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

JUN 16 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **Oxyfluorfen.** Guideline 171-4(b) Nature of the Residue in Ruminants. Reregistration Case No. 2490. Chemical No. 111601. MRID #42670601. DP Barcode D188906. CBRS #11,526.

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THRU: Andrew Rathman, Section Head
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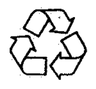
Attached is a review of a oxyfluorfen goat metabolism study submitted by Rohm and Haas Co. in response to the Phase 4 Review (S.Funk, 3/16/91). This study was reviewed by Acurex Corp. under the supervision of CBRS. This study has undergone secondary review in CBRS and has been revised to reflect Branch Policies.

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 numerous racs and food additives, including but not limited to: fat, meat and mbyp of sheep, poultry, horses, hogs, goats and cattle at 0.05 ppm; eggs at 0.05 ppm; and milk at 0.05 ppm [40 CFR §180.381 (a), (b), and §185.4600].

The submitted goat metabolism study is not adequate, but is upgradeable. In separate experiments, goats were dosed with [^{14}C]oxyfluorfen, uniformly radiolabeled in either the chlorophenyl (CPR) or nitrophenyl (NPR) ring, at approximately 16 ppm (168X maximum calculated dietary burden) for 7 consecutive days. The data indicate that [^{14}C]oxyfluorfen

1



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radioisotopes had a similar pattern of distribution and characterization in milk and tissues. As in the poultry metabolism study (S.Knizner, 6/10/93, CBRS #11,303, MRID #42624701), TRR was highest in the fat, with concentrations of 0.692 ppm for the CPR labeled compound and 0.534 ppm for the NPR labeled compound. TRR levels for the CPR and NPR radiolabeled compounds respectively in liver were 0.169 and 0.378 ppm, in kidney 0.052 and 0.052 ppm, and in muscle 0.030 and 0.024 ppm.

CPR and NPR radioactive residues in milk were highest in the Day 4 sample, at 0.252 and 0.211 ppm, respectively. For the other 6 milk samples (days 1-3 and 5-7), average TRR levels in the CPR and NPR dosed goats were 0.059 ± 0.024 ppm and 0.063 ± 0.018 ppm respectively. The TRR level in the Day 4 milk sample is more than 6 standard deviations larger than the average results obtained on all other study days. In a preliminary review of results from the goat metabolism study (C.Olinger, 6/15/92, CBRS #9913), the registrant was asked to provide an explanation for the sudden increase in radioactive residues in the Day 4 milk. The registrant did not provide an explanation. This is a deficiency.

Oxyfluorfen was the principal metabolite detected in fat (74-85% TRR), muscle (73-85% TRR), and milk (68-83% TRR). N-acyl oxyfluorfen (RH 35450) was identified in muscle (3.4% TRR in CPR sample) and tentatively identified in milk (2.9% TRR in CPR sample). In kidney, 6-14% of the TRR was accounted for by oxyfluorfen, and the majority of the residue (69-72% TRR) was characterized as polar.

In liver, 1-6% of the TRRs from various samples were tentatively identified as oxyfluorfen. The registrant stated that further characterization and identification of liver metabolites is continuing. Adequacy of this study is reserved pending the submission of the additional liver data.

Samples from the metabolism study were stored for up to 21 months prior to analysis. Storage stability data on milk and tissues are required to support the storage conditions and intervals of this study. Additionally, the registrant stated that a freezer thaw occurred for 48 hours where the temperature reached approximately 20 °C. Several liver subsamples and kidney samples were in the freezer. The registrant must identify the samples involved in the freezer thaw and demonstrate that this event did not influence the results of the study.

Representative samples from the goat metabolism study must be analyzed using enforcement analytical methods for radiovalidation purposes.

If you need additional input please advise.

