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

JUN 10 1993

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **Oxyfluorfen. Guideline 171-4(b) Nature of the Residue in Poultry.** Reregistration Case No. 2490. Chemical No. 111601. MRID #42634701. DP Barcode D187615. CBRS #11,303.

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Attached is a review of a oxyfluorfen hen 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 poultry metabolism study is adequate. In separate experiments, hens were fed [^{14}C]oxyfluorfen, radiolabeled in either the chlorophenyl (CPR) or nitrophenyl (NPR) ring, at approximately 15 ppm (300X maximum calculated dietary burden) in the diet for 7 consecutive days. The data indicate that [^{14}C]oxyfluorfen radioisotopes had a similar pattern

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of distribution and characterization in eggs and tissues. TRR was highest in fat, with concentrations ranging from 14.408 ppm for the CPR labeled compound to 15.932 ppm for the NPR labeled compound. CPR and NPR radioactive residues in eggs were highest in day 7 samples, at 1.509 and 2.003 ppm, respectively. TRR levels in liver were 1.261 and 1.680 ppm and in breast muscle were 0.190 and 0.246 ppm, respectively for the CPR and NPR radiolabeled compounds.

Oxyfluorfen was the principal metabolite detected in eggs (60-69% TRR), liver (52-62% TRR), breast muscle (76-77% TRR), thigh muscle (85-88% TRR), and fat (93-96% TRR). Hydroxy-oxyfluorfen (RH 34670) was identified in eggs (16-22% TRR), fat (3-5% TRR), liver (6-16% TRR), and muscle (3-5% TRR). A sulfate conjugate of OH-oxyfluorfen (Metabolite B), was detected in eggs (14-15% TRR), breast muscle (7-8.5% TRR), and thigh muscle (3-4% TRR), but not in liver or fat. The data indicate that O-deethylation followed by conjugation with a sulfate moiety is the major oxyfluorfen metabolic pathway.

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

If you need additional input please advise.

Attachment 1 - Review of Oxyfluorfen Hen Metabolism Study.

cc: S.F., circ., R.F., List B File, S.Knizner, ACUREX
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OXYFLUORFEN
(Chemical Code 111601)
(CBRS No. 11303; DP Barcode D187615)

TASK 2B

Phase 5 - Reregistration Review
Residue Chemistry

May 20, 1993

Contract No. 68-DO-0142

Submitted to:

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OXYFLUORFEN

(Chemical Code 111601)

(CBRS No. 11303; DP Barcode D187615)

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 poultry. Representative samples from the metabolism study were required to be analyzed by current or proposed enforcement methods. After reviewing the preliminary results from the hen metabolism study, the Agency (C. Olinger, 6/15/92, CBRS No. 9913) stated that the most important work remaining was identification of metabolite B, hydrolysis of the liver post-extraction solids, and characterization of the water-soluble residues from the liver. Subsequently, Rohm and Hass submitted data (1993; MRID 42634701) pertaining to the metabolism of [^{14}C]oxyfluorfen in poultry. 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 poultry metabolism study is adequate. Total radioactive residues (TRR) in hens fed [^{14}C]oxyfluorfen, radiolabeled in either the chlorophenyl (CPR) or nitrophenyl (NPR) ring, at approximately 15 ppm (300x) for 7 consecutive days were highest in fat with concentrations ranging from 14.408 ppm for the CPR compound to 15.932 ppm for the NPR compound. The data indicate that [^{14}C]oxyfluorfen radioisotopes had a similar pattern of distribution and characterization in eggs and tissues. CPR and NPR radioactive residues in eggs were highest in day 7 samples, at 1.509 and 2.003 ppm, respectively. Oxyfluorfen was the principal metabolite detected in eggs (60-69% TRR), liver (52-62% TRR), breast muscle (76-77% TRR), thigh muscle (85-88% TRR), and fat (93-96% TRR). Hydroxy-oxyfluorfen (RH 34670) was detected in eggs and tissues (3-22% TRR). Metabolite B, a sulfate conjugate of OH-oxyfluorfen, was detected in eggs (14-15% TRR), breast muscle (7-8.5% TRR), and thigh muscle (4% TRR). The data indicate that O-deethylation followed by conjugation with a sulfate moiety is the major oxyfluorfen metabolic pathway.

