171-4J

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

AUG 19 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **Oxyfluorfen.** Livestock Feeding Study - Meat/Milk/Poultry/Eggs Magnitude of the Residue Reregistration Case No. 2490. Chemical No. 111601. MRID #43152201 43152202 DP Barcode D200532 CBRS #13395

FROM: Steven A. Knizner, Chemist
Special Review Section I
Chemistry Branch II - Reregistration Support
Health Effects Division (7509C)

THRU: Andrew Rathman, Section Head
Special Review Section I
Chemistry Branch II - Reregistration Support
Health Effects Division (7509C)

TO: Bruce Sidwell, PM Team 53
Accelerated Reregistration Branch
Special Review and Reregistration Division (7508W)

The Oxyfluorfen Phase 4 Review (S.Funk, 3/16/91) required livestock feeding studies and analysis of representative samples from the animal metabolism studies using preferred enforcement analytical methods. In response, Rohm and Haas Company has submitted (MRIDs 443152201 and 43152202) dairy cattle and poultry feeding studies and analytical method radiolabeled validation data. These studies were reviewed by Dynamac Corp. (see Attachment), under the supervision of CBRS, and have undergone secondary review in CBRS to reflect Branch Policies.

The dairy cattle feeding study is adequate pending submission of acceptable storage stability data and pending receipt of data required in an earlier review of a goat metabolism study (S.Knizner, 6/16/93, CBRS #11526). Oxyfluorfen residues in milk and tissues did not exceed established tolerances (0.05 ppm for milk and fat, meat, and meat byproducts of cattle, goats, hogs, horses, and sheep) following oral dosing of dairy cows with oxyfluorfen at 0.278, 0.834, and 2.78 ppm (4x, 13x, and 43x, respectively, the maximum dietary burden). The available data indicate that a tolerance of 0.01 ppm (LOQ) would be appropriate for residues of oxyfluorfen *per se* in milk, fat, meat, and meat by-products of cattle, goats, hogs, horses, and sheep.

(1)

As noted above, additional data from the submitted goat metabolism study are required. No additional ruminant feeding data will be required provided the ruminant metabolism study does not identify additional residues of concern and acceptable storage stability data are provided.

The poultry feeding study is adequate pending submission of acceptable storage stability data. Except for fat, residues of oxyfluorfen *per se* were below established tolerances (0.05 ppm for eggs, meat, and meat by-products) following oral dosing of laying hens with oxyfluorfen at 0.086 ppm (2x). Residues of oxyfluorfen *per se* in fat exceeded the tolerance level of 0.05 ppm after treatment with oxyfluorfen at 0.086 ppm. The available data indicate that the following tolerances for oxyfluorfen *per se* would be appropriate for poultry commodities: 0.03 ppm for eggs, 0.01 ppm for meat and meat by-products, and 0.2 ppm for fat.

Samples from the ruminant and poultry feeding studies were stored for up to 12 months prior to analysis. Storage stability data on oxyfluorfen residues in milk, eggs, and tissues are required to support the storage conditions and intervals of these feeding studies.

Samples from the poultry and ruminant metabolism studies were analyzed by Rohm and Haas GLC Methods TR 34-93-17 and TR 34-93-72. indicate that Method TR 34-93-17 adequately recovers oxyfluorfen *per se* from milk. The data also indicate that Method TR 34-93-72 adequately recovers oxyfluorfen *per se* from fat and muscle. Analysis of egg samples from the hen metabolism study using a preferred enforcement analytical method is still required.

Based on the submitted radiolabeled validation data, Method TR 34-93-72 does **not** adequately recover oxyfluorfen residues from hen liver and its adequacy in recovering residues of concern from goat liver cannot be determined until the required additional information from the ruminant metabolism study is submitted. On the basis of the available poultry liver data, a new and/or modified analytical method will be required for analysis of liver. This method should be validated by analysis of liver samples from the poultry and goat metabolism studies.