Attachment 1 - Review of Oxyfluorfen Goat Metabolism Study.

cc: S.F., circ., R.F., List B File, S.Knizner, ACUREX
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H7509C:CBRS:CM#2:305-6903:SAK:sak:oxyflugt.met:6/14/93

OXYFLUORFEN
(Chemical Code 111601)
(CBRS No. 11526; DP Barcode D188906)

TASK 2B

Phase 5 - Reregistration Review
Residue Chemistry

May 17, 1993

Contract No. 68-DO-0142

Submitted to:

U.S. Environmental Protection Agency
Arlington, VA 22202

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3

OXYFLUORFEN

(Chemical Code 111601)

(CBRS No. 11526; DP Barcode D188906)

PHASE 5 - REREGISTRATION REVIEW RESIDUE CHEMISTRY

Task 2B

BACKGROUND

The Oxyfluorfen Phase 4 Review dated 3/91 required data depicting the distribution and metabolism of oxyfluorfen in ruminants. Representative samples from the metabolism study were required to be analyzed by current or proposed enforcement methods. After reviewing the preliminary results from the goat metabolism study, the Agency (C. Olinger, 6/15/92, CBRS No. 9913) required that the registrant provide an explanation for the sudden increase of radioactive residues in milk on Day 4 of dosing. Subsequently, Rohm and Hass submitted data (1993; MRID 42670601) pertaining to the metabolism of [^{14}C]oxyfluorfen in lactating goats. This submission is reviewed here to determine its adequacy in fulfilling residue chemistry data requirements. The Conclusions and Recommendations stated in this review pertain only to the nature of oxyfluorfen residues in animals.

The nature of the residue in plants and animals is not adequately understood. Adequate methodology is available for the enforcement of tolerances for oxyfluorfen residues in or on plant and animal commodities. Two GLC/electron capture detector (ECD) methods are listed in PAM Vol. II as Methods I and II for the determination of oxyfluorfen residues in or on soybean grain, milk, and the fat, meat, and meat byproducts of cattle. Method I has undergone EPA validation. Agency validation of Method II for eggs and liver is still required.

Tolerances for residues of oxyfluorfen [2-chloro-1-(3-ethoxy-4-nitrophenoxy)-4-(trifluoromethyl)benzene] in or on raw agricultural commodities and processed foods are currently expressed in terms of oxyfluorfen and its metabolites containing the diphenyl ether linkage (40 CFR §180.381 and §185.4600).

As there are no Codex MRLs for residues of oxyfluorfen, there are no questions concerning Codex/U.S. tolerance compatibility.

CONCLUSIONS/RECOMMENDATIONS

1a. The submitted goat metabolism study is not adequate, but is upgradeable pending receipt of additional information. Total radioactive residues (TRR) in goats fed [^{14}C]oxyfluorfen, radiolabeled in the chlorophenyl (CPR) and nitrophenyl (NPR) rings, at approximately 16 ppm (168x) for 7 consecutive days were highest in fat with concentrations ranging from 0.692 ppm for the CPR compound to 0.534 ppm for the NPR compound. TRR levels for the CPR and NPR radiolabeled compounds respectively in liver were 0.169 and 0.378 ppm, in kidney 0.052 and 0.052 ppm, and in muscle 0.030 and 0.024 ppm.

1b. CPR and NPR radioactive residues in milk were highest in the Day 4 sample, at 0.252 and 0.211 ppm, respectively. For the other 6 milk samples (days 1-3 and 5-7), average TRR levels in the CPR and NPR dosed goats were 0.059 ± 0.024 ppm and 0.063 ± 0.018 ppm respectively. The TRR level in the Day 4 milk sample is more than 6 standard deviations larger than the average results obtained on all other study days. In a preliminary review of results from the goat metabolism study (C.Olinger, 6/15/92, CBRS #9913), the registrant was asked to provide an explanation for the sudden increase in radioactive residues in the Day 4 milk. The registrant did not provide an explanation. This is a deficiency.

2a. Oxyfluorfen was the principal metabolite detected in milk (68-83% TRR), muscle (73-85% TRR), and fat (74-85% TRR). In kidney, 6-14% of the TRR was accounted for by oxyfluorfen, and the majority of the residue (69-72% TRR) was characterized as polar.

2b. In liver, 1-6% of the TRRs from various samples were tentatively identified as oxyfluorfen. The registrant stated that further characterization and identification of liver metabolites is continuing. Adequacy of this study is reserved pending the submission of the additional liver data.