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

DETAILED CONSIDERATIONS

Qualitative Nature of the Residue in Animals

Hens. In response to Phase 4 requirements, Rohm and Haas Company submitted data (1993; MRID 42634701) pertaining to the metabolism in poultry of [^{14}C]oxyfluorfen radiolabeled in either the chlorophenyl ring (CPR) or nitrophenyl ring (NPR). 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 20 hens for 7 consecutive days at 15 ppm (as a function of feed intake). The dose level is equivalent to 300x the maximum theoretical dietary exposure based on the established tolerance of 0.05 ppm for oxyfluorfen residues in or on corn grain and soybean seed (Table 1). A group of 20 hens served as the control group. Eggs were collected twice daily, composited by test group, homogenized, and stored frozen. Hens were sacrificed within 24 hours of administering the final dose. Samples of breast and thigh muscle, liver, and fat were collected, composited by treatment group, homogenized, and stored frozen (approximately -20 °C) until they were shipped to the analytical laboratory where they were stored at -15 °C. The samples were stored for 11-12 months prior to the initial extractions and analyses. The analytical phase of the study lasted for another 11 months.

To determine storage stability, egg, thigh muscle, and fat samples were re-extracted 8 months after the initial sample extractions. Selected fractions were subjected to HPLC analysis, and the results compared to the initial HPLC profile. The percent distribution of the TRR in egg, muscle, and fat was similar to that from the first extractions. Comparison of the initial egg, muscle, and fat HPLC profiles with the second HPLC profiles indicated that the residues in the samples were stable during 260-266 days of frozen storage.

The storage stability data are adequate even though the initial extractions and HPLC profiles were conducted approximately 11 months after the samples were collected. Although no samples were extracted at the beginning of the study, because the data demonstrate that oxyfluorfen per se is the major residue in egg and tissue samples, the storage stability will be considered adequate.

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

Table 1. Calculation of maximum dietary exposure in poultry.

Commodity	Tolerance (ppm)	% in diet	Dietary exposure (ppm)
Soybean seed	0.05	30.0	0.015
Corn grain	0.05	70.00	0.035
Total		100.0	0.05

Total Radioactive Residues (TRR)

Radioactive residues in liquid samples were determined directly by liquid scintillation spectrometry (LSS). Radioactive residues in solids were determined by combustion to $^{14}CO_2$ and LSS. All egg and tissue samples were radioassayed in duplicate or triplicate. Detection limits for the radioassays were not reported. Sample calculations were submitted.

Total radioactive residues in eggs and tissues from the treated goats are reported in Table 2. Levels of radioactive residues were highest in fat with concentrations of 14.408 ppm for the CPR radioisotope and 15.932 ppm for the NPR radioisotope. CPR and NPR radioactive residues in eggs were highest in day 7 samples (1.509 and 2.003 ppm, respectively).

Extraction and Hydrolysis of Residues

At least one CPR and NPR sample from eggs and tissues was extracted and analyzed. The distribution of ^{14}C-residues in eggs (day 7) and tissue samples is presented in Table 2.

Egg (day 7) residues were extracted with acetonitrile (ACN)/hexane (1:1, v/v) resulting in a solid fraction that was not analyzed further, and hexane and ACN fractions. The hexane fraction was concentrated, reconstituted in methanol (MeOH), and placed in a dry ice/acetone bath to precipitate lipids. The remaining MeOH fraction was concentrated and analyzed by HPLC. The ACN fraction was partitioned with ethyl acetate (EtOAc) resulting in an aqueous fraction that was not analyzed further and an EtOAc fraction that was analyzed by HPLC and TLC.