The residue methods tested in this study represent a substantial modification of Method II in PAM, Vol. II. Therefore, if the registrant is proposing these methods as tolerance enforcement methods, an independent laboratory validation (described in PR Notice 88-5, dated 7/15/88) of Methods TR 34-93-17 and TR 34-93-72 must be submitted. Non-confidential copies of the methods must also be submitted for Agency validation.

Attachment.

cc: S.F., circ., R.F., List B File, S.Knizner, DYNAMAC
RDI: A. Rathman, 8/8/94 M.Metzger, 8/15/94 E.Zager, 8/19/94
7509C:CBRS:CM#2:305-6903:SAK:sak:oxyfluor:8/2/94

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DYNAMAC
CORPORATION
Environmental Services

Final Report

OXYFLUORFEN
Shaughnessy No. 111601
Case No. 2490
(CBRS No. 13395, DP Barcode D200532)

TASK 4
Phase 5 - Reregistration Review of Residue Chemistry Data

July 15, 1994

Contract No. 68-D4-0010

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

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

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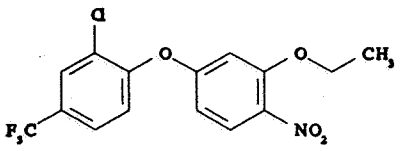
OXYFLUORFEN



Shaughnessy No. 111601; Case No. 2490

(CBRS No. 13395; DP Barcode D200532)

Task 4

PHASE 5 - REREGISTRATION REVIEW OF RESIDUE CHEMISTRY DATA

BACKGROUND

The Oxyfluorfen Phase 4 Review dated 3/91 required livestock feeding studies and analysis of representative samples from the animal metabolism studies using preferred enforcement analytical methods. In response, Rohm and Haas Company has submitted (1994; MRIDs 443152201 and 43152202) dairy cattle and poultry feeding studies and analytical method radiolabeled validation data. These data are reviewed in this document for their adequacy in fulfilling Phase 4 data requirements. The Conclusions and Recommendations stated in this document apply only to the magnitude of oxyfluorfen residues in ruminants and poultry and residue analytical methods. Other data requirements stated in the Oxyfluorfen Phase 4 Review are not addressed herein.

The qualitative nature of the residue in plants is adequately understood based on the results of tomato, onion, and peach plant metabolism studies (CBRS Nos. 12522, 13212, 12513, and 13338; DP Barcodes D194785, D199266, D194789, and D200012; 4/8/94; S. Knizner). The submitted alfalfa metabolism study is upgradeable following receipt of additional information. The nature of the residue in poultry is adequately understood (CBRS No. 11303, DP Barcode D187615, 6/10/93, S. Knizner). The adequacy of the submitted ruminant metabolism study will be determined pending the submission of additional liver data and additional information concerning storage stability (CBRS No. 11526, DP Barcode D188906, 6/16/93, S. Knizner). Based on the adequate plant and animal metabolism studies, the residue of concern is oxyfluorfen *per se*.

Adequate methodology is available for the enforcement of tolerances for oxyfluorfen residues in/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/on almonds, corn, grapes, soybeans, stone fruit, milk, and the fat, meat, and meat byproducts of cattle. Method I has undergone EPA validation. 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/on raw agricultural and processed commodities are currently expressed in terms of oxyfluorfen and its metabolites containing the diphenyl ether linkage [40 CFR §180.381 (a) and (b) 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

1. The dairy cattle feeding study is adequate pending submission of acceptable storage stability data and pending receipt of data required in an earlier review of a goat metabolism study (S.Knizner, 6/16/93, CBRS #11526). Oxyfluorfen residues in milk and tissues did not exceed established tolerances (0.05 ppm for milk and fat, meat, and meat byproducts of cattle, goats, hogs, horses, and sheep) following oral dosing of dairy cows with oxyfluorfen at 0.278, 0.834, and 2.78 ppm (4x, 13x, and 43x, respectively, the maximum dietary burden). The available data indicate that a tolerance of 0.01 ppm (LOQ) would be appropriate for residues of oxyfluorfen *per se* in milk, fat, meat, and meat by-products of cattle, goats, hogs, horses, and sheep.