3. Samples from the metabolism study were stored for up to 21 months prior to analysis. Storage stability data on milk and tissues are required to support the storage conditions and intervals of this study. Additionally, the registrant stated that a freezer thaw occurred for 48 hours where the temperature reached approximately 20 °C. Several liver subsamples and kidney samples were in the freezer. The registrant stated that documentation of the freezer thaw was included in the raw data. However, the reviewer could not find the necessary information. The registrant must identify the samples involved in the freezer thaw and demonstrate that this event did not influence the results of the study.

4. Representative samples from the goat metabolism study must be analyzed using enforcement analytical methods for radiovalidation purposes.

DETAILED CONSIDERATIONS

Qualitative Nature of the Residue in Animals

Goats. In response to Phase 4 requirements, Rohm and Hass Company submitted data (1993; MRID 42670601) pertaining to the metabolism of [^{14}C]oxyfluorfen radiolabeled in either the chlorophenyl ring (CPR) or nitrophenyl ring (NPR) in lactating goats. The CPR labeled compound had a radiochemical purity of 100% and a specific activity of 11.5 μCi/mg (25,530 dpm/μg) and the NPR labeled compound had a radiochemical purity of 95% and a specific activity of 10.5 μCi/mg (23,198 dpm/μg). Each label was administered orally to one goat for 7 consecutive days. The actual dose level as a function of feed intake was 15.62 ppm for the CPR label and 15.58 ppm for the NPR label. The dose levels are equivalent to 168x the maximum theoretical dietary exposure based on the established oxyfuorfen tolerances of 0.01 ppm in/on mint hay (60% of a dairy cattle diet), 0.025 ppm in/on almond hulls (25% of a dairy cattle diet), and 0.05 ppm in/on corn grain (15% of a dairy cattle diet). A third goat was used as a control. Milk was collected twice a day. Goats were sacrificed within 24 hours of administering the final dose, and samples of liver, kidney, fat (omental and perirenal), and muscle (longissimus dorsi, semimembranous, and triceps) were collected. Equal quantities of each type of fat and muscle were pooled by tissue type to yield composited fat and muscle samples.

Samples were stored at -20 °C for at least 21 months prior to extraction and analysis. The registrant stated that a freezer thaw occurred for 48 hours where the temperature reached approximately 20 °C. Several liver subsamples and kidney samples were in the freezer. The registrant stated that documentation of the freezer thaw was included in the raw data. However, the reviewer could not find the necessary information. The registrant must identify the samples involved in the freezer thaw and demonstrate that this event did not influence the results of the study.

The in-life portion of the study and initial radioanalyses were conducted by ABC Laboratories, Inc. Subsequent analyses and identifications were conducted by Rohm and Haas.

Total Radioactive Residues (TRR)

Radioactive residues in milk samples were determined directly by liquid scintillation spectrometry (LSS). Radioactive residues in fat were determined by direct LSS of solubilized fat samples. Radioactive residues in other tissues were determined by combustion to $^{14}CO_2$ and LSS. All milk and tissue samples were radioassayed in duplicate. Detection limits for the radioassays were not reported. Sample calculations were submitted.

Total radioactive residues in milk and tissues from the treated goats are reported in Table 1. Totals of 85.6% (CPR) and 79.6% (NPR) of the radioactivity ingested were recovered.

Levels of radioactive residues were highest in fat with concentrations ranging from 0.534 ppm for the NPR to 0.692 ppm for the CPR radioisotype.

CPR and NPR radioactive residues in milk were highest in the Day 4 sample, at 0.252 and 0.211 ppm, respectively. For the other 6 milk samples (days 1-3 and 5-7), average TRR levels in the CPR and NPR dosed goats were 0.059±0.024 ppm and 0.063±0.018 ppm respectively. The TRR level in the Day 4 milk sample is more than 6 standard deviations larger than the average results obtained on all other study days. In a preliminary review of results from the goat metabolism study (C.Olinger, 6/15/92, CBRS #9913), the registrant was asked to provide an explanation for the sudden increase in radioactive residues in the Day 4 milk. The registrant did not provide an explanation. This is a deficiency.

