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

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **Oxyfluorfen.** Nature of the Residue in Tomatoes, Onions, Stone Fruit, and Alfalfa. Reregistration Case No. 2490. Chemical No. 111601. MRID #42865001, 42913201, 42873301, and 92136114. DP Barcodes D194785, D199266, D194789, and D200012. CBRS #12,522, 13,212, 12,513, and 13,338.

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In response to the Phase 4 Review of oxyfluorfen (S.Funk, 3/22/91), Rohm and Haas Co. has submitted nature of the residue studies for tomatoes, onion, and stone fruit (peaches). The Phase 4 Review also noted that a previously submitted alfalfa metabolism study (MRID #92136101) was suitable for Phase 5 review (S.Funk, 12/31/91). These metabolism studies are reviewed below.

Tolerances are established for residues of the herbicide oxyfluorfen [2-chloro-1-(3-ethoxy-4-nitrophenoxy)-4-(trifluoromethyl)benzene] and its metabolites containing the diphenyl ether linkage in or on the following commodities: almond hulls and mint hay (peppermint and spearmint) at 0.10 ppm; fat, meat and mbyp of sheep, poultry, horses, hogs, goats and cattle at 0.05 ppm; eggs at 0.05 ppm; milk at 0.05 ppm; artichokes, avocados, bananas (including plantain), broccoli, cabbage, cauliflower, coffee, corn grain, cottonseed, dates, feijoa, figs, grapes, kiwifruit, olives, onions (dry bulb), persimmons, pistachios, pome fruits group,

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pomegranates, soybeans, stone fruits group and tree nuts group (except almond hulls) at 0.05 ppm [40 CFR §180.381 (a)].

Tolerances with regional registration are established for residues of the herbicide oxyfluorfen and its metabolites containing the diphenyl ether linkage in or on the raw agricultural commodities guava, papaya and taro (corms and leaves) at 0.05 ppm [40 CFR §180.381 (b)].

A food additive tolerance of 0.25 ppm is established for residues of oxyfluorfen and its metabolites containing the diphenyl ether linkage in or on the processed commodities cottonseed oil, mint oil (peppermint and spearmint) and soybean oil as a result of application of the herbicide to the growing crops [40 CFR §185.4600].

CBRS notes that oxyfluorfen is not currently registered for use on alfalfa and no tolerances for oxyfluorfen residues in/on alfalfa are currently established. In conjunction with an EUP, a temporary tolerance for residues of oxyfluorfen [2-chloro-1-(3-ethoxy-4-nitrophenoxy)-4-(trifluoromethyl)benzene] and its metabolites containing the diphenyl ether linkage was established for alfalfa at 0.1 ppm (PP#5G3263). This temporary tolerance expired 12/31/87.

Recommendations

The submitted tomato, onion, and stone fruit metabolism studies are adequate. No additional data for tomato, onion, and stone fruit metabolism are required. The alfalfa metabolism study is not adequate, but is upgradeable following receipt of information requested in Conclusions 15, 17a and 20.

Because oxyfluorfen is not currently registered for use on alfalfa, CBRS at this time considers the nature of the residue in plants to be adequately understood. Based on the results of the tomato, onion and peach plant metabolism studies and the previously reviewed ruminant and poultry metabolism studies (S.Knizner, CBRS #11,526, 7/16/93 and CBRS #11,303, 7/10/93), the residue requiring regulation and to be included in the tolerance expression is parent oxyfluorfen only.

Conclusions

Nature of the Residue in Tomatoes, MRID #42865001

1. CBRS concludes that the test material was adequately described and characterized. Two radiolabeled versions of oxyfluorfen were used in this study. Either the chlorophenyl ring (CPR) or nitrophenyl ring (NPR) was uniformly labeled with ^{14}C.

2. CBRS concludes that the test system was adequately described. Thirty two (32) days prior to transplanting tomato (Rutgers variety, about 1 inch high) crops, two plots were treated with CPR test material and another two with NPR material. The nominal application rate of 2.5 lb ai/A used represents approximately 5X the maximum seasonal usage rate.

Immediately prior to transplanting tomatoes, soil was incorporated (roto-tilled to depth of 5 inches). Tomatoes were harvested as they became ripe (red). Four harvest were made, corresponding to PHIs of 103, 113, 126, and 147 days.

3. The TRR level in CPR treated tomatoes ranged from 0.009 to 0.016 ppm. Residue levels in NPR treated tomatoes were below the limit of detection (<0.0050 ppm). Therefore, characterization of residues was only required for CPR treated tomatoes. Because the two treatments differed only in the position of the radiolabel, the differing TRR results suggest cleavage of the diphenyl ether bond.

4. Following fractionation of radioactive residues in CPR treated tomatoes, the majority of the radioactivity was recovered in the ethyl acetate fraction of the aqueous phase of the MeOH extract (81% TRR, 0.013 ppm). The combined methylene chloride fractions had no detectable radioactivity. The radioactivity in the ethyl acetate fraction was characterized as being volatile, and the registrant suggested that the volatile radioactive component was trifluoroacetic acid (TFA).

5. Storage Stability - Combustion analyses were completed within one month of sample harvest. Samples were stored frozen for up to approximately 7 months from harvest to the start of extraction/characterization.

Nature of the Residue in Onions, MRID #42913201

6. CBRS concludes that the test material was adequately described and characterized. Two radiolabeled versions of oxyfluorfen were used in this study. Either the chlorophenyl ring (CPR) or nitrophenyl ring (NPR) was uniformly labeled with ^{14}C.

7. CBRS concludes that the test system was adequately described. Two applications of test material, at a nominal rate of 1.25 lb ai/A/application were made (first application at 4-leaf stage, followed by another application 24 days later). The total nominal application rate of 2.5 lb ai/A used in this study represents approximately 5X the maximum seasonal usage rate. Minor injury to onion leaves was noted after each application. Mature onions were harvested by hand 77 days after the first treatment, which corresponds to 53 days after the last treatment (DALT).

8. A deviation from the study protocol was noted in that harvested onions, with tops, skins, roots, and soil attached were let dry at ambient temperature for 10 days before being processed and frozen. This sample handling procedure is not in accordance with Agency guidelines for metabolism studies. However, based on the results of this study and the tomato and stone fruit metabolism studies, this study will not be rejected because of improper sample storage.

9. The TRR level in CPR treated onions was approximately 0.017 ppm. Results for TRR levels in NPR-treated onions were 0.0513 and 0.0646 ppm.

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9.a. CPR Treated Onions - The ethyl acetate fraction (0.0042 ppm, 2.7% TRR) was the only fraction subjected to characterization. Based on the solubility, volatility under acidic conditions and extractability into organic phase in acidic form, the registrant proposed that the majority of the radioactivity in the ethyl acetate fractions was ^{14}C-trifluoroacetic acid (TFA).

9.b. NPR Treated Onions - The aqueous extract contained the majority of the TRR (72.7%, 0.047 ppm). The registrant attempted to identify/characterize residues present in the aqueous fraction. Techniques used included: Supelco Supelclean method development kits (polar, non-polar, anion-exchange and cation-exchange chromatography); butanol partitioning; acid hydrolysis (1 M and 6 M HCl); and derivatization (acetylation). Analysis of derivatized products indicated that the aqueous fraction contained at least four components. The largest of these components accounted for 38.5% TRR (0.0249 ppm), and attempts at identification using TLC were not successful.

10. Storage Stability - Combustion analyses were performed 10 weeks after harvest, and residue extractions were begun 19 weeks after harvest. No storage stability data were provided.

Nature of the Residue in Stone Fruit, MRID #42873301

11. CBRS concludes that the test material was adequately described and characterized. Two radiolabeled versions of oxyfluorfen were used in this study. Either the chlorophenyl ring (CPR) or nitrophenyl ring (NPR) was uniformly labeled with ^{14}C.

12. CBRS concludes that the test system was adequately described. Soil under dormant peach trees was treated with ^{14}C-oxyfluorfen (either CPR or NPR labeled) at a nominal application rate of 10 lb ai/A (5X). Mature peaches were harvested 126 days after soil treatment. Small amounts of twigs, leaves, and immature fruits were also harvested at 8, 16, 30, 63, and 91 days after application. Samples were processed within 3 to 6 days of harvest, and combustion analysis for TRR determinations were performed within 7 days of harvest.

13. Combustion analysis yielded no detectable residues (<0.004 ppm) for all mature peach samples. Ten subsamples were combusted for each study sample. Raw LSC data were provided for each sample. Because the TRR was <0.010 ppm, characterization of radioactive residues was not required.

14. Storage stability data are not required because all samples were analyzed within 7 days of harvest.

Nature of the Residue in Alfalfa, MRID #92136114

15. CBRS concludes that the test material was not adequately described and characterized. Two radiolabeled versions of oxyfluorfen were used in this study. Either the chlorophenyl

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ring (CPR) or nitrophenyl ring (NPR) was uniformly labeled with ^{14}C. The chemical purity of non-radiolabeled oxyfluorfen (lot RPO 8674FP) used to dilute the radioactive material was not stated. This information is available (Rohm and Haas Notebook #48285, page 43, M.Spina) and should be provided. The test material was formulated with emulsifiers and spray adjuvants as specified in the Goal 1.6E Herbicide formulation. Details on the treatment are found in Rohm and Haas Research Notebook #49068, pages 4-5, but were not provided in this report. This is a deficiency. Radioanalysis data for spray solutions, if available, should be supplied.

16. CBRS concludes that the test system was adequately described. Plots were sprayed with the test material at a rate of approximately 2.0 lb ai/A. The registrant stated that represents approximately 8X the expected use rate for alfalfa. Alfalfa plants were in the post bud break stage at the time of application. Plots were harvested by hand at approximately 6, 10, 14, and 20 weeks after application. Samples were stored frozen immediately after harvest, chopped in a Hobart food processor with dry ice, and then returned to the freezer at -20 C until analyzed (3.5 years).

17. Results -
17.a. The report stated that plants taken for autoradiography showed the radiolabel to be distributed throughout the plant. No autoradiography data were provided. This is a deficiency. The registrant should provide representative autoradiograms of control and treated plants (both labels). A discussion of the autoradiographic procedure should be included.

17.b. For all harvests, TRR levels were higher (2x to 3x) in the ^{14}C-CPR treated plants versus the ^{14}C-NPR treated plants. Because the two treatments differed only in the position of the radiolabel, the differing TRR results suggest cleavage of the diphenyl ether bond. For the CPR label, TRR levels ranged from 0.093 - 0.199 ppm and for the NPR label 0.031 - 0.073 ppm, with the lower values being corresponding to the earlier harvests.

18. Identification/Characterization of Residues in ^{14}C-CPR Treated Plants -
18.a. $MeCl_2$ Fraction - Oxyfluorfen was found at 2% TRR (0.004 ppm) in the $MeCl_2$ fraction of the first harvest alfalfa sample (45 day PHI), but was not detected in any of the later harvests. The remainder of the activity in this fraction remained at the origin ("polar material", 3 to 7% TRR, 0.004 to 0.012 ppm) or was identified as "unknowns" (4 to 5% TRR, 0.004 to 0.010 ppm).

18.b. Aqueous Fraction - CBRS concludes that sufficient data (co-distillation, mass spectrometry, and GC) has been provided to identify trifluoroacetic acid in the aqueous extract. TFA was the most abundant metabolite in the aqueous fraction (17 - 53% TRR, 0.016 - 0.106 ppm). The percentage of TFA increased with time (first harvest 17% TRR, second 37%, third 53%, and last 50%).

19. Identification/Characterization of Residues in ^{14}C-NPR Treated Plants - CBRS concludes

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that the radiolabel in NPR treated alfalfa has been adequately characterized. Because of the low levels of radioactivity in the fractions ($\leq$0.018 ppm), identification of residues was not accomplished. Qualitative analysis of the TLC plates for the aqueous and methylene chloride extracts showed that most of the radiolabeled material remained at the origin (polar material). A small amount of radiolabel in the methylene chloride extract co-migrated with oxyfluorfen standard, but the exact quantity could not be determined.

20. Storage Stability - No storage stability data were provided. This is a deficiency. Samples were stored for up to 3.5 years from harvest to analysis. The registrant must provide data demonstrating the stability of oxyfluorfen and its metabolites in alfalfa for this time period.

Nature of the Residue in Tomatoes, MRID #42865001

Detailed Considerations

This study was designed to support the reregistration of Goal 1.6E herbicide. Goal 1.6E Herbicide is registered for use as a preemergence and/or postemergence herbicide for control of certain weeds in fallow beds to be planted with either seeded or transplanted crops.

Test Material

Two radiolabeled versions of oxyfluorfen were used in this study. Either the chlorophenyl ring (CPR) or nitrophenyl ring (NPR) was uniformly labeled with ^{14}C, as shown in Figure 1. Additionally, some ^{13}C-CPR labeled material was used to aid in identification of metabolites. The ^{14}C-CPR material (lot 734.01) had a radiochemical purity of 97.2%, chemical purity of 96.3% and specific activity of 49705 dpm/ug (22.39 mCi/g). The ^{14}C-NPR material (lot 731.01) had a radiochemical purity of 92.3%, chemical purity of 93.5% and specific activity of 41669 dpm/ug (18.77 mCi/g). The chemical purity of the ^{13}C-CPR test material (lot MWS15-92-2) was 94.9%. Non-radiolabeled oxyfluorfen (lot EG2322) used to dilute the radioactive material had a chemical purity of 98.0%.

Figure 1. Position of radiolabel, with ^{14}C in the chlorophenyl ring (CPR) or nitrophenyl ring (NPR).

The test material was formulated with emulsifiers and spray adjuvants as specified in the Goal 1.6E Herbicide formulation. The spray emulsions were made immediately before application by mixing the formulated oxyfluorfen with a volume of water to represent a spray volume of 100 gal/A. Composition of the spray material is given in Table 1. CBRS concludes that the test material was adequately described and characterized.

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Table 1. Composition of Active Ingredient Used in Study.

Test Plot	^{12}C (mg)	^{13}C (mg)	^{14}C (mg)	Total AI[a]	SA dpm/mg	SA mCi/g	Total mCi
CPR-1	207	263	54.66	525	5175	2.331	1.224
CPR-2	212	261	55.39	528	5214	2.349	1.240
NPR-1	454	-	66.39	520	5320	2.396	1.246
NPR-2	453	-	66.16	519	5316	2.395	1.243

[a] Not corrected for chemical purities of the test substance.

Test System

Test plots were located at the Newtown Research Farm of Rohm and Haas Co. in Pennsylvania. The soil was characterized as silt loam. Four fallow test plots, each 2 ft. x 10 ft., and approximately 5 ft. apart were used in the study. On May 21, 1992, thirty two (32) days prior to transplanting tomato (Rutgers variety, about 1 inch high) crops, two plots were treated with CPR test material and another two with NPR material. On June 22, soil was incorporated (roto-tilled to depth of 5 inches) and approximately 7 tomato plants were transplanted as a single row in each plot. A control tomato plot was located about 500 ft from the treatment plots.

The formulated test materials were transferred to spray bottles and water (172 mL) was added. The spray solutions were applied using a hand sprayer (CO_2 backpack sprayer). Triplicate samples of each spray solution were radioassayed to verify the application rate. The nominal application rate of 2.5 lb ai/A used in this study represents approximately 5X the maximum seasonal usage rate. Actual application rates are presented below in Results.

Tomatoes were harvested as they became ripe (red). Four harvest were made, corresponding to PHIs of 103, 113, 126, and 147 days. The first harvest was the beginning of the harvest season, and the last harvest was followed by frosty weather which destroyed the crops. Although sticks and wires were used to support crops during growth, many tomatoes were harvested from the ground and touched by soil. Soil was removed by washing with water before processing samples.

Harvested tomatoes were driven to the Spring House Laboratories, processed and frozen the next day. At least ten tomatoes, when available, were processed for each sample. Processing consisted of rinsing in water, cutting into pieces and grinding with dry ice in a Waring Commercial Food Processor. Homogenized samples were stored frozen until analysis. A table was provided showing the quantity and average weights of all tomatoes harvested at the various harvest dates.

CBRS concludes that the test system was adequately described.

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Analytical Methods

LSC - Liquid scintillation counting was performed using a Packard Tri-Carb Model 1900 or 3255 Liquid Scintillation Spectrometer. Counting efficiency was determined by external standard channels ratio method.

Combustion analyses were performed using a Packard Tri-Carb Oxidizer. Samples were oxidized and $^{14}CO_2$ evolved was trapped in vials containing Oxisorb-Oxiprep solution (1:2, v:v). The trapped radioactivity was counted by LSC. Combustion efficiency was determined by combusting a control samples fortified with a known amount of ^{14}C. Ten subsamples were combusted for each study sample and the average of the ten results was used for calculations.

Raw counting data was processed using the registrants in house data reduction program. Sample dpm were determined by subtracting control cpm from sample cpm and dividing by percent counting efficiency. Sample ppm were calculated by dividing sample dpm by sample size multiplied by the specific activity of the test substance. The limit of detection was 0.0050 ppm, based on a nominal specific activity of 5228 dpm/ug, 0.35 g sample size, and 7 cpm being the least significant cpm.

Extraction and Fractionation

Tomato homogenate was processed in two blender assemblies (Eberbach 8470). MeOH was added to each of the blender assemblies and the resulting suspension was blended at high speed for about 5 minutes. The resulting suspensions were filtered (Whatman Filter Paper No. 54) and filtrates combined. The filter cakes were combined and returned to one of the blender assemblies. The blending and filtering were repeated three more times. All filtrates were combined. Aliquots of the combined filtrate were radioassayed. The remaining filter cake was allowed to dry at room temperature overnight and was then analyzed by combustion analysis.

The MeOH from the methanol extract was removed in vacuo at less than 50 C using a Buchii Rotovapor-R. The residue left was taken up in a mixture of water and methylene chloride. The two layers were separated and the organic layer was removed from the separatory funnel. The aqueous layer was washed twice more with methylene chloride and the combined methylene chloride extracts were radioassayed.

The aqueous fraction was acidified to pH 1 by addition of concentrated HCl. Six ethyl acetate extractions were performed. Layers were separated by centrifugation (Beckman AccuSpin FR) at 3000 rpm for 5 min. All resulting fractions were radioassayed.

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Results

TRR - Combustion results for the four tomato harvests are presented in Table 2. Each number is the average of ten combustion subsamples. Raw LSC data were provided for each sample. The TRR level in CPR treated tomatoes ranged from 0.009 to 0.016 ppm. Residue levels in NPR treated tomatoes were below the limit of detection (<0.0050 ppm).

The registrant stated that all water rinses from washing soiled tomatoes had no detectable radioactivity, indicating that residues were not on the surface but instead distributed in the fruit.

Table 2. TRR found in Tomatoes Harvested at indicated PHIs. Values presented are averages of ten combustions. Limit of detection 0.0050 ppm.

Sample	Applic. Rate (lb ai/A)[a]	TRR at Indicated PHI (days)			
		103 days	113	126	147
CPR-1	2.54	0.016	0.010	0.010	0.012
CPR-2	2.56	0.014	0.010	0.013	0.009
NPR-1	2.63	ND[b]	ND	ND	ND
NPR-2	2.53	ND	ND[c]	ND[d]	ND

[a] Application rate as determined by radioassay of test material subsample. Registered application rate is 0.5 lb ai/A.
[b] ND = not detected, two of the ten samples combusted for this sample had detectable residues at 0.0069 and 0.0135 ppm.
[c] Two of the ten samples combusted for this sample had detectable residues at 0.0076 and 0.0052 ppm.
[d] Two of the ten samples combusted for this sample had detectable residues at 0.0100 and 0.0067 ppm.

Characterization of Residues

Characterization of residues was only required for CPR treated tomatoes because they had TRR levels >0.010 ppm. The distribution of radioactivity in the extracts of CPR treated samples is given in Table 3.

The majority of the radioactivity was recovered in the ethyl acetate fraction of the aqueous phase of the MeOH extract. The combined methylene chloride fractions had no detectable radioactivity.

Table 3. Distribution of Radioactivity in Extracts of CPR Treated Tomatoes. TRR in sample was 0.0164 ppm.

Fraction	ppm	% TRR
MeOH Extract	0.0162	98.8
Aqueous Phase		
Acidified Aqueous	0.0029	17.8
Ethyl Acetate	0.0133	81.1
PES	0.0002	1.2

Characterization of the radioactivity in the ethyl acetate fraction was accomplished as follows:

Volatility Measurement: An aliquot of this fraction was taken and trifluoroacetic acid was added. Solvent was evaporated to dryness under N_2 at 50 C for one hour. The remaining (non-volatile) material was redissolved in ethyl acetate and radioassayed. No detectable radioactivity was found.

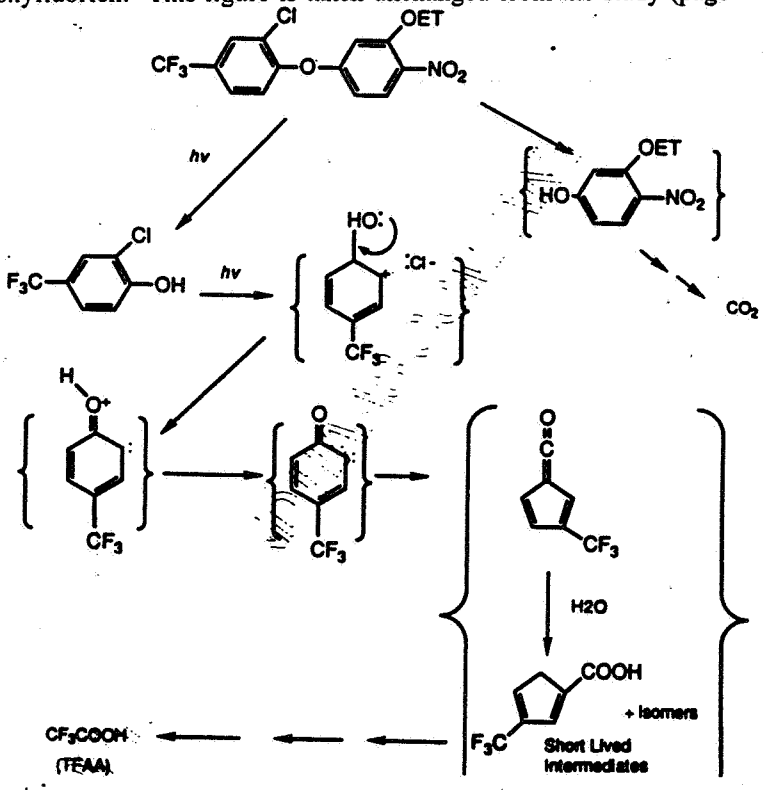
Distillation: The ethyl acetate fraction was distilled in vacuo at room temperature using a rotovap. The distribution of radioactivity between the distillates and non-volatile remains was 91.7% and 8.3%. The distillates were then neutralized by ammonia and redistilled. No detectable radioactivity was found in the ethyl acetate distillates in this second distillation.

The registrant suggested that the volatile radioactive component was trifluoroacetic acid.

Metabolic Pathway

The registrant proposed a metabolic pathway for oxyfluorfen as shown in Figure 2. This figure is taken unchanged from the study (page 33, figure 4 of study).

Figure 2. Proposed metabolic pathway for oxyfluorfen. This figure is taken unchanged from the study (page 33, figure 4 of study).



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Nature of the Residue in Onions, MRID #42913201

Detailed Considerations

This study was designed to support the reregistration of Goal 1.6E herbicide. Goal 1.6E Herbicide is registered for a postemergence use on onions at an application rate of 0.12 to 0.25 lb ai/A/application, with a maximum seasonal rate of 0.5 lb ai /A.

Test Material

Two radiolabeled versions of oxyfluorfen were used in this study. Either the chlorophenyl ring (CPR) or nitrophenyl ring (NPR) was uniformly labeled with ^{14}C. Additionally, some ^{13}C-CPR labeled material was used to aid in identification of metabolites. The ^{14}C-CPR material (lot 734.01) had a radiochemical purity of 97.2%, chemical purity of 96.3% and specific activity of 49705 dpm/ug (22.39 mCi/g). The ^{14}C-NPR material (lot 731.01) had a radiochemical purity of 92.3%, chemical purity of 93.5% and specific activity of 41669 dpm/ug (18.77 mCi/g). The chemical purity of the ^{13}C-CPR test material (lot MWS15-92-2) was 94.9%. Non-radiolabeled oxyfluorfen (lot EG2322) used to dilute the radioactive material had a chemical purity of 98.0%.

The test material was formulated with emulsifiers and spray adjuvants as specified in the Goal 1.6E Herbicide formulation. The spray emulsions were made immediately before application by mixing the formulated oxyfluorfen with a volume of water to represent a spray volume of 100 gal/A. Composition of the spray material is given in Table 4.

CBRS concludes that the test material was adequately described and characterized.

Table 4. Composition of Active Ingredient Used in Study.

Test Plot	^{12}C (mg)	^{13}C (mg)	^{14}C (mg)	Total AI[a]	SA dpm/mg	SA mCi/g	Total mCi
CPR-1	204	261	54.52	519.5	5216	2.350	1.221
CPR-2	207	260	55.69	522.7	5296	2.386	1.247
NPR-1	457	-	65.98	523.0	5257	2.368	1.238
NPR-2	458	-	65.66	523.7	5225	2.354	1.232

[a] Not corrected for chemical purities of the test substance.

Test System

Test plots were located at the Newtown Research Farm of Rohm and Haas Co. in Pennsylvania. The soil was characterized as silt loam. Two soil plots (4 ft x 5 ft) were used for each of the treatment (CPR-1, CPR-2, NPR-1, and NPR-2). Approximately 90 onion

bulbs (Stuttgarter) were planted in each plot on May 22, 1992 and grown to the 4 leaf stage before the first application (June 16). A second application was made 24 days later (July 10). Minor injury to onion leaves was noted after each application.

The formulated test materials were transferred to spray bottles and water (172 mL) was added. The spray solutions were applied using a hand sprayer (CO_2 backpack sprayer). Triplicate samples of each spray solution were radioassayed to verify the application rate.

Each application was made at a nominal rate of 1.25 lb ai/A/application. The total nominal application rate of 2.5 lb ai/A used in this study represents approximately 5X the maximum seasonal usage rate. Actual application rates are presented below in Results.

Mature onions were harvested by hand 77 days after the first treatment, which corresponds to 53 days after the last treatment (DALT). Immature onion samples were also collected on days 15, 24, 43, and 56 after the first treatment.

Harvested onions, with tops, skins, roots, and soil attached were let dry at ambient temperature for 10 days before being processed. The registrant noted that this procedure deviated from the study protocol, but reflects common agricultural practices. The tops and roots of the onions were then removed and the dry outer skin peeled. Processing of onions consisted of cutting into pieces and grinding with dry ice in a Waring Commercial Food Processor. Homogenized samples were stored frozen until analysis. Combustion analyses were performed on November 16, 10 weeks after harvest, and residue extractions were begun on January 22, 1993, 19 weeks after harvest.

CBRS concludes that the test system was adequately described.

Analytical Methods

LSC - Liquid scintillation counting was performed using a Packard Tri-Carb Model 1900 or 3255 Liquid Scintillation Spectrometer. Counting efficiency was determined by external standard channels ratio method.

Combustion analyses were performed using a Packard Tri-Carb Oxidizer. Samples were oxidized and $^{14}CO_2$ evolved was trapped in vials containing Oxisorb-Oxiprep solution (1:2, v:v). The trapped radioactivity was counted by LSC. Combustion efficiency was determined by combusting a control samples fortified with a known amount of ^{14}C. Ten subsamples were combusted for each study sample and the average of the ten results was used for calculations.

Radioassay of solutions were performed by placing the aliquots of known size in Hydrofluor in a polyethylene vial and counting for either 15 min (3 rounds of 5 min, using external standard channel for determining counting efficiency) or 3 min (3 rounds of 1 min, quick counting). The quick counting method was used because of strong chemical luminescence

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interference in some samples. Only cpm values were reported because there was no counting efficiency data available in this case.

Raw counting data was processed using the registrants in house data reduction program. Sample dpm were determined by subtracting control cpm from sample cpm and dividing by percent counting efficiency. Sample ppm were calculated by dividing sample dpm by sample size multiplied by the specific activity of the test substance. The limit of detection was 0.005 ppm, based on a nominal specific activity (SA) of 5228 dpm/ug, 0.35 g sample size, and 7 cpm being the least significant cpm. For all calculations, a SA of 5228 dpm/ug was used instead of the SA of each treatment solution as presented in Table 1. This discrepancy had minimal effect on calculated values.

Extraction and Fractionation of Radioactivity in the CPR Samples

Onion homogenate was processed in an Eberbach 8470 blender. MeOH was added to each of the blender assemblies and the resulting suspension was blended at high speed in a Waring Laboratory Blender for about 5 minutes. The resulting suspensions were filtered (Whatman Filter Paper No. 54) and filtrates combined. The filter cake was returned to the blender blending and filtering were repeated three more times. All filtrates were combined. Aliquots of the combined filtrate were radioassayed. The remaining filter cake was allowed to dry at room temperature overnight and was then analyzed by combustion analysis.

The MeOH from the methanol extract was removed in vacuo at less than 50 C using a Buchii Rotovapor-R. The residue left was taken up in a mixture of water and methylene chloride. The two layers were separated and the organic layer was removed from the separatory funnel. The aqueous layer was washed twice more with methylene chloride and the combined methylene chloride extracts were radioassayed.

The aqueous fraction was acidified to pH 1 by addition of concentrated HCl. Six ethyl acetate extractions were performed. Layers were separated by centrifugation (Beckman AccuSpin FR) at 3000 rpm for 5 min. The acidified aqueous fraction was further extracted four times with n-butanol. All resulting fractions were radioassayed.

Extraction and Fractionation of Radioactivity in the NPR Samples

The same extraction scheme used for CPR treated samples was used for NPR treated samples, except that the dried MeOH residue was taken up in water and extracted four times with ethyl acetate. All resulting fractions were radioassayed.

Results

TRR - Combustion results for mature onions are presented in Table 5. Each number is the average of ten combustion subsamples. Raw LSC data were provided for each sample. The TRR level in CPR treated onions was approximately 0.017 ppm. Results for TRR levels in NPR treated onions were 0.0513 and 0.0646 ppm.

Table 5. TRR found in Mature Onions Harvested 53 Days After Last Treatment. Each treatment was made at a nominal rate of 1.25 lb ai/A, and there were 24 days between treatments. Limit of detection 0.005 ppm.

Sample	Total Application (lb ai/A)[a,b]	TRR (ppm)[b]
CPR-1	2.47	0.0170
CPR-2	2.43	0.0166
NPR-1	2.25	0.0513
NPR-2	2.40	0.0646

[a] Application rate as determined by radioassay of test material subsample.
[b] In calculating TRR a specific activity (SA) of 5228 dpm/ug was used for all calculations instead of the SA of each treatment solution as presented in Table 1. This discrepancy had minimal effect on calculated values.

Characterization of Residues

CPR-1 Sample - The distribution of radioactive residues in fractions of the CPR-1 treated sample is given in Table 6. The ethyl acetate fraction (0.0042 ppm, 24.7% TRR) was the only fraction subjected to characterization.

The volatility of radioactive residues in the ethyl acetate fraction was characterized as follows. An aliquot of this fraction was taken and trifluoroacetic acid was added. Solvent was evaporated to dryness under N_2 at 50 C for one hour. The remaining (non-volatile) material was redissolved in ethyl acetate and radioassayed. Most of the radioactivity (62.3%) was evaporated. Based on the solubility, volatility under acidic conditions and extractability into organic phase in acidic form, the registrant proposed that the volatile component is trifluoroacetic acid (TFA).

Table 6. Distribution of Radioactivity in Extracts of CPR-1 Treated Onions. TRR by combustion analysis was 0.0170 ppm.

Fraction	ppm	% TRR
MeOH Extract	0.0179	105.2
Aqueous Phase		
Ethyl Acetate	0.0042	24.7
Aqueous Acidified	0.0130	76.1
Aqueous Acidified	0.0102	60.0
Butanol	0.0014	8.0
Methylene Chloride	0.0003	1.6
PES	0.0026	15.2
Total of Fractions	0.0187	110.0

NPR-2 Sample - The distribution of radioactivity in fractions of the NPR-2 sample is given in Table 7. The aqueous extract contained the majority of the TRR (72.7%, 0.047 ppm)

The registrant attempted to identify/characterize residues present in the aqueous fraction. Techniques used included: Supelco Supelclean method development kits (polar, non-polar, anion-exchange and cation-exchange chromatography); butanol partitioning; acid hydrolysis (1 M and 6 M HCl); and derivatization (acetylation).

Analysis of derivatized products indicated that the aqueous fraction contained at least four components. The largest of these components accounted for 38.5% TRR (0.0249 ppm), and attempts at identification using TLC were not successful.

Table 7. Distribution of Radioactivity in Extracts of NPR-2 Treated Onions. TRR by combustion analysis was 0.0646 ppm.

Fraction	ppm	% TRR
MeOH Extract	0.0421	65.1
Aqueous Phase		
Aqueous	0.0470	72.7
Ethyl Acetate	0.0070	10.9
PES	0.0073	11.3
Activity Lost During Fractionation	0.0153	23.6
Total of Fractions	0.0766	118.6

Metabolic Pathway

The registrant proposed metabolic pathway for oxyfluorfen in onions is exactly that like that proposed for tomatoes.

Nature of the Residue in Stone Fruit, MRID #42873301

Detailed Considerations

This study was designed to support the reregistration of Goal 1.6E herbicide. Goal 1.6E Herbicide is registered for use as a preemergence or postemergence herbicide for control of certain weeds in certain treefruit/nut/vine plantings. Oxyfluorfen is applied to the ground at the base of dormant fruit trees at 0.5 to 2.0 lb ai/A for postemergence weed control or 1.2 to 2.0 lb ai/A for preemergence control.

Test Material

Two radiolabeled versions of oxyfluorfen were used in this study. Either the chlorophenyl ring (CPR) or nitrophenyl ring (NPR) was uniformly labeled with ^{14}C. The ^{14}C-CPR material (lot 734.01) had a radiochemical purity of 97.2%, chemical purity of 96.3% and specific activity of 49705 dpm/ug (22.39 mCi/g). The ^{14}C-NPR material (lot 731.01) had a radiochemical purity of 92.3%, chemical purity of 93.5% and specific activity of 41669 dpm/ug (18.77 mCi/g). Non-radiolabeled oxyfluorfen (lot EG2322) used to dilute the radioactive material had a chemical purity of 98.0%.

The test material was formulated with emulsifiers and spray adjuvants as specified in the Goal 1.6E Herbicide formulation. The spray emulsions were made immediately before application by mixing the formulated oxyfluorfen with a volume of water to represent a spray volume of 100 gal/A. Composition of the spray material is given in Table 8.

CBRS concludes that the test material was adequately described and characterized.

Table 8. Composition of Active Ingredient Used in Study.

Test Plot	^{12}C (g)	^{14}C (mg)	Total AI[a] (g)	SA dpm/ug	SA mCi/g	Total mCi
CPR-1	2.330	274.02	2.604	5230	2.356	6.135
CPR-2	2.333	274.58	2.608	5234	2.358	6.148
NPR-1	2.281	327.60	2.609	5233	2.357	6.149
NPR-2	2.282	327.75	2.610	5233	2.357	6.152

[a] Not corrected for chemical purities of the test substance.

Test System

Test plots were located in the peach orchard (K-1 field) of the Newtown Research Farm of Rohm and Haas Co. in Newtown, PA. The soil in the field is classified as silt loam.

The soil in four test plots (5 ft. x 5 ft. each) under a peach tree (Red Haven) was treated with ^{14}C-oxyfluorfen (two with CPR labeled and two with NPR labeled). Application was made on April 7, 1992, when the trees were still dormant. Two control peach trees were located at least 100 ft. away from the treated trees.

Applications were made using a hand sprayer. Triplicate aliquots of each spray solution were radioassayed to verify the actual dosage applied. The nominal application rate was 10 lb ai/A, representing 5X the maximum registered use. Actual application rates for the test plots are presented in Results section of this review.

Mature peaches were harvested 126 days after soil treatment. Small amounts of twigs, leaves, and immature fruits were also harvested at 8, 16, 30, 63, and 91 days after application. About 70 mature peaches were harvested from each plot. Samples were frozen the day of harvest and stored frozen until processing. A subsample of 25 peaches from each plot was subjected to processing. Processing consisted of cutting the peaches into pieces, removing pits, and chopping in a Hobart Chopper with dry ice followed by further grinding in a Waring Commercial Food Processor. Samples were processed within 3 to 6 days of harvest, and combustion analysis for TRR determinations were performed within 7 days of harvest. Processed samples were stored frozen until analysis.

CBRS concludes that the test system was adequately described.

Analytical Methods

LSC - Liquid scintillation counting was performed using a Packard Tri-Carb Model 1900 or 3255 Liquid Scintillation Spectrometer. Counting efficiency was determined by external standard channels ratio method.

Combustion analyses were performed using a Packard Tri-Carb Oxidizer. Samples were oxidized and $^{14}CO_2$ evolved was trapped in vials containing Oxisorb-Oxiprep solution (1:2, v:v). The trapped radioactivity was counted by LSC. Combustion efficiency was determined by combusting a control samples fortified with a known amount of ^{14}C. Ten subsamples were combusted for each study sample and the average of the ten results was used for calculations.

Raw counting data was processed using the registrants in house data reduction program. Sample dpm were determined by subtracting control cpm from sample cpm and dividing by percent counting efficiency. Sample ppm were calculated by dividing sample dpm by sample size multiplied by the specific activity of the test substance. The limit of detection was 0.004 ppm, based on a nominal specific activity of 5228 dpm/ug, 0.50 g sample size, and 7 cpm being the least significant cpm.

Results

TRR - Combustion analysis yielded no detectable residues (<0.004 ppm) for all treated peach samples. Ten subsamples were combusted for each study sample. Results and application rates based on radioassay of spray solutions are summarized in Table 9. Raw LSC data were provided for each sample. Because TRR was <0.010 ppm, characterization of radioactive residues was not required.

Table 9. TRR found in Mature Peaches (126 day PHI). Target application rate was 10 lb ai/A (5X). TRR values presented are averages of ten combustions. Limit of detection 0.004 ppm (ND = not detected).

Sample	Applic. Rate (lb ai/A)[a]	TRR
CPR-1	9.9	ND[b]
CPR-2	19.2[c]	ND
NPR-1	11.0	ND
NPR-2	11.4	ND

[a] Application rate as determined by radioassay of test material subsample.
[b] ND = not detected, one of the ten samples combusted for this sample had detectable residues at 0.0049 ppm.
[c] Registrant postulated that this result was higher than expected possibly because of sampling inhomogeneous spray solution.

Small amounts of radioactivity were detected in twigs ($\leq$0.013 ppm), leaves ($\leq$0.055 ppm) and immature fruit ($\leq$0.020 ppm). Table 10 presents a summary of results obtained from the analysis of immature fruits, leaves, and twigs.

Table 10. Results for analysis of immature fruits, leaves, and twigs. Days after treatment (DAT) on which samples were collected are noted. Limit of detection was 0.004 ppm (ND = not detected).

		TRR (ppm) found on indicated DAT				
Treatment	Sample	8 DAT	16 DAT	30 DAT	63 DAT	91 DAT
CPR-1	Twigs Leaves Immature Peaches	ND	ND	0.007	0.009 0.055 0.020	 0.012
CPR-2	Twigs Leaves Immature Peaches	ND	ND	ND	0.009 0.060 0.005	 0.006
NPR-1	Twigs Leaves Immature Peaches	ND	0.111	ND	0.013 0.027 0.007	 0.006
NPR-2	Twigs Leaves Immature Peaches	ND	ND	ND	0.007 0.015 ND	 0.006

Nature of the Residue in Alfalfa, MRID #92136114

Detailed Considerations

Test Material

Two radiolabeled versions of oxyfluorfen were used in this study. Either the chlorophenyl ring (CPR) or nitrophenyl ring (NPR) was uniformly labeled with ^{14}C. The ^{14}C-CPR material (lot 528.0101) had a radiochemical purity of 96.9% and specific activity of 5.16 mCi/g, ~11,100 dpm/ug. The ^{14}C-NPR material (lot 527.0103) had a radiochemical purity of 93.5% and specific activity of 4.99 mCi/g, ~11,100 dpm/ug. The chemical purity of non-radiolabeled oxyfluorfen (lot RPO 8674FP) used to dilute the radioactive material was not stated. This information is available (Rohm and Haas Notebook #48285, page 43, M.Spina) and should be provided.

The test material was formulated with emulsifiers and spray adjuvants as specified in the Goal 1.6E Herbicide formulation. Details on the treatment are found in Rohm and Haas Research Notebook #49068, pages 4-5, but were not provided in this report . This is a deficiency. Radioanalysis data for spray solutions, if available, should be supplied.

CBRS concludes that the test material was not adequately described.

Test System

Test plots were located in and established alfalfa field at the Newtown Research Farm of Rohm and Haas Co. in Pennsylvania. The soil was characterized as silt loam. Plots were sprayed (backpack sprayer) with the test material at a rate of approximately 2.0 lb ai/A on April 4, 1986. The registrant stated that represents approximately 8X the expected use rate for alfalfa. Alfalfa plants were in the post bud break stage at the time of application. Because no canopy had formed, the registrant stated that much of the oxyfluorfen was applied to bare ground. The emerging trifoliate leaves were killed by the oxyfluorfen, delaying overall plant growth by 3 to 4 weeks.

Plots were harvested by hand at approximately 6, 10, 14, and 20 weeks after application. At the time of the first harvest, growth in the treated plots still lagged behind that of the control plots, and the canopy was still not completely closed. Plants were cut just above ground level with grass clippers. For the 6 week harvest, one-half of each plot was harvested. For the 10 week harvest, the other half of the plot was harvest, For the 14 week harvest, the first half of the plot was harvested again. For the final 20 week harvest, each half was harvested and kept separately. Samples were stored frozen immediately after harvest, chopped in a Hobart food processor with dry ice, and then returned to the freezer at -20 C until analyzed (3.5 years).

CBRS concludes that the test system was adequately described.

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Extraction and Fractionation of Radioactivity

MeOH was added to chopped frozen tissue in a blender and blended at high speed. The resulting suspension was filtered (Whatman Filter Paper No. 3). The filter cake was returned to the blender and blending with MeOH and filtering were repeated three more times. All filtrates were combined and reduced in volume using a rotovap, followed by transfer to a separatory funnel. Methylene chloride and water were added to the separatory funnel. The funnel was shaken and phases allowed to separate. The methylene chloride phase was removed and the aqueous phase was washed 2 more times with methylene chloride. The aqueous and methylene chloride phases were rotovaped , reconstituted in MeOH, and aliquots were removed for LSC.

The remaining filter cake was stored at room temperature in a glass jar. Bound residues were extracted using acid, base and enzymes. Samples of filter cakes were incubated at 60 C for 1 hour following addition of 1.0 N HCl. Samples were then filtered and filter cakes were dried and aliquots were analyzed by combustion analysis. Filtrates were concentrated and radioassayed. The filter cakes were then treated with 0.1 N NaOH for 1.5 hours at 70 C. Following filtration the cakes were dried, weighed, and aliquots removed for combustion. Filtrates were concentrated and radioassayed. The filter cakes were then treated with an enzyme solution containing hemicellulase, cellulase, and pectinesterase. The enzyme mixtures were incubated 18 hours at 40 C. Following filtration cakes were dried an aliquots taken for combustion analysis.

An unknown component from the CPR aqueous fraction was purified using a quaternary aminoethyl (QAE) Sephadex anion exchange column. The column was equilibrated with 1 N NaOH, washed with deionized water, and the sample applied. The column was eluted with 1 N HCl. The HCl fraction was partitioned 2 times with ethyl acetate. The ethyl acetate fractions were combined, adjusted to pH 10, rotovaped to dryness, reconstituted in MeOH and radioassayed.

Analytical Methods

LSC - Liquid scintillation counting was performed using a Packard Tri-Carb Model 1900 or 3255 Liquid Scintillation Spectrometer. Counting efficiency was determined by external standard channels ratio method.

Combustion analyses were performed using a Packard Tri-Carb Oxidizer. Samples (approximately 0.3 g) were oxidized and $^{14}CO_2$ evolved was trapped in vials containing Carbo-Sorb-2 and mixed with Permafluor-V scintillation cocktail. The trapped radioactivity was counted by LSC. Combustion efficiency was determined by combusting a control samples fortified with a known amount of ^{14}C. Ten subsamples were combusted for each study sample and the average of the ten results was used for calculations. Radioassay of solutions were performed by placing the aliquots of known size in Hydrofluor in a polyethylene vial and counting.

Raw counting data was processed using the registrants in house data reduction program. Sample dpm were determined by subtracting control cpm from sample cpm and dividing by percent counting efficiency. Sample ppm were calculated by dividing sample dpm by sample size multiplied by the specific activity of the test substance. The limit of detection was 0.0011 ppm, based on a nominal specific activity (SA) of 11,100 dpm/ug, 0.3 g sample size, and 3 cpm being the least significant cpm.

Because of the presence of colored pigments in some samples, it was necessary to decolorize the samples to minimize the effects on LSC. Decolorization was accomplished by: 10 pipetting sample into scintillation vial; 2) diluting to 1.0 mL with MeOH; 3) adding 2 drops 6 N HCl and mixing; 4) adding 100 uL saturated $KMnO_4$ in H_2O and mixing; 5) adding 2 drops 30% H_2O_2 and mixing; 6) adding scintillation cocktail and counting. Background counting using this procedure was determined by subjecting 1.0 mL MeOH to the same decolorization procedure.

TLC - The aqueous and methylene chloride extracts were analyzed by TLC (Merck Silica Gel Plates). The aqueous extracts were developed with a chloroform/MeOH/triethylamine (80/20/0.5) solvent system. The methylene chloride plates were developed with a acetone/toluene (95/5) solvent system.

HPLC - A Waters HPLC system equipped with a Merck LiChrosorb Si 60 column and a LKB 2221 Superac Fraction collector was used to remove silica gel and other trace contaminants prior to MS analysis. Chloroform/MeOH (80/20) was used as the mobile phase. UV and radioactivity detectors (IN/US beta-RAM) were used. Fractions were also collected for LSC.

GC- A Hewlett Packard Model 5890a GC equipped with a Supelco Nukol 0.53 mm column, FID and radioactivity monitor was used for GC analyses.

MS - Electron impact mass spectra were obtained using a Direct Exposure Probe (DEP) Mass Spectrometry with a Finnigan TSQ-46 MS.

Results

Autoradiography - The report stated that plants taken for autoradiography showed the radiolabel to be distributed throughout the plant. For both labels, the lower portion of the plant appeared to be more highly labeled than the upper portions. The registrant went on to say that the distribution of radiolabel in the plant was indicative of systemic accumulation. No autoradiography data were provided. This is a deficiency. The registrant should provide representative autoradiograms of control and treated plants (both labels). A discussion of the autoradiographic procedure should be included.

TRR - Combustion results for alfalfa harvest at various PHIs are presented in Table 11. Each number is the average of five combustion subsamples. Raw LSC data were provided

for each sample.

For all harvests, TRR levels were higher (2x to 3x) in the ^{14}C-CPR treated plants versus the ^{14}C-NPR treated plants. Because the two treatments differed only in the position of the radiolabel, the differing TRR results for the treatments suggest cleavage of the diphenyl ether bond. For the CPR label, TRR levels ranged from 0.093 - 0.199 ppm and for the NPR label 0.031 - 0.073 ppm, with the lower values being corresponding to the earlier harvests.

Because of the manner in which plots were harvested, the 45 and 76 day PHI samples represent residues accumulated from the time of application to harvest. The radiolabel in the 109 day PHI sample represents accumulation of radiolabel in plants following harvest of the 45 day PHI samples. The radiolabel in the 158 day PHI samples resulted from residues accumulated in plants after the 76 day PHI harvest for half the plot and after the 109 day PHI for the other half of the plot.

CBRS concludes that the TRR results demonstrate continual accumulation of radiolabel throughout the growing season.

Table 11. TRR found in Alfalfa treated with oxyfluorfen at 2.0 lb ai/A at the indicated PHIs.

PHI (days)	CPR Label (ppm)[a]	NPR Label (ppm)[a]
45	0.093	0.044
76	0.129	0.031
109	0.199	0.059
158	0.184	0.073

[a] Expressed in terms of oxyfluorfen.

Characterization of Residues

CPR Label - The distribution of radioactive residues in fractions of the ^{14}C-CPR treated sample is given in Table 12. For all samples, the majority of the radioactivity was present in the aqueous fraction of the MeOH extract (48% to 71% TRR).

Table 12. Distribution of Radioactivity in Extracts of ^{14}C-CPR Treated Alfalfa.

Fraction	45 day PHI (TRR 0.093 ppm)		76 day PHI (TRR 0.129 ppm)		109 day PHI (TRR 0.199 ppm)		158 day PHI (TRR 0.184 ppm)	
	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR
MeOH Extract	0.057	61	0.088	68	0.157	79	0.127	69
$MeCl_2$	0.012	13	0.013	10	0.016	8	0.015	8
Aqueous	0.045	48	0.075	58	0.141	71	0.112	61
PES	0.018	19	0.018	14	0.036	18	0.039	21
Acid	0.006	6	0.005	4	0.010	5	0.009	5
Base	0.005	5	0.005	4	0.010	5	0.013	7
Enz.	0.0004	0.4	0.0006	0.5	0.001	0.6	0.001	0.5
PES-2	0.006	6	0.006	5	0.014	7	0.015	8
Unaccounted For	0.001	1.6	0.0006	0.5	0.008	0.4	0.001	0.5
"Lost"	0.019	20	0.023	18	0.006	3	0.018	10

$MeCl_2$ Fraction - The $MeCl_2$ fraction was analyzed by TLC, followed by quantitation by scrapping the plates and LSC. Oxyfluorfen was found at 2% TRR (0.004 ppm) in the first harvest alfalfa sample (45 day PHI), but was not detected in any of the later harvests. The remainder of the activity in this fraction remained at the origin (3 to 7% TRR, 0.004 to 0.012 ppm) or was identified as "unknowns" (4 to 5% TRR, 0.004 to 0.010 ppm).

Aqueous Fraction - TFA Identification - The aqueous fraction was passed through an anion exchange column (QAE Sephadex) and the majority of the radiolabel was retained by the column and could only be eluted by 1 N HCl. The material that eluted from the column was found to be extractable into ethyl acetate and to be volatile if left in the acidic form. All radiolabel was lost during concentration by rotary evaporation. If the radiolabeled material was converted to the salt form (by adjusting to near pH 10 with NH_4OH) it was not volatilized. Therefore, before concentration, the eluted material was adjusted to pH 10. The concentrated sample was further purified by 1-D TLC followed by additional purification with 2-D TLC, then HPLC to remove the silica gel. The purified sample was analyzed by Direct Exposure Probe (DEP) Mass Spectrometry.

Electron Impact spectra were generated using a Finnigan TSQ-46 MS. The mass spectrum obtained showed peaks at m/z 114, 69, 60, 51, 45, 36, and 30. TFA could give rise to the ions with m/z 114, 69, 51, 50, and 45. The registrant did not provide a mass spectrum of a TFA standard obtained under the same conditions.

The volatile metabolite was also characterized by GC. A portion of the purified sample was mixed with "authentic" TFA and subjected to GC analysis with both radioactivity monitoring and FID. The radioactivity peak coeluted with the "authentic" TFA peak detected by FID. The source and purity of the "authentic" TFA were not provided.

CBRS concludes that sufficient data has been provided to identify trifluoroacetic acid in the aqueous extract. TFA was the most abundant metabolite identified in the aqueous fraction

(17 - 53% TRR, 0.016 - 0.106 ppm). The percentage of TFA increased with time (first harvest 17% TRR, second 37%, third 53%, and last 50%).

NPR Label - The distribution of radioactivity in fractions of the ^{14}C-NPR treated alfalfa is given in Table 13.

Table 13. Distribution of Radioactivity in Extracts of ^{14}C-NPR Treated Alfalfa.

Fraction	45 day PHI (TRR 0.044 ppm)		76 day PHI (TRR 0.031 ppm)		109 day PHI (TRR 0.059 ppm)		158 day PHI (TRR 0.073 ppm)	
	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR
MeOH Extract	0.015	34	0.009	29	0.015	25	0.015	21
Aqueous	0.010	22	0.006	20	0.010	18	0.009	12
$MeCl_2$	0.005	12	0.003	9	0.005	8	0.006	8
PES	0.029	65	0.020	64	0.041	70	0.053	72
Acid	0.007	16	0.004	13	0.006	11	0.009	13
Base	0.013	30	0.006	19	0.008	14	0.013	18
Enz.	0.0004	1	0.0006	2	0.001	2	0.001	2
PES-2	0.007	17	0.007	22	0.016	27	0.018	25
Unaccounted For	0.0004	1	0.003	11	0.011	18	0.012	16
"Lost"	0.0004	1	0.002	7	0.003	5	0.006	8

Because of the low levels of radioactivity in the fractions, identification of residues was not accomplished. The NPR autoradiograms required darkroom exposure of up to 1.5 years to allow for visualization of as little of 100 to 200 dpm/plate. Qualitative analysis of the TLC plates for the aqueous and methylene chloride extracts showed that most of the radiolabeled material remained at the origin. A small amount of radiolabel in the methylene chloride extract co-migrated with oxyfluorfen standard, but the exact quantity could not be determined.

CBRS concludes that the radiolabel in NPR treated alfalfa has been adequately characterized.

Metabolic Pathway

The registrant proposed a pathway for generation of TFA, primarily be photolytic reactions, as shown in Figure 2 above.

cc: S.F., circ., R.F., List B File, S.Knizner
RDI: A. Rathman, 4/5/94 M.Metzger, 4/5/94 E.Zager, 4/6/94
7509C:CBRS:CM#2:305-6903:SAK:sak:Oxyflr:4/4/94