Liver residues were extracted with chloroform ($CHCl_3$)/MeOH/water (5:11:5, v/v/v) resulting in MeOH/water, $CHCl_3$, and solid fractions. The MeOH/water fraction was analyzed by HPLC after cleanup using a C-18 column and evaporation of the MeOH. The $CHCl_3$ fraction was concentrated and reconstituted in hexane/ACN (1:1, v/v). The resulting ACN fraction was analyzed by HPLC and TLC. Lipids were precipitated from the hexane fraction as described for eggs, and the resulting MeOH fraction was concentrated and analyzed by HPLC. Subsamples of liver NPR and CPR solid fractions (solids-1) were enzyme hydrolyzed (protease in phosphate buffer, pH 7.5, 37 °C for 24 hours) resulting in solid (solids-2) and hydrolysate-1 fractions. The hydrolysate-1 fraction obtained from the CPR sample was partitioned with EtOAc resulting in an EtOAc and an aqueous fraction (AQ-1). The AQ-1 fraction was eluted through successive C-18 columns resulting in an aqueous fraction (AQ-2) and a MeOH-1b fraction. The EtOAc and the MeOH-1b fractions were combined and subjected to HPLC analysis. The hydrolysate-1 fraction from the NPR sample was eluted through successive C-18 columns with MeOH and MeOH/acetic acid (HOAc) (1:1, v/v) resulting in an aqueous (AQ-1) fraction and MeOH-1a and MeOH-2 fractions. The two MeOH fractions were combined and analyzed by HPLC and the AQ-1 fraction was not analyzed further. Solids-2 fractions from CPR and NPR liver samples were acid hydrolyzed (1 N HCl, 4 hours at 100 °C) resulting in hydrolysate-2 and solids-3 fractions. The hydrolysate-2 fractions were concentrated and analyzed by HPLC and TLC. The Solids-3 fractions were acid hydrolyzed (6N HCl, 24 hours, 103 °C). The resulting hydrolysate-3 fractions were concentrated and analyzed by HPLC and TLC. The remaining solid fractions were not analyzed further.

Thigh and breast muscle residues were extracted similarly to liver residues with $CHCl_3$/MeOH/water (5:11:5, v/v/v) resulting in a solid fraction that was not analyzed further and MeOH/water and $CHCl_3$ fractions. The MeOH/water fraction was cleaned up using a C-18 column, and the resulting eluant MeOH fractions were analyzed by HPLC. The $CHCl_3$ fraction was concentrated and dissolved in hexane/ACN (1:1, v/v) resulting in an ACN fraction that was analyzed by HPLC, and a hexane fraction. The hexane fraction from CPR thigh muscle was eluted through a Florisil column. MeOH eluant fractions were combined, concentrated, and analyzed by HPLC. Lipids in the hexane fraction from NPR thigh muscle were precipitated from the hexane fraction as described for eggs and liver. The resulting MeOH fraction was concentrated and analyzed by HPLC.

Residues in fat were sequentially extracted with hexane and MeOH. The MeOH and solid fractions were not analyzed further. The hexane extract (hexane-1) was concentrated and

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partitioned with ACN resulting in an ACN fraction that was analyzed by HPLC and a hexane-2 fraction. The hexane-2 fraction from the CPR sample was sequentially eluted through a Florisil column with hexane, methylene chloride (CH_2Cl_2)/hexane (1:4, v/v), and MeOH. The MeOH/CH_2Cl_2 and MeOH fractions were concentrated and subjected to HPLC analysis. The hexane-2 fraction from the NPR sample was eluted through a Florisil column and the resulting CH_2Cl_2/hexane (1:4 and 1:1, v,v) fractions were combined, concentrated and subjected to HPLC analysis.

Table 2. Distribution and characterization of ^{14}C-residues in eggs and tissues from hens fed with [^{14}C]oxyfluorfen labeled in the chlorophenyl (CPR) or nitrophenyl (NPR) rings at 15 ppm (300x).

Sample/Fraction	%TRR[a]	ppm[a]	Characterization/Identification
Eggs (Day 7) 1.509 ppm (2.003 ppm)			
ACN/Hexane			
Hexane	4.15 (4.52)	0.06 (0.09)	CPR and NPR samples analyzed by HPLC; 2.6-2.8% of the TRRs, were identified as oxyfluorfen, and 0.9-1.2% as RH 34670. Identity of oxyflurofen confirmed by TLC.
ACN	95.39 (94.62)	1.44 (1.90)	Solvent partitioned
EtOAc	95.29 (94.24)	1.438 (1.888)	CPR and NPR samples analyzed by TLC and HPLC; of the TRRs, 58-66% was identified as oxyfluorfen, 15-21% as RH 34670, and 14-15% identified as metabolite B; Identities of oxyfluorfen and RH 34670 were confirmed by GC/RAM.
Aqueous	0.10 (0.38)	0.002 (0.008)	Not analyzed further
Solids	0.46 (0.86)	0.007 (0.017)	Not analyzed further
Liver 1.261 ppm (1.680 ppm)			
$CHCl_3$/MeOH/H_2O			
MeOH/H_2O	13.30 (17.84)	0.168 (0.300)	C-18 column cleanup, MeOH eluant fractions of CPR and NPR samples analyzed by HPLC and TLC; of the TRRs, 0.4-3% was identified as oxyfluorfen, 4.6-7% as metabolite A, 3.8% as metabolite E (CPR sample only); four unknowns were also detected, none of which accounted for >3% of the TRR.
$CHCl_3$	73.64 (71.84)	0.928 (1.207)	Solvent partitioned
Hexane	5.49 (7.77)	0.069 (0.131)	HPLC; of the TRRs, 0.7-1.8% identified as oxyfluorfen, 1% as RH 34670, and three unknowns, each accounting for <5% of the TRR
ACN	68.15 (64.07)	0.859 (1.076)	CPR and NPR samples were analyzed by HPLC and TLC; of the TRRs, 47-61% was identified as oxyfluorfen, 6-14% as RH 34670. Identity of oxyfluorfen was confirmed by GC/RAM and GC/MS.

Continued.

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Table 2 continued.

Sample/Fraction	%TRR[a]	ppm[a]	Characterization/Identification
Solids-1	13.06 (10.32)	0.17 (0.17)	Protease hydrolysis
Hydrolysate-1	1.69 (1.94)	0.02 (0.03)	CPR hydrolysate solvent partitioned; NPR hydrolysate subjected to C18 column chromatography, retained components eluted with MeOH and MeOH/HOAc
MeOH-1a[c]	(0.68)	(0.011)	MeOH-1a and 2 were combined and subjected to HPLC analysis; one unknown (1.07% TRR) was detected.
MeOH-2[c]	(0.39)	(0.007)	
EtOAc[b]	0.28	0.004	EtOAc and MeOH-1b (below) fractions were combined and subjected to HPLC analysis; two components detected, each accounting for <0.7% of the TRR.
AQ-1	1.41 (0.87)	0.02 (0.015)	C-18 column cleanup of CPR sample; retained components eluted with MeOH; NPR samples not further analyzed.
MeOH-1b[b]	0.65	0.008	Fraction combined with EtOAc fraction above.
AQ-2[b]	0.76	0.010	Not analyzed further
Solids-2	11.37 (8.38)	0.14 (0.14)	1N HCl hydrolysis
Hydrolysate-2	2.52 (2.41)	0.032 (0.040)	HPLC and TLC analyses; No component detected >1.8% of the TRR.
Solids-3	8.85 (5.97)	0.11 (0.10)	6N HCl hydrolysis
Hydrolysate-3	5.51 (3.82)	0.069 (0.064)	HPLC and TLC analyses; No component detected >3.4% of the TRR.
Solids-4	3.34 (2.15)	0.042 (0.036)	Not analyzed further
Muscle (Breast) 0.190 ppm (0.246 ppm)			
$MeOH/H_2O/CHCl_3$			
$MeOH/H_2O$	6.16 (5.84)	0.012 (0.014)	C-18 column cleanup, MeOH eluant fractions analyzed by HPLC and TLC; metabolite B accounted for 5.8-6% TRR in both CPR and NPR samples.
$CHCl_3$	84.91 (84.83)	0.161 (0.209)	Solvent partitioned
Hexane	1.44 (1.28)	0.003 (0.003)	Not analyzed further
ACN	83.47 (83.55)	0.159 (0.206)	CPR and NPR samples analyzed by TLC and HPLC; Of the TRRs, 76-77% was identified as oxyfluorfen, 4.6-5% as RH 34670, and 1-2% as metabolite B.
Solids	8.93 (9.34)	0.017 (0.023)	Not analyzed further
Muscle (Thigh) 1.191 ppm (1.308 ppm)			
$MeOH/H_2O/CHCl_3$			

Continued.

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Table 2 continued.

Sample/Fraction	%TRR[a]	ppm[a]	Characterization/Identification
MeOH/H_2O	2.66 (2.43)	0.032 (0.032)	C-18 column cleanup, MeOH eluant fractions analyzed by HPLC and TLC; metabolite B accounted for all the residues in this fraction in both CPR and NPR samples, except for 0.26% of the TRR in the CPR sample that was identified as RH 34670.
$CHCl_3$	95.52 (95.04)	1.14 (1.23)	Solvent partitioned
Hexane	1.30 (3.51)	0.015 (0.046)	CPR sample: Florisil column cleanup, MeOH eluant fractions analyzed by HPLC; six components detected; no component > 0.78% of the TRR; NPR sample: Lipids precipitated, MeOH fraction analyzed by HPLC; 1.5% of the TRR identified as oxyfluorfen, three components detected, none accounted for >1.5% of the TRR.
ACN	94.22 (91.53)	1.122 (1.197)	CPR and NPR samples analyzed by TLC and HPLC; of the TRRs, 84-88% was identified as oxyfluorfen, 3.8-4.4% as RH 34670, and 1.4% as metabolite B; two other components were detected, neither accounted for >2.6% of the TRR.
Solids	1.82 (2.53)	0.022 (0.033)	Not analyzed further
Fat 14.408 ppm (15.932 ppm)			
Hexane/MeOH			
MeOH	0.13 (0.04)	0.019 (0.006)	Not analyzed further
Hexane-1	99.85 (99.96)	14.39 (15.93)	Solvent partitioned
Hexane-2	2.34 (5.05)	0.337 (0.805)	CPR and NPR samples purified using Florisil columns and analyzed by HPLC and TLC; of the TRRs, 0.4-3% was identified as oxyfluorfen and 0.4-0.5% as RH 34670; two other components were detected, neither accounted for >1.3% of the TRR.
ACN	97.51 (94.91)	14.05 (15.12)	CPR and NPR samples analyzed by TLC and HPLC; of the TRRs, 90-95% was identified as oxyfluorfen, and 2-4% as RH 34670.
Solids	0.02 (0.0)	0.003 (0.00)	Not analyzed further

[a]NPR values in parentheses. [b]CPR sample only. [c]NPR sample only.

Characterization of Residues

One or two dimensional normal-phase TLC analyses were conducted on silica gel plates using several solvent systems. Standards were co-chromatographed with the samples. TLC plates were scanned for radioactivity and analyzed by direct integration from the scanner. Non-radioactive standards were visualized under short wavelength UV. Representative TLC chromatograms were provided. The molecular structures and chemical names of oxyfluorfen and suspected metabolites are presented in Figure 1.

Reverse-phase HPLC analyses were performed on a system equipped with a radioactivity detector, a UV absorbance detector at 254 nm, and several solvent systems. The reference standards were subjected to HPLC analysis using the same conditions as those used for the treated samples. Representative chromatograms were provided.

Oxyfluorfen from egg and liver samples was isolated and confirmed by GC/radioactivity monitoring (RAM) and GC/MS. Metabolites A, B and E were isolated and identified by GC/MS and FAB/MS and enzymatic hydrolysis.

Metabolite E was isolated from excreta and purified by HPLC and TLC and was subsequently used as a standard for characterizing the residues in egg and tissues. The metabolite was also subjected to sulfatase hydrolysis (acetate buffer, pH 5, 24 hours at 37 °C). The sulfatase hydrolysate and the hydrolysate obtained without enzyme were subjected to TLC analysis.

Metabolite A was subjected to β-glucuronidase hydrolysis (acetate buffer, pH 5, 24 hours at 37 °C). The resulting enzyme and control hydrolysates were subjected to TLC analysis.

Metabolites A, B, and E were subjected to acid hydrolysis (0.1 N HCl, 24 hours at ambient temperature for metabolites A and E; 85 °C for one hour for excreta). The resulting hydrolysates were subjected to TLC, HPLC, or mass spectroscopy. Metabolite A was also subjected to 1 N HCl and 6 N HCl hydrolysis, and the resulting hydrolysates subjected to mass spectroscopy.

A summary of the distribution of oxyfluorfen and its metabolites is presented in Tables 3 and 4. In eggs and tissues, 87-100% of the TRR was extracted; Of the TRRs, 52-95% were identified as oxyfluorfen, and 3-22% as the hydroxy-oxyfluorfen. Metabolite B, a sulfate conjugate of OH-oxyfluorfen, was detected in eggs (14-15% TRR), breast muscle (7-8.5% TRR), and thigh muscle (4% TRR). Metabolites A, C, and E and several unknowns were also detected, but no individual component accounted for >8 % of the TRR.

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Table 3. Characterization of ^{14}C-residues in eggs and tissues from hens fed [^{14}C]oxyfluorfen labeled in the chlorophenyl (CPR) ring.

Metabolite ID	Egg		Liver		Breast Muscle		Thigh Muscle		Fat	
	%	PPM	%	PPM	%	PPM	%	PPM	%	PPM
Oxyfluorfen	68.66	1.037	61.94	0.781	76.19	0.145	87.63	1.044	95.63	13.779
RH-34670	15.76	0.238	5.54	0.070	5.00	0.010	4.70	0.056	2.62	0.378
Metabolite A	0.47	0.007	5.17	0.065						
Metabolite B	14.39	0.217			8.44	0.016	3.79	0.046		
Metabolite C	0.16	0.002	6.95	0.088			0.88	0.010	0.59	0.085
Metabolite E			4.71	0.059						
Unknowns			11.6[a]	0.146			1.2	0.014	1.02	0.147

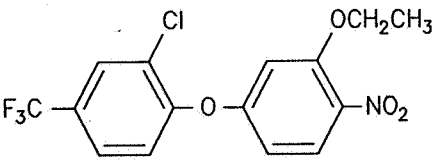
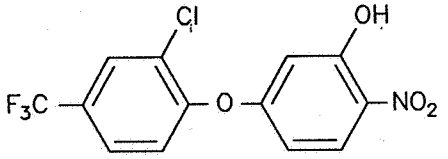
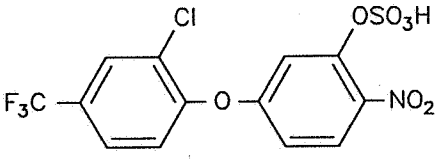
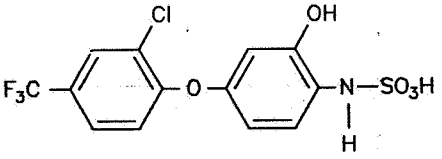
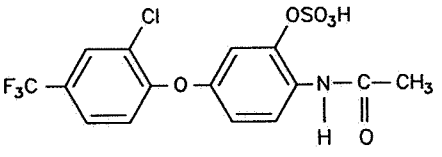
[a]Includes six components, none of which accounted for >5.2% of the TRR.

Table 4. Characterization of ^{14}C-residues in eggs and tissues from hens fed [^{14}C]oxyfluorfen labeled in the nitrophenyl (NPR) ring.

Metabolite ID	Egg		Liver		Breast Muscle		Thigh Muscle		Fat	
	%	PPM	%	PPM	%	PPM	%	PPM	%	PPM
Oxyfluorfen	60.25	1.206	52.11	0.875	76.57	0.188	85.30	1.116	93.09	14.831
RH-34670	21.70	0.435	15.62	0.262	4.61	0.011	4.15	0.055	4.88	0.777
Metabolite A	0.97	0.019	8.05	0.135						
Metabolite B	14.77	0.296			6.83	0.016	3.83	0.050		
Metabolite E			0.47	0.008						
Oxyfluorfen Isomer[a]	1.06	0.021	0.86	0.014	1.37	0.003	2.55	0.033	0.71	0.113
Unknowns			19.0[b]	0.319			1.63	0.021	1.28	0.204

[a]2′-NO_2-oxyfluorfen isomer. Registrant stated that this isomer was associated with the NPR-labeled test substance. [b]Includes nine components, none of which accounted for >4% of the TRR.

Figure 1. Chemical names and structures of oxyfluorfen and its metabolites in poultry tissues and eggs.

Common/Chemical Name	Structure	Hen Matrices
Oxyfluorfen **[2-chloro-1-(3-ethoxy-4-nitrophenoxy)-4-(trifluoromethyl)benzene]**		**eggs** **liver** **breast muscle** **thigh muscle** **fat**
Hydroxy-oxyfluorfen **RH34670**		**eggs** **liver** **breast muscle** **thigh muscle** **fat**
Metabolite B **(a sulfate conjugate of OH-oxyfluorfen)**		**eggs** **breast muscle** **thigh muscle**
Metabolite A **(an N-sulfamic acid conjugate of the hydroxy-amino-oxyfluorfen)**		**eggs** **liver**
Metabolite E **(a sulfate conjugate of the hydroxy-N-acetyl oxyfluorfen)**		**liver**

Continued.

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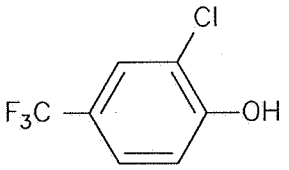
Continued.

Common/Chemical Name	Structure	Hen Matrices
Metabolite C 3-chloro-4-hydroxy-benzotrifluoride RH34800		eggs liver thigh muscle fat

The following compounds were also used as reference standards: amino-oxyfluorfen, 5-CF_3-oxyfluorfen isomer, 6′-NO_2-oxyfluorfen isomer, 2′-NO_2-oxyfluorfen isomer, 5-CF_3-6′-NO_2-oxyfluorfen isomer, N-acetyl-oxyfluorfen, 2-nitrophenol, 2-nitroresorcinol, hydroxy-N-acetyl-oxyfluorfen, hydroxy-amino-oxyflurfen, and 2-nitrohydroquinone.

References

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

42634701 Kim-Kang, H. (1993) Metabolism of (carbon 14)-Oxyfluorfen in the Laying Hen--Analytical Phase: Identification and Quantitation of Metabolites in Eggs and Tissues: Lab Project Number: XBL 92002: RPT00111: 3107.13: Unpublished study prepared by Xenobiotic Labs Inc. 299 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):