Table 1. Total radioactive residues in milk and tissues from goats dosed orally with [^{14}C]oxyfluorfen labeled in the chlorophenyl (CPR) and nitrophenyl (NPR) rings at approximately 16 ppm each (168x) for 7 consecutive days.

	Total Radioactive Residues (ppm)[a]	
Matrix	CPR	NPR
Liver	0.169	0.378
Kidney	0.052	0.052
Composited Muscle[b]	0.030	0.024
Composited Fat[c]	0.692	0.534
Milk		
Day 1	0.049	0.067
Day 2	0.046	0.040
Day 3	0.039	0.051
Day 4	0.252	0.211
Day 5	0.050	0.055
Day 6	0.104	0.089
Day 7	0.067	0.075

[a]Expressed in oxyfluorfen equivalents. [b]Composited from equal amounts of longissimus dorsi, semimembranous, and triceps muscle. [c]Composited from equal amounts of perirenal and omental fat.

Extraction and Hydrolysis of Residues

At least one CPR and NPR sample from each tissue was extracted and analyzed. Day 2, 4, and 6 CPR milk samples and Day 4 NPR milk samples were extracted and analyzed individually. The distribution ^{14}C-residues in milk (Day 4) and tissue samples is presented in Tables 2 and 3.

Milk residues were extracted with chloroform ($CHCl_3$)/methanol (MeOH) (1:2, v/v) resulting in aqueous and solid fractions that were not analyzed further and a $CHCl_3$/MeOH fraction. The $CHCl_3$/MeOH fraction was concentrated, dissolved in heptane, and partitioned with acetonitrile (ACN). The resulting heptane fraction was not analyzed further and the ACN fractions were analyzed by TLC, HPLC, and GC/MS.

Composited muscle homogenates were extracted with ACN resulting in solid fractions that were not analyzed further and ACN fractions that were partitioned with heptane and ACN. The resulting heptane fraction was not analyzed further. The ACN fraction was concentrated and analyzed by TLC.

Radioactive residues in the composited fat sample were extracted with $CHCl_3$/MeOH (5:7, v/v) as described for milk. The heptane and solid fractions were not analyzed further. Residues in the ACN fraction were concentrated, dissolved in ethyl ether, and analyzed by TLC. The major radioactive zone was eluted from the TLC plate and analyzed by GC/MS.

Homogenized kidney samples were extracted with ACN/MeOH. Solids were not analyzed further; the ACN/MeOH fractions were concentrated and analyzed by TLC.

Residues in liver (NPR) were extracted with $CHCl_3$/MeOH, concentrated, and partitioned with heptane and ACN (Extraction I). The heptane and ACN fractions were analyzed by TLC. In addition, subsamples of the heptane fraction were subjected to column chromatography and selected column fractions were analyzed by TLC. Soluble fractions were radioassayed and not analyzed further. Residues in the solid fractions were extracted with 70% ACN or ACN containing either 1 N HCl, 1 N NaOH, or 30% acetic acid. Following centrifugation, the solids were resuspended in their respective extraction solvents and placed in a boiling water bath for 1 hour. The soluble fractions from the HCl/ACN and NaOH/ACN extractions were partitioned with ethyl ether. The acid and base ether fractions were analyzed by TLC. The non-acid and base heat extracts and the weak acetic acid heat extract were not analyzed further.

Residues in liver (CPR) were extracted with 1.2 N HCl in ACN at 85 °C for 15 minutes resulting in HCl/ACN and solid fractions (Extraction II). The HCl/ACN fraction was partitioned with ethyl acetate (EtOAc) resulting in an aqueous fraction that was not analyzed further and an EtOAc-1 fraction. The EtOAc-1 fraction was concentrated and a subsample was analyzed by TLC. An additional subsample was base hydrolyzed (1 N NaOH in ACN, 100 °C) resulting in an EtOAc-2 fraction that was analyzed by TLC and a hydrolysate that

was partitioned with EtOAc resulting in EtOAc-3 and aqueous fractions. The EtOAc-3 fraction was analyzed by TLC. In addition, subsamples of the EtOAc-3 and aqueous fractions were eluted through a C-18 cartridge. Eluant fractions from both subsamples were combined and subjected to TLC. Liver solids were extracted with NaOH/ACN (pH 10, 85 °C, one hour). The resulting NaOH/ACN fraction was partitioned with EtOAc and butanol resulting in aqueous and butanol fractions that were not analyzed further and an EtOAc fraction. The EtOAc fraction was eluted through a column. The MeOH column eluant was not analyzed further. The ether column eluant was analyzed by TLC.

Residues in liver (CPR) were extracted with 1 N NaOH in ACN (reluxed for 2 hours) resulting in a solid fraction that was not analyzed further and a NaOH/ACN fraction (Extraction III). The NaOH/ACN fraction was neutralized with HCl and partitioned with EtOAc resulting in EtOAc and aqueous fractions. The EtOAc fraction was concentrated and eluted with ether and MeOH through a silica gel column. Ether and MeOH eluant fractions were analyzed by TLC. The aqueous fraction was adjusted to pH 3 with HCl and partitioned with EtOAc. The resulting precipitate, aqueous, and EtOAc fractions were not analyzed further.

Residues (CPR) from an additional liver sample were extracted with ACN resulting in ACN and solid (ACN solid) fractions (Extraction IV). The ACN fraction was concentrated to dryness and resuspended in EtOAc. The EtOAc fraction was concentrated and partitioned with heptane and ACN resulting in ACN, heptane, and solid (EtOAc solid) fractions. The ACN fraction was eluted through a column and the fractions containing radiolabel were analyzed by TLC and HPLC. The heptane fraction was not analyzed further. The EtOAc solid fraction was extracted with MeOH and the resulting post-extraction solids (PES) and MeOH fractions were not analyzed further. The ACN solid fraction was sequentially extracted with 0.12 N HCl in ACN followed by sonication with 5% NaOH in ACN; partitioned with EtOAc, heptane, MeOH; eluted through a C 18 cartidge; analyzed by TLC and HPLC; and the HPLC fractions combined and treated with sulfatase, but the registrant reported that no fractions were obtained which afforded reasonable characterization.

Table 2. Distribution and characterization of ^{14}C-residues in milk and tissues from goats fed [^{14}C]oxyfluorfen labeled in the chlorophenyl (CPR) or nitrophenyl (NPR) rings at approximately 16 ppm (168x) for 7 consecutive days.

Sample/Fraction	%TRR[a]	ppm[a]	Characterization/Identification
Milk Day 4 0.252 ppm (0.211 ppm)			
$CHCl_3$/MeOH			
Heptane	3.6 (6.8)	0.009 (0.014)	Not analyzed
ACN	93.7 (76.5)	0.236 (0.16)	Analyzed by TLC; 0.209 ppm (82.8% TRR), 0.142 ppm (67.5% TRR) identified as oxyfluorfen in CPR and NPR samples, respectively; 0.007 ppm (2.9% TRR) tentatively identified as RH-35450 in CPR sample; other components in CPR and NPR samples comprised ≤9% of the TRR; Identity of oxyfluorfen confirmed by HPLC and GC/MS. In Day-3 and Day-6 CPR samples, oxyfluorfen accounted for 67% and 74.5% of the TRR, respectively.
Aqueous	2.5 (12.8)	0.006 (0.027)	Not analyzed
Solids	1.2 (0.6)	0.003 (0.001)	Not analyzed
Muscle 0.03 ppm (0.024 ppm)			
ACN			
Heptane	5.1 (5.2)	0.002 (0.001)	Not analyzed
ACN	90.8 (104.5)	0.028 (0.026)	TLC; 0.022 ppm (73.2% TRR) and 0.02 ppm (85.1% TRR) identified as oxyfluorfen in CPR and NPR samples, respectively; 0.001 ppm (3.4% TRR) was identified as RH-35450 in the CPR sample; other components comprised ≤12% of the TRR (≤0.003 ppm).
Solids	5.3 (10.5)	0.002 (0.003)	Not analyzed
Fat 0.692 ppm (0.534 ppm)			
$CHCl_3$/MeOH			
Heptane	6.4 (7.1)	0.044 (0.038)	Not analyzed
ACN	77.3 (85.8)	0.532 (0.458)	TLC analysis identified 0.511 ppm (73.9% TRR) as oxyfluorfen in CPR sample and 0.451 ppm (84.5% TRR) in the NPR sample; GC/MS confirmed identity of oxyfluorfen. Other components comprised ≤1.4% of the TRR in both samples.
Solids	0.6 (1.1)	0.004 (0.006)	Not analyzed
Kidney 0.052 ppm (0.052 ppm)			
ACN/MeOH			
ACN	90.3 (99)	0.048 (0.051)	TLC analysis identified 0.003 ppm (5.7% TRR) and 0.007 ppm (14% TRR) as oxyfluorfen in the CPR and NPR samples, respectively; The majority of the residue in both samples (69-72% TRR) remained at the origin and was characterized as polar; Other components comprised ≤6% of the TRR.
Solids	11.4 (18)	0.006 (0.009)	Not analyzed

[a]Values for NPR samples are in parentheses.

Table 3. Distribution and characterization of ^{14}C-residues in liver of goats fed [^{14}C]oxyfluorfen labeled in the chlorophenyl (CPR) or nitrophenyl (NPR) ring, at approximately 16 ppm (168x) for 7 consecutive days.

Sample/Fraction	%TRR	ppm	Characterization/Identification
Liver			
Extraction I (NPR; 0.378 ppm)			
$CHCl_3$/MeOH	55.6	0.21	Solvent partitioned
Heptane	25.6	0.10	Analyzed by column chromatography and TLC; 0.023 ppm (6% TRR) identified as oxyfluorfen, 0.064 ppm (17% TRR) characterized as polar.
ACN	19.8	0.07	TLC; 0.03 ppm (8% TRR) characterized as polar, 0.02 ppm (5% TRR) unknown.
Solids	69.5	0.26	Acid hydrolyzed
HCl/ACN			
No heat	18	0.07	Not analyzed
Mild heat	43	0.16	
Ether	22	0.08	TLC; further characterization pending
Aqueous	15	0.06	
NaOH/ACN			Base hydrolyzed
No heat	15	0.06	Not analyzed
Mild heat	35	0.13	
Ether	16	0.06	TLC; further characterization pending
Aqueous	12	0.05	
70% ACN			
No heat	7	0.03	Not analyzed
Mild heat	12	0.05	
30% Acetic Acid/ACN			
No heat	6	0.02	Not analyzed
Mild heat	11	0.04	Not analyzed
Extraction II (CPR; 0.169ppm)			
HCl/ACN	66	0.11	Solvent partitioned
Aqueous	13	0.02	Not analyzed
EtOAc-1	42	0.07	Subsample analyzed by TLC; 26% of the TRR remained at the origin; Additional subsample base hydrolyzed.
EtOAc-2	24	0.04	TLC; 5.7% of the TRR remained at the origin, 4% unknown.
Base Hydrolysate	13	0.02	
EtOAc-3	6	0.01	Column chromatography and TLC
Aqueous	7	0.01	Selected column eluant fractions combined with EtOAc-3 column eluant fractions and subjected to TLC; approximately 2% of the TRR tentatively identified each as oxyfluorfen and RH 34670; further characterization pending.
Solids	34	0.06	
NaOH/ACN	32	0.05	Solvent partitioned

(continued).

11

Table 3. (continued).

Sample/Fraction	%TRR	ppm	Characterization/Identification
EtOAc	22	0.04	C-18 Column chromatography
Ether eluant	14	0.02	TLC; further characterization pending
MeOH eluant	4	0.01	
Butanol	3	0.01	Not analyzed
Aqueous	13	0.02	Not analyzed
Solids	2	0.003	Not analyzed
Extraction III (CPR; 0.169 ppm)			
NaOH/ACN	81	0.14	Solvent partitioned
EtOAc	50	0.08	Fractionated further by column chromatography
Ether eluant	17	0.03	TLC;11.5% of the TRR remained at the origin, 1.1% tentatively identified as oxyfluorfen, and 0.5% of the TRR identified as RH 35450.
MeOH eluant	16	0.03	TLC; 16% of the TRR remained at the origin, 2% unknown; further characterization pending.
Aqueous	25	0.04	Solvent partitioned
EtOAc	8	0.01	Not analyzed
Aqueous	8	0.01	Not analyzed
Precipitate	6	0.01	Not analyzed
Solids	19	0.03	Not analyzed
Extraction IV (CPR; 0.169 ppm)			
ACN			Solvent partitioned
EtOAc	42	0.07	Solvent partitioned
Heptane	5	0.01	Not analyzed
ACN	39	0.07	Column chromatography, TLC, HPLC; 1.7% of the TRR identified as oxyfluorfen, 3.1% identified as RH 35450.
Hydrolysate	12	0.02	
Aqueous			
EtOAc	6	0.01	Not analyzed
Solids	11	0,02	
MeOH	18	0.03	Not analyzed
PES	4	0.01	Not analyzed
Solids	42	0.07	See text for explanation

Characterization of Residues

Normal phase TLC analyses were conducted on silica gel plates using several solvent systems. TLC plates were scanned for radioactivity and analyzed by direct integration from the scanner. Non-radioactive standards were visualized under UV. Representative TLC chromatograms were provided. The molecular structures and chemical names of oxyfluorfen and suspected metabolites are presented in Figure 1.

Selected fractions were fractionated by silica gel or silicic acid column chromatography. Fractions eluting as the same peak were combined, concentrated, and characterized further.

Reverse-phase HPLC analyses were performed on a system equipped with a radioactivity detector and UV absorbance detector at 280 nm. Samples were eluted using a water/MeOH (66:34, v/v) solvent system. Representative chromatograms were provided.

The identification of oxyfluorfen in purified subsamples of milk and fat was confirmed using GC/MS equipped with a mass selective detector.

In milk, fat, and muscle, 83-100% of the TRR was extracted, 68-85% of the TRR was identified as oxyfluorfen, and other components comprised 1-9% of the TRR. In kidney, 90-99% of the TRR was extracted, 6-14% of the TRR was identified as oxyfluorfen, 69-72% of the TRR was characterized as polar, and unidentified components comprised $\leq$6% of the TRR.

In liver (Extraction I), a recovery of 120% was reported which included a soluble fraction that comprised 85% of the TRR and a solid fraction that comprised 40%. In the soluble fraction, only 6% of the TRR was identified as oxyfluorfen, 25% of the residue was characterized as polar, and 5% was reported as unknown. With liver Extractions II and III, 81-98% of the TRR was extracted and 0.5-2% was tentatively identified as oxyfluorfen. The presence of RH 34670 and 35450 were suggested from the TLC analyses. Liver extraction IV solubilized approximately 60% of the TRR. Approximately 2% of the TRR was tentatively identified as oxyfluorfen, and 3% identified as RH 35450. Sulfatase hydrolysis had no effect on liver solids. The registrant stated that further characterization and identification of liver residues is continuing.

Figure 1.

Common/Chemical Name	Structure	Matrices/MRID
Oxyfluorfen **RH 32915**	Cl, OCH_2CH_3, F_3C, O, NO_2	goat milk muscle fat kidney liver
RH 34670	Cl, OH, F_3C, O, NO_2	goat liver
N-Acyl Goal **RH 35450**	Cl, OCH_2CH_3, F_3C, O, $NCOCH_3$, H	goat milk muscle liver

14

References

Citations for the MRID documents referenced in this review are presented below. Submissions reviewed in this document are indicated by shaded type.

42670601 Reibach, P. (1993) Metabolism of (carbon 14)-Oxyfluorfen in Lactating Dairy Goats: Lab Project Number: 34-93-4. Unpublished study prepared by Rohm and Haas Co. and ABC Labs., Inc. 332 p.

Agency Memoranda

CBRS No. 9913
Subject: Reregistration of Oxyfluorfen: Time Extension Request.
From: C. Olinger
To: M. Wilhite/B.Sidwell
Dated: 6/15/92
MRID(s):