   As noted above, additional information from the submitted goat metabolism study is required. No additional ruminant feeding data will be required provided the ruminant metabolism study does not identify additional residues of concern and acceptable storage stability data are provided.

2. The poultry feeding study is adequate pending submission of acceptable storage stability data. Except for fat, residues of oxyfluorfen *per se* were below established tolerances (0.05 ppm for eggs, meat, and meat by-products) following oral dosing of laying hens with oxyfluorfen at 0.086 ppm (2x). Residues of oxyfluorfen *per se* in fat exceeded the tolerance level of 0.05 ppm after treatment with oxyfluorfen at 0.086 ppm. The available data indicate that the following tolerances for oxyfluorfen *per se* would be appropriate for poultry commodities: 0.03 ppm for eggs, 0.01 ppm for meat and meat by-products, and 0.2 ppm for fat.

3. Samples from the ruminant and poultry feeding studies were stored for up to 12 months prior to analysis. Storage stability data on oxyfluorfen residues in milk, eggs, and tissues are required to support the storage conditions and intervals of these feeding studies.

4a. Samples from the poultry and ruminant metabolism studies were analyzed by Rohm and Haas GLC Methods TR 34-93-17 and TR 34-93-72. The submitted radiolabeled validation data indicate that Method TR 34-93-17 adequately recovers oxyfluorfen *per se* from milk. The data also indicate that Method TR 34-93-72 adequately recovers oxyfluorfen *per se* from fat and muscle. Analysis of egg samples from the hen metabolism study using a preferred enforcement analytical method is still required.

4b. Based on the submitted radiolabeled validation data, Method TR 34-93-72 does **not** adequately recover oxyfluorfen residues from hen liver and its adequacy in recovering residues of concern from goat liver cannot be determined until the required additional information from the ruminant metabolism study is submitted. On the basis of the available poultry liver data, a new and/or modified analytical method will be required for analysis of liver. This method should be validated by analysis of liver samples from the poultry and goat metabolism studies.

4c. The residue methods tested in this study represent a substantial modification of Method II in PAM, Vol. II. Therefore, if the registrant is proposing these methods as tolerance enforcement methods, an independent laboratory validation (described in PR Notice 88-5, dated 7/15/88) of Methods TR 34-93-17 and TR 34-93-72 must be submitted. Non-confidential copies of the methods must also be submitted for Agency validation.

DETAILED CONSIDERATIONS

Residue Analytical Methods

Rohm and Haas (1994; MRIDs 43252201 and 43252202) submitted descriptions of Methods TR 34-93-17, TR 34-93-46, and TR 34-93-72 along with the dairy cattle and poultry feeding studies.

Milk samples were analyzed for residues of oxyfluorfen and its isomers, RH-2382, RH-4672, and RH-0671 (Table 1) using Method TR 34-93-17. Milk samples are homogenized, a 10% NaCl solution is added, and residues are extracted twice with hexane/acetone (1:1, v/v). The hexane-soluble residues are combined, passed through a bed of anhydrous sodium sulfate, and evaporated to dryness. The residues are then redissolved in toluene and purified using a Florisil column eluted with toluene/methanol (8:2, v/v). Residues are evaporated to dryness, redissolved in toluene, and quantified by GLC/ECD.

Egg samples were analyzed for residues of oxyfluorfen and its isomers using Method TR 34-93-46. Egg samples are homogenized and the residues are extracted with acetonitrile (ACN), filtered, diluted with a saturated NaCl solution, partitioned into petroleum ether, and concentrated. Residues are then purified using a Florisil column eluted with 50% diethyl ether in petroleum ether. The purified residues are concentrated, redissolved in hexane and quantified by GLC/ECD.

Fat and tissue samples from the cattle and poultry feeding studies were analyzed for residues of oxyfluorfen and its isomers using Method TR 34-93-72. Fat and tissue samples are homogenized with dry ice and the dry ice is sublimated overnight in the freezer. Residues in fat are extracted with hexane and partitioned into ACN; residues in muscle, liver, and kidney

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are extracted with ACN. Residues in the ACN fractions are washed with petroleum ether and concentrated. The partially purified ACN-soluble residues are then diluted with a saturated NaCl solution, partitioned into petroleum ether (2x) and concentrated. Residues from muscle and kidney samples are further purified using a silica gel column eluted with petroleum ether/ethyl ether (6:4, v/v), and residues from fat and liver samples are purified using a Florisil column eluted with petroleum ether/ethyl ether (1:9, v/v). Residues are then evaporated to dryness, redissolved in toluene, and quantified by GLC/ECD.

The limit of quantitation (LOQ) for all analytes in all matrices is 0.01 ppm and the limit of detection (LOD) is 0.003 ppm.

Method validation data are presented in Tables 2 and 3 and concurrent method recovery data are presented in Table 4. Raw data, sample calculations, and representative chromatograms were submitted. Methods TR 34-93-17, TR 34-93-46, and TR 34-93-72 are adequate for residue data collection of oxyfluorfen and its isomers from milk, eggs, and tissue samples from the dairy cattle and poultry feeding studies. Based on the submitted radiolabeled validation data, Method TR 34-93-72 does **not** adequately recover oxyfluorfen residues from hen liver and its adequacy in recovering residues of concern from goat liver cannot be determined until the required additional information from the ruminant metabolism study is submitted. On the basis of the available poultry liver data, a new and/or modified analytical method will be required for analysis of liver. This method should be validated by analysis of liver samples from the poultry and goat metabolism studies.

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Table 1. Oxyfluorfen and its isomers.

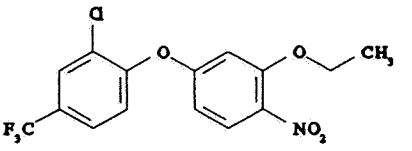
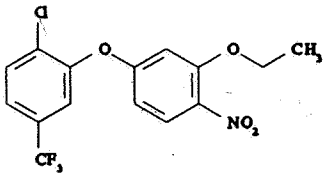
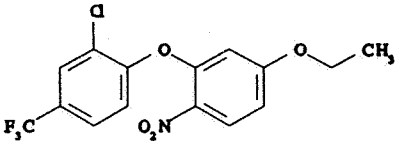
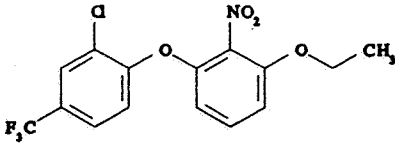
Common Name Chemical Name	Structure
Oxyfluorfen 2-chloro-1-(3-ethoxy-4-nitrophenoxy)-4-(trifluoromethyl)benzene	
RH-2382 2-chloro-1-(3-ethoxy-4-nitrophenoxy)-5-(trifluoromethyl)benzene	
RH-4672 2-chloro-1-(3-ethoxy-6-nitrophenoxy)-4-(trifluoromethyl)benzene	
RH-0671 2-chloro-1-(3-ethoxy-2-nitrophenoxy)-4-(trifluoromethyl)benzene	

Table 2. Recoveries of oxyfluorfen and its isomers from cow's milk (Method TR 34-93-17) and tissues (Method TR 34-93-72) separately fortified with each analyte.

Fortification Level (ppm)	No. of Samples	Percent Recovery			
		Oxyfluorfen	RH-0671	RH-2382	RH-4672
Milk					
0.01	6	70-114	60-140 (2)[a]	55-107 (1)	61-111 (2)
0.02	3	89-126	82-120	93-103	98-102
0.05	5-6	72-117	75-109	73-106	75-109
Muscle					
0.01	2	87.4, 86.1	71.8, 76.2	83.7. 83.7	83.5, 81.4
0.02	2	86.5, 86	73, 72.5	88.6, 88.1	83.5, 83
0.04	2	101, 104	82, 84.8	102, 106	97.3, 101
0.05	2	86.2, 96.8	72, 88.4	84.8, 95.2	83, 92.6
0.25	4	86.5-96.1	67.7-80.3 (1)	86.5-96.2	85.2-93.4
1.0	4	87.8-99.6	69.2-95.7 (1)	86.5-99.9	86.6-98.8

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Fortification Level (ppm)	No. of Samples	Percent Recovery			
		Oxyfluorfen	RH-0671	RH-2382	RH-4672
Fat					
0.01	3	108-156 (1)	101-155 (1)	109-159 (1)	103-151 (1)
0.05	3	109-140 (1)	101-131 (1)	107-136 (1)	105-138 (1)
0.2	1	113	99	107	110
0.25	2	97, 107	94.8, 103	97.2, 105	95.1, 104
1.0	2	96.6, 99.5	95, 97.6	94.8, 99.4	95.3, 98.5
Liver					
0.01	4	69.5-93.3 (1)	60-77.6 (1)	70-86.6	67.3-82.4 (1)
0.05	4	81.2-95.2	64.2-85.2 (2)	79.3-94	76.8-91
0.25	4	77.8-102	62.6-81.3 (1)	76.5-99.5	76.4-98.4
1.0	4	90.1-105	77.4-91.8	87.7-105	87.6-103
Kidney					
0.01	4	86-92.5	66.7-87.8 (1)	77.3-83.8	82.6-89.3
0.05	4	86.2-96	70.4-84.2	82.8-91.8	83-94.4
0.25	4	94.6-104	90-98.4	93.1-101	92.7-103
1.0	4	87.7-98.5	81.9-99.3	87.6-95.7	87.8-99.6

[a] Values in parentheses represent the number of samples with recoveries outside of the 70-120% range.

Table 3. Recoveries of oxyfluorfen and its isomers from poultry eggs (Method TR 34-93-46) and tissues (Method TR 34-93-72) separately fortified with each analyte.

Fortification Level (ppm)	No. of Samples	Percent Recovery			
		Oxyfluorfen	RH-0671	RH-2382	RH-4672
Eggs					
0.01	12	70.2-91.8	72.3-97.4	67-96.4 (1)[a]	70.6-89.4
0.05	12	71.8-102	76-100	48.6-93.1 (1)	63.8-96.6 (1)
1.0	11	77.8-103	75.6-104	73.4-96.8	75.6-103
5.0	6	86.8-95	88-96.8	86.4-92.2	85.4-90.6
Muscle					
0.01	4	65.4-82.9 (2)	67.3-78.4 (3)	72.5-85.9	59.9-79.9 (3)
0.05	4	77.2-84.4	70.2-78.2	76.6-84.0	74.2-80.4
0.25	4	87.0-92.7	79.9-88.0	86.4-92.6	85.3-90.5
1.0	4	79.0-86.8	74.6-79.3	64.8-86.1 (1)	81.8-84.9

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Fortification Level (ppm)	No. of Samples	Percent Recovery			
		Oxyfluorfen	RH-0671	RH-2382	RH-4672
Fat					
0.01	3	96.6-105	86.3-94.2	99.6-116	89.2-98.7
0.05	3	100-105	90.8-96.6	98.5-104	95.0-99.8
0.2	1	110	100	104	107
0.25	2	113, 106	109, 95.2	116, 104	103, 98.4
1.0	2	100, 97.9	83.7, 90.1	96.5, 95.6	91.5, 91.5
Liver					
0.01	4	76.1-92.0	69.6-87.9 (2)	66.9-85.4 (1)	72.7-89.1
0.05	4	85.0-92.0	72.2-82.7	78.0-82.5	83.0-90.4
0.1	1	101	97.9	98.3	98.9
0.25	4	89.2-96.8	76.5-92.6	87.2-93.0	86.9-94.8
1.0	4	88.7-108	86.6-102	87.7-106	87.0-105

[a] Values in parentheses represent the number of samples with recoveries outside of the 70-120% range.

Table 4. Recoveries of oxyfluorfen and its isomers from animal samples fortified and analyzed concurrently with residue samples from the cattle and poultry feeding studies (MRIDs 43142201 and 43142201).

Fortification Level (ppm)	No. of Samples	Percent Recovery			
		Oxyfluorfen	RH-0671	RH-2382	RH-4672
Milk					
0.01	19	55.9-120 (1)[a]	57.4-113 (1)	52.5-119 (2)	45.1-113 (2)
0.02	3	79.5-89	78.5-88.5	78.5-92	75-89.5
0.05	2	80.8, 82.4	82.6, 81.8	82.2, 85.2	78, 80.6
0.075	3	69.6-103 (1)	70.8-97.2	69.9-101 (1)	68.8-98.8 (1)
0.10	5	73.2-95.5	70.4-96.7	73-95.9	72.2-95.3
0.15	5	60.9-120 (1)	60.5-119 (1)	60.3-119 (1)	61.1-117 (1)
0.2	4	78.5-107	72-137 (1)	78-108	78-109
Cattle Muscle					
0.01	1	76.5	75.2	80.6	71.6
0.02	1	84.5	81.5	84.7	81.5
0.1	2	76.5, 82	75.4, 80.5	76.3, 80.2	74.1, 78.8
Cattle Liver					
0.01	2	71.8, 79.4	69.3, 73	73.4, 77.2	64.4, 64.4
0.1	2	85.4, 94.4	83.6, 91.3	84, 93.2	82.7, 91.1
Cattle Fat					
0.01	2	108, 71	109, 71.8	102, 75.8	104, 64.4
0.02	1	90	91.5	78	86.5
0.1	3	67.2-85.5 (1)	67.3-85.5 (1)	68.4-80.8 (1)	65.1-83.8 (1)

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Table 4. Continued.

Fortification Level (ppm)	No. of Samples	Percent Recovery			
		Oxyfluorfen	RH-0671	RH-2382	RH-4672
Cattle Kidney					
0.01	2	87.2, 89.4	85.4, 85.9	136, 83.5	81.1, 82.4
0.1	2	89.5, 105	85.3, 100	86.4, 102	88.6, 101
Eggs					
0.01	14	87.0-114	83.4-111	90.5-124 (1)	79.5-108
0.02	1	96.0	95.0	96.0	93.0
0.05	3	96.8-104	93.0-101	104-108	89.2-99.8
0.1	16	94.2-111	90.0-111	90.4-113	90.0-110
0.25	1	72.6	105	43.4	106
Poultry Muscle					
0.01	1	92.7	88.8	91.8	86.5
0.1	2	81.9, 92.5	78.9, 89.3	81.1, 89.6	80.2, 90.6
Poultry Fat					
0.01	1	98.2	92.5	73.9	94.7
0.1	2	110, 115	104, 104	108, 107	105, 105
Poultry Liver					
0.01	1	87.8	110	83.6	71.7
0.1	1	88.0	86.5	86.3	84.1

[a] Values in parentheses represent the number of samples with recoveries outside of the 70-120% range.

Radiolabeled Method Validation. Rohm and Haas tested analytical Methods TR 34-93-17 and TR 34-93-72 described above using milk, fat, and tissue samples from the previously submitted ruminant and poultry metabolism studies (1993; MRIDS 42634701 and 42670601). Recoveries from fortification with oxyfluorfen and its isomers of poultry control fat and tissue samples from the metabolism study and of goat fat and tissues purchased locally are presented in Table 5. Results from analysis of fortified samples indicate that Method TR 34-93-72 adequately recovers oxyfluorfen *per se* to 0.02 ppm in poultry and ruminant fat and tissues. Recoveries from fortification with oxyfluorfen and its isomers of milk controls are presented in Table 2. Results from analysis of fortified samples indicate that Method TR 34-93-17 adequately recovers residues of oxyfluorfen *per se* to 0.01 ppm in milk.

Samples bearing radioactive residues from the animal metabolism studies were analyzed using Methods TR 34-93-17 and TR 34-93-72. Comparison of the metabolism data with results from Methods TR 34-93-17 and TR 34-93-72 are summarized in Table 6. Method TR 34-93-72 adequately recovered radiolabeled oxyfluorfen from fat and muscle samples generated in the poultry metabolism study but did not adequately recover residues from the hen liver sample. Methods TR 34-93-17 and TR 34-93-72 adequately recovered oxyfluorfen *per se* from goat milk, fat, and tissues generated in the ruminant metabolism study.

The submitted radiolabeled validation data indicate that Method TR 34-93-17 is adequate for tolerance enforcement of oxyfluorfen *per se* in milk. The data also indicate that Method TR 34-93-72 adequately recovers oxyfluorfen *per se* from hen and goat fat and muscle. However, Method TR 34-93-72 does not adequately recover oxyfluorfen residues from hen liver and its adequacy in recovering residues of concern from goat liver cannot be determined until the required additional information from the ruminant metabolism study are submitted. Analysis of egg samples from the hen metabolism study using a preferred enforcement analytical method is still required.

The residue methods tested in this study represent a substantial modification of Method II in PAM, Vol. II. Therefore, if the registrant is proposing these methods as the tolerance enforcement methods, data from an independent laboratory validation (described in PR Notice 88-5, dated 7/15/88) of Methods TR 34-93-17 and TR 34-93-72 must be submitted. Nonconfidential copies of the methods must be submitted for Agency validation so their adequacy as enforcement methods can be determined.

Table 5. Recoveries from control ruminant and poultry samples fortified with oxyfluorfen and its isomers.

Fortification Level (ppm)	Recovery (%)			
	Oxyfluorfen	RH-0671	RH-2382	RH-4672
Hen Breast Muscle [a]				
0.02	85.2	92.5	45.5	93.5
0.10	86.1	85.4	73.1	95.4
Hen Liver				
0.02	63.8	74.5	71.6	85.0
0.10	87.7	77.5	89.0	102
Hen Fat				
0.02	89.2	96.9	68.1	93.5
0.10	86.4	89.8	83.5	94.5
Goat Fat [a]				
0.02	78.9	91.5	129	89.5
0.05	92.3	99.2	112	94.0
0.10	101	107	111	112
Goat Liver				
0.02	67.7	84.0	95.5	70.0
0.10	88.4	86.7	111	99.8
Goat Kidney				
0.01	69.4	87.3	156	87.1
0.02	67.7	84.0	95.5	70.0
0.10	88.4	86.7	111	99.8
Goat Muscle				
0.02	84.6	99.0	119	87.0
0.05	91.6	91.0	104	96.8
0.10	96.0	98.3	103	110

[a] Poultry fat and tissue samples from the metabolism study (MRID 42634701); Goat fat and tissue samples were purchased locally due to an unavailability of control goat fat and tissues from the metabolism study (MRID 42670601).

Table 6. Results from analysis of poultry and ruminant metabolism samples using the preferred enforcement methods compared to the data from the metabolism studies.

Matrix	Residues (ppm)					
	Metabolism Study[a]		Enforcement Method[b]			
	Oxyfluorfen-CPR	Oxyfluorfen-NPR	Oxyfluorfen	RH-0671	RH-2382	RH-4672
Hen						
Breast muscle	0.145	0.188	0.187, 0.184	<0.003, <0.003	<0.003, 0.0362	<0.003, <0.003
Thigh muscle	1.044	1.116	0.903, 0.937	<0.003, <0.003	<0.003, <0.003	<0.003, <0.003
Fat	13.78	14.83	11.2, 11.0, 10.7	<0.003, <0.003, <0.003	<0.003, <0.003, <0.003	<0.003, <0.003, <0.003
Liver	0.781	0.875	0.291, 0.233	<0.003, <0.003	<0.003, <0.003	<0.003, <0.003
Eggs	1.037	1.206	NR[3]	NR	NR	NR
Goat						
Muscle	0.022	0.020	0.022, 0.024	<0.003, <0.003	<0.003, <0.003	<0.003, <0.003
Fat	0.511	0.451	0.425, 0.454	<0.003, <0.003	<0.003, <0.003	<0.003, <0.003
Liver	--[d]	--[d]	<0.003, <0.003	<0.003, <0.003	<0.003, <0.003	<0.003, <0.003
Kidney	0.003	0.007	<0.003, <0.003	<0.003, <0.003	<0.003, <0.003	<0.003, <0.003
Milk	0.209	0.142	0.13	<0.003	<0.003	<0.003

[a] The animals in the poultry and ruminant metabolism studies were fed [^{14}C]oxyfluorfen radiolabeled in either the chlorophenyl (CPR) or nitrophenyl (NPR) ring. These data were taken from the Agency's reviews of the ruminant and poultry metabolism studies (CBRS Nos. 11303 and 11526). [b] The preferred enforcement methods used were Method TR 34-93-17 for milk and Method TR 34-93-72 for fat and tissues. The registrant did not identify which samples from the metabolism studies were tested with the enforcement methods. [c] NR-data not reported. [d] Data on liver from the ruminant metabolism study (MRID 42670601) are still required.

Storage Stability Data

The registrant stated that storage stability studies to support these animal feeding studies are currently in progress. Milk and tissue samples from the cattle feeding study were stored prior to analysis for up to 246 and 368 days, respectively. Egg and tissue samples from the poultry feeding study were stored prior to analysis for up to 187 and 312 days, respectively.

Magnitude of the Residue in Meat, Milk, Poultry, and Eggs

Cattle. A tolerance of 0.05 ppm has been established for residues of oxyfluorfen and its metabolites containing the diphenyl ether linkage in milk, meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep [40 CFR §180.381(a)].

Rohm and Haas submitted (1994; MRID 43152201) data depicting the magnitude of the residue of oxyfluorfen and its isomers in milk and tissues of dairy cows. Twelve lactating cows (four per dose group) were orally dosed with technical grade oxyfluorfen (71.7% purity) via gelatin capsules for 28 consecutive days at dietary levels of 0.278, 0.834, and 2.78 ppm, based on daily feed consumption of 18.4 kg/animal. Four control cows were placebo-dosed. The in-life portion of the feeding study was conducted by Bio-Life Associates, Ltd. Calculations for deriving the daily dose of oxyfluorfen as well as information pertaining to feed consumption, milk production, and general health of the test animals were submitted.

The maximum reasonable dietary intake of oxyfluorfen residues by dairy and beef cattle based on feed items with established tolerances are 0.065 and 0.07 ppm, respectively. Therefore, the administered doses of 0.278, 0.834, and 2.78 ppm are equivalent to approximately 4x, 13x, and 43x, respectively, the maximum dietary burden for dairy cattle; and are approximately 4x, 12x, and 40x, respectively, the maximum dietary burden for beef cattle. The calculations of the dietary burden are presented in Table 7.

The registrant's determination of the dietary burden included residues of 0.1 ppm in alfalfa. However, CBRS notes that oxyfluorfen is not currently registered for use on alfalfa and no tolerances for oxyfluorfen residues in/on alfalfa are currently established. The maximum dietary burden, including the proposed 0.1 ppm tolerance for residues in/on alfalfa, is also presented in Table 7.

Table 7. Calculation of maximum dairy and beef cattle dietary burdens for oxyfluorfen.

Feed Item	% Diet	% Dry Matter	Tolerance (ppm)	ppm in Diet
Almond hulls	15 (25) [a]	90	0.1	0.017 (0.028)
Soybean seed	20 (15)	89	0.05	0.011 (0.008)
Corn grain and meal	65 (60)	89	0.05	0.037 (0.034)
Current maximum dietary burden [b]	100			0.065 (0.070)
Alfalfa forage	70 (50)	35	0.1	0.200 (0.143)
Corn grain and meal	30 (50)	89	0.05	0.017 (0.028)
Proposed maximum dietary burden [b]	100			0.217 (0.171)

[a] Numbers used to calculate beef cattle dietary burden are in parentheses. