phenol sulfone derivatives (4.7% TRR, 0.05 ppm), and TLC origin (3.5% TRR, 0.03 ppm).
Non-extractable	24	0.24	NA.

(continued)

Table 5 *(continued)*.

Fraction	% TRR	ppm	Characterization/Identification
120-DAT wheat grain (0.73 ppm)			
Organosoluble	7	0.05	Phenol sulfone (2.2% TRR, 0.02 ppm), fenamiphos sulfone (2.9% TRR, 0.02 ppm), phenol sulfoxide (0.5% TRR, <0.01 ppm), fenamiphos sulfoxide (1.1% TRR, 0.01 ppm), and TLC origin (0.6% TRR, <0.01 ppm).
Aqueous-soluble	25	0.18	Hydroxymethylphenol sulfone and phenol sulfone (5.3% TRR, 0.04 ppm), phenol sulfoxide (1.7% TRR, 0.01 ppm), phenol sulfone glucoside (8.0% TRR, 0.06 ppm), phenol sulfoxide glucoside (2.6% TRR, 0.02 ppm), phenol sulfone conjugate (2.7% TRR, 0.02 ppm), and TLC origin (5.0% TRR, 0.04 ppm).
Non-extractable	68	0.49	NA.
269-DAT wheat grain (0.20 ppm)			
Organosoluble	4	<0.01	Fenamiphos (0.1% TRR, <0.01 ppm), phenol sulfone (0.9% TRR, <0.01 ppm), fenamiphos sulfone (1.9% TRR, <0.01 ppm), phenol sulfoxide (0.2% TRR, <0.01 ppm), fenamiphos sulfoxide (1.0% TRR, <0.01 ppm), and TLC origin (<0.1% TRR, <0.01 ppm).
Aqueous-soluble	17	0.03	Hydroxymethylphenol sulfone and phenol sulfone (1.2% TRR, <0.01 ppm), phenol sulfone glucoside (5.1% TRR, 0.01 ppm), phenol sulfone conjugate, Metabolite 13, phenol sulfone derivatives, and des-amino fenamiphos sulfoxide (3.7% TRR, 0.02 ppm), and TLC origin (3.3% TRR, 0.01 ppm).
Non-extractable	79	0.16	NA.

Table 6. Summary of identification of [^{14}C]fenamiphos residues in/on rotational crops.

Metabolite	Swiss Chard		Garden beet roots		Garden beet Tops		Wheat Forage		Wheat Straw		Wheat Grain	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
30-DAT												
Identified												
Fenamiphos	0.4	0.03	--	--	0.4	0.03	--	--	--	--	--	--
Fenamiphos sulfoxide	28.1	2.45	12.4	0.57	19.0	1.39	31.3	5.41	10.4	4.83	4.0	0.04
Fenamiphos sulfone	20.2	1.76	7.3	0.33	11.1	0.81	18.0	3.11	14.1	6.55	7.8	0.08
Phenol sulfoxide	3.1	0.27	4.6	0.21	2.1	0.16	12.1	2.10	5.6	2.60	3.8	0.04
Phenol sulfone	4.9	0.43	8.1	0.38	3.4	0.25	10.6	1.84	5.9	2.74	15.1	0.15
Hydroxymethyl-phenol sulfone	1.2	0.10	1.0	0.05	0.2	0.01	2.4	0.42	0.5	0.23	11.2	0.11
Phenol sulfoxide glucoside	2.0	0.17	5.5	0.25	4.1	0.30	3.4	0.59	10.3	4.78	9.4	0.09
Phenol sulfone glucoside	1.0	0.09	4.1	0.19	3.7	0.27	5.2	0.90	13.5	6.27	15.9	0.16
Phenol sulfone conjugate	15.7	1.37	7.0	0.32	18.0	1.32	1.4	0.24	1.7	0.79	--	--
Des-amino fenamiphos sulfoxide	13.9	1.21	--	--	13.2	0.96	2.3	0.40	--	--	--	--
Phenol sulfone derivatives	--	--	6.6	0.30	7.5	0.55	5.5	0.95	16.6	7.71	4.7	0.05
Subtotal	**90.5**	**7.88**	**56.7**	**2.60**	**82.7**	**6.05**	**92.2**	**15.96**	**78.6**	**36.50**	**71.9**	**0.72**
Characterized												
Metabolite 6	0.3	0.03	--	--	0.4	0.03	1.6	0.28	0.9	0.42	--	--
Metabolite Group 10	--	--	5.5	0.25	4.3	0.31	--	--	--	--	--	--
Metabolite 13	2.1	0.18	3.3	0.14	4.3	0.31	--	--	--	--	--	--
Metabolites 16a and 16b	4.7	0.41	--	--	--	--	--	--	6.4	2.97	--	--
TLC origin	1.8	0.16	14.4	0.66	5.9	0.43	0.6	0.10	4.3	2.00	3.9	<0.04
Subtotal	**8.9**	**0.78**	**23.2**	**1.05**	**14.9**	**1.08**	**2.2**	**0.38**	**11.6**	**5.39**	**3.9**	**<0.04**
Total characterized/identified	**99.4**	**8.66**	**79.9**	**3.65**	**97.6**	**7.13**	**94.4**	**16.34**	**90.2**	**41.89**	**75.8**	**<0.76**
Non-extractable	0.5	0.04	20.4	0.94	2.5	0.18	5.5	0.95	9.9	4.60	24.2	0.24
120-DAT												
Identified												
Fenamiphos sulfoxide	1.4	0.02	3.1	0.01	7.2	0.20	19.1	2.90	5.3	1.05	1.1	0.01
Fenamiphos sulfone	1.8	0.02	3.6	0.02	6.1	0.17	18.6	2.82	8.6	1.70	2.9	0.02
Phenol sulfoxide	0.3	<0.01	0.4	<0.01	0.2	0.01	10.3	1.56	3.3	0.66	2.2	<0.02
Phenol sulfone	7.2	0.09	7.2	0.03	3.2	0.09	24.6	3.73	6.3	1.24	4.9	0.04
Hydroxymethyl-phenol sulfone	1.3	0.01	4.6	0.02	--	--	1.5	0.23	0.4	0.09	2.6	0.02
Phenol sulfoxide glucoside	--	--	8.8	0.04	10.4	0.29	0.9	0.14	8.1	1.60	2.6	0.02
Phenol sulfone glucoside	2.5	0.03	--	--	8.6	0.24	2.0	0.30	9.4	1.86	8.0	0.06

(continued)

Table 6 (continued).

Metabolite	Swiss Chard		Garden beet roots		Garden beet Tops		Wheat Forage		Wheat Straw		Wheat Grain	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
269-DAT (continued)												
Characterized												
Metabolite 6	--	--	--	--	--	--	--	--	0.2	0.01	--	--
Metabolite Group 10	--	--	10.4	0.01	--	--	--	--	--	--	--	--
Metabolite 13	4.3	0.02	--	--	11.7	0.04	--	--	--	--	1.9	<0.01
Metabolites 16a and 16b	10.5	0.06	--	--	--	--	--	--	--	--	--	--
TLC origin	3.2	0.03	15.0	<0.02	30.5	<0.12	2.0	0.05	6.2	0.29	3.3	<0.02
Subtotal	**18.0**	**0.11**	**25.4**	**<0.03**	**42.2**	**0.16**	**2.0**	**0.05**	**6.4**	**0.30**	**5.2**	**<0.03**
Total characterized/identified	**89.3**	**<0.53**	**54.1**	**<0.11**	**83.4**	**<0.33**	**91.1**	**2.16**	**<79.3**	**<3.80**	**21.3**	**<0.14**
Non-extractable	10.9	0.06	45.9	0.05	16.7	0.06	9.0	0.21	20.6	0.98	78.6	0.16

Storage stability

Samples used in this study were stored frozen at -18 C until analyzed; dates of sample extraction and analysis were not provided. Based on the study start and completion dates, samples were analyzed within ~ two years of harvest. The registrant provided data from a concurrent storage stability study using 30-DAT wheat straw samples. Subsamples were extracted at ~ 1 month and ~ 16 months following harvest by the methods previously described. The extracts were analyzed by TLC, and the metabolite profiles depicting the amounts of selected organosoluble metabolites, aqueous-soluble residues, and non-extractable residues for each sampling interval were compared. The data indicated that representative radiolabeled residues in wheat straw sample extracts did not change following ~ 16 months of frozen storage. These data are adequate to support the present confined rotational crop study.

Study summary

The submitted confined rotational crop study is adequate to satisfy the 165-1 guideline requirements for purposes of reregistration.

The study indicates that ^{14}C-residues (expressed as fenamiphos equivalents) accumulated at levels >0.01 ppm in/on all commodities of beets, Swiss chard, and wheat that were planted 30, 120, and 269 days after ring-labeled [1-^{13}C/^{14}C]fenamiphos was applied to sandy loam soil at 1.1x the maximum registered rate for annual food/feed crops. Accumulation was highest in the 30-day rotation and declined thereafter. The ranges of total radioactive residues (TRR) accumulation were: garden beet roots (0.10-4.62 ppm), garden beet tops (0.36-7.31 ppm), Swiss chard (0.57-8.71 ppm), wheat forage (2.36-17.30 ppm), wheat straw (4.78-46.43 ppm), and wheat grain (0.20-0.98 ppm).

The majority of the total radioactive residues (TRR) in/on the matrices of rotated crops were adequately characterized and identified, except for garden beet roots and wheat grain from the 269-DAT rotation interval. The ranges of characterized and identified radioactivity in/on rotated commodities were: garden beet tops (83-98% of TRR), garden beet roots (54-80% of TRR), Swiss chard (89-99% of TRR), wheat forage (91-97% of TRR), wheat straw (79-90% of TRR), and wheat grain (21-76%).

No further analytical work is required on the following fractions from the 269-day rotation because adequate data from primary plant metabolism studies, including those from root and tuber vegetables and cereal grains, are available: (i) bound residues (45.9% of TRR, 0.05 ppm) in/on garden beet roots; and (ii) unidentified wheat grain bound residues (79% of TRR, 0.16 ppm).

Fenamiphos sulfone and fenamiphos sulfoxide, the two metabolites of concern (in addition to the parent), were the principal organosoluble residues identified from the 30-day rotations, and collectively accounted for 12-49% of the radioactivity; the proportion of these two residues declined at subsequent intervals. The parent, fenamiphos, was a minor (<1% of TRR) residue at all intervals.

The principal aqueous-soluble residues identified were phenol sulfone conjugate (maximum of 25% TRR in Swiss chard), des-amino fenamiphos sulfoxide (maximum of 37% TRR in Swiss chard), and phenol sulfone derivatives (maximum of 35% TRR in wheat straw). Other organosoluble- and aqueous-soluble metabolites present at various levels were phenol sulfoxide, phenol sulfone, hydroxymethyl-phenol sulfone, phenol sulfoxide glucoside, and phenol sulfone glucoside.

The metabolism of fenamiphos in primary crops is consistent with metabolism in rotational crops. Except for the identification of des-amino fenamiphos sulfoxide in the present study, the metabolites identified were similar. The metabolism of fenamiphos in primary crops and in rotational crops involves the oxidation of fenamiphos to fenamiphos sulfoxide and/or fenamiphos

sulfone, subsequent hydrolysis to fenamiphos sulfoxide phenol and fenamiphos sulfone phenol, and the formation of glucosides or other conjugates.

GLN 165-2: Limited Field Rotational Crop Studies (MRID 42043601)

Two field rotational crops were planted in each of three test locations (KS, MS, and TX). A single broadcast soil application of the 3 lb/gal EC formulation was made to bare soil at 6 lb ai/A (1x the maximum seasonal rate for annual crops) in a finished spray volume of 16-31 gal/A. The following rotational crops were planted at 1 and 4 months posttreatment and cultivated according to established farming practices: (i) in KS: turnips, spinach, and sorghum; (ii) in MS: turnips, spinach, sorghum, and wheat; and (iii) in TX: turnips, mustard greens, and wheat. In addition, sorghum was planted in MS at 8 months posttreatment. All rotational crops were harvested at maturity; in addition, immature wheat and sorghum green forage samples were harvested at 45 days postplanting. Samples were not collected from the 4-month turnip and spinach crops in MS because of crop failure. Control samples were harvested from co-located, untreated plots at each test site.

The magnitude of the residue in the commodities of rotational crops is presented in Table 7. The apparent combined residues of fenamiphos, fenamiphos sulfoxide and fenamiphos sulfone (expressed as fenamiphos equivalents), were <0.01 ppm (nondetectable) in/on the following untreated controls (number of samples in parentheses): turnip tops (5), turnip roots (5), mustard leaves (3), spinach leaves (3), sorghum forage (4), sorghum straw (4), sorghum grain (4), wheat forage (3), wheat straw (3), and wheat grain (2).

Residue analytical methods

Samples were analyzed for the combined residues of fenamiphos, fenamiphos sulfoxide, and fenamiphos sulfone using a GC/FPD method (Mobay Method No. 100163), modified to incorporate a permanganate oxidation procedure that converts the parent and its sulfoxide metabolite to fenamiphos sulfone. The combined residues are expressed as fenamiphos equivalents. The limit of detection is 0.01 ppm. Briefly, residues were extracted by homogenization with acetone and water. The homogenate was then vacuum filtered and partitioned three times with chloroform. After each partition the chloroform fractions were filtered through anhydrous sodium sulfate. The chloroform filtrates were combined, concentrated just to dryness by rotary evaporation at 40 C, and redissolved in acetone. Residues were then mixed sequentially with 20% magnesium sulfate and 0.1 M potassium permanganate. The resulting mixture was partitioned three times with chloroform, filtered through anhydrous sodium sulfate, and the combined chloroform filtrates were evaporated just to dryness by rotary evaporation at 40 C. Dried residues from all matrices were redissolved in ethyl acetate prior to analysis by GC/FPD. Dried straw (wheat and sorghum) residues were subject to additional partitioning with acetonitrile and hexane prior to GC/FPD analysis. All GC analyses were conducted on an OV1701 fused silica column (15 m x 530 μm x 3.0 μm) equipped with a flame photometric detector (FPD) operated in the phosphorous mode. Residue concentration in rotational crop matrices was determined by comparing the instrument response for sample extracts to an external standard. Confirmatory analyses for residues of fenamiphos in/on crop matrices were conducted using a GC/MS method equipped with a mass selective detector (MSD).

The registrant presented data and chromatograms demonstrating that the detector response for fenamiphos and fenamiphos sulfoxide (after conversion to the sulfone metabolite), and fenamiphos sulfone was linear in the 0.01-0.10 ppm range for peanut green forage, wheat straw and grain, and turnip roots and tops; correlation coefficients ranged 0.9798-0.9994.

Table 7. Combined residues of fenamiphos, fenamiphos sulfoxide, and fenamiphos sulfone found in/on the commodities of rotational crops grown in test plots treated with a single broadcast soil application of the 3 lb/gal EC fenamiphos formulation at 1x the maximum rate.

Rotational Crop	Rotation Interval (Months) [a]	RAC	Harvest Interval (Days) [b]	No. of Samples	Combined Residues [c] (ppm)
Turnips	1	Tops	37-77	3	<0.01-0.05
		Roots		3	<0.01
	4	Tops	36, 66	2	<0.01
		Roots		2	<0.01
Mustard	1	Leaves	47	1	0.03
	4	Leaves	45	1	<0.01
Spinach	1	Leaves	56, 197	2	0.02, 0.10
	4	Leaves	56	1	0.03
Sorghum	1	Forage	45	1	0.05
		Straw	125	1	0.03
		Grain		1	<0.01
	4	Forage	45, 48	2	0.01, 0.44
		Straw	115, 125	2	<0.01, 0.02
		Grain		2	<0.01
	8	Forage	48	1	<0.01
		Straw	115	1	<0.01
		Grain		1	<0.01
Wheat	1	Forage	45, 46	2	0.02, 0.75
		Straw	182, 259	2	<0.01, 0.18
		Grain		1	<0.01
	4	Forage	44	1	<0.01
		Straw	164	1	<0.01
		Grain		1	<0.01

[a] Rotational interval is the period between soil treatment and planting.
[b] Harvest interval is the period between planting and harvest.
[c] Combined residues include the sum of fenamiphos, fenamiphos sulfoxide, and fenamiphos sulfone determined as fenamiphos sulfone and expressed as fenamiphos equivalents *per se*.

The method validation recoveries and concurrent recoveries obtained during analysis of samples from the limited field rotational crop study are presented in Table 8; peanut green forage was used in place of wheat and sorghum forage for method validation. For method validation untreated crop samples were fortified with fenamiphos, fenamiphos sulfoxide, and fenamiphos sulfone at 0.01-0.05 ppm; peanut green forage was fortified only at 0.05 ppm. For concurrent recoveries, untreated control samples were fortified with fenamiphos sulfoxide at 0.10 ppm. The registrant provided raw data which included representative chromatograms of standard, control, treated and fortified samples, and examples of residue calculations. The recovery data indicate that this Mobay Method is adequate for collecting data on residues of fenamiphos, fenamiphos sulfoxide, and fenamiphos sulfone in/on the rotational crop matrices used in this study.

Table 8. Method validation and concurrent recoveries of fenamiphos, fenamiphos sulfoxide, and fenamiphos sulfone from untreated crop matrices fortified with fenamiphos, fenamiphos sulfoxide, and fenamiphos sulfone at 0.01-0.05 ppm (for method validation) and with fenamiphos sulfoxide at 0.10 ppm (for concurrent recoveries.

Matrix	Number of Samples	Fortification (ppm)	Percent Recovery •		
			Fenamiphos	Fenamiphos sulfoxide	Fenamiphos sulfone
Method validation recoveries - fortification with fenamiphos, fenamiphos sulfoxide, and fenamiphos sulfone					
Turnip roots	4	0.01-0.05	94-113	74-112	78-117
Turnip tops	4	0.01-0.05	85-104	75-89	81-89
Peanut green forage	1	0.05	70	88	74
Wheat straw	4	0.01-0.05	73-88	73-83	67-109
Wheat grain	4	0.01-0.05	76-97	71-92	80-117
Concurrent recoveries - fortified with fenamiphos sulfoxide only					
Turnip tops	3	0.10	--	81-119	--
Turnip roots	3	0.10	--	75-100	--
Mustard greens	2	0.10	--	75, 82	--
Sorghum forage	3	0.10	--	78-110	--
Sorghum straw	3	0.10	--	70-93	--
Sorghum grain	2	0.10	--	88	--
Wheat forage	1	0.10	--	84	--
Wheat straw	1	0.10	--	77	--
Wheat grain	1	0.10	--	82	--

• Determined as fenamiphos sulfone and expressed as fenamiphos equivalents.

Storage stability

Samples were stored frozen (ca. -20 C) for the following maximum intervals prior to residue extraction: wheat and sorghum commodities (388 days), turnip tops and roots (360 days), spinach and mustard leaves (348 days). All samples were analyzed within 2-10 days of extraction, except for the following commodities: two turnip top samples (20 days), two turnip root samples (17 days), and one sample each of spinach and mustard (16 days).

No concurrent storage stability data were submitted with the field rotational crop study. The registrant presented a summary of storage stability data from previously submitted studies (Mobay Report Nos. 27100, 36132, 36318-36320, and 66221). These data indicate that fenamiphos, fenamiphos sulfoxide, and fenamiphos sulfone are stable for 95-1052 days in broccoli, carrot root, potato, corn grain, corn green forage, peanut nutmeat, and/or peanut vines when stored at ca. -23 C. The Fenamiphos Product and Residue Chemistry RED (CBRS No. 11213, D187029 dated 1/26/94) concludes that storage stability studies have generally demonstrated stability of fenamiphos and metabolites up to 1170 days on tested raw and processed plant commodities.

In summary, the limited field rotational study indicates that residues of fenamiphos and its metabolites, fenamiphos sulfoxide and fenamiphos sulfone, expressed as fenamiphos equivalents, were detected at levels >0.01 ppm in/on several commodities from the 4-month rotation grown in test plots that had been broadcast-treated with the 3 lb/gal EC formulation at 1x the maximum seasonal rate for annual crops. The maximum combined residues from the 4-month rotation, which represents the registrant's established plantback interval, were found in/on spinach leaves (0.03 ppm), and sorghum forage (0.44 ppm) and straw (0.02 ppm).

Although additional data are required to support rotational crop tolerances, sufficient data are presently available to conclude that residues may be found in rotational crops at levels which will require rotational crop tolerances at plantback intervals of less than 8 months.

In order to assure that illegal residues are not found in rotational crops, and to facilitate inclusion of rotational crop residues in dietary risk assessment, the registrant should either amend product labels to include an 8-month plantback interval so that residues of fenamiphos and its regulated metabolites will not be found in rotational crops, or (2) based on the limited field trial data, propose rotational crop tolerances for crops which are specified on product labels. If the registrant elects the later, extensive field rotational crop studies will be required. The requirement for number of trials would be the same as that to establish primary tolerances on all crops (or crop groups) which the registrant intends to have as rotational crops. If the registrant desires to allow the "universe" of crop groups to be rotated, then magnitude of the residue data will be required on representative crops [see 40 CFR §180.34 (f)] for all crop groups which could be planted in a typical crop rotation sequence.

MASTER RECORD IDENTIFICATION NUMBERS

Citations for the MRID documents referred to in this review are presented below.

41659301 Linke-Ritzer, P. and Brauner, A. (1990) [RING-1-^{14}C]Fenamiphos: Residues in Rotational Crops and Soil. Performing Laboratory ID No.: M 130 0 183-6, Mobay Report Number 100246. Unpublished study conducted by BAYER AG, Leverkusen-Bayerwerk, Federal Republic of Germany, and sponsored by Mobay Corporation. 108 p.

42043601 Pither, K. (1991) Fenamiphos (3) - Residues in Field Rotational Crops. Performing Laboratory ID No.: PTRL Project No. 380. Submitting Laboratory ID No.: NE850089R01. Mobay Report No. 101317. Unpublished study prepared by Mobay Corporation. 1259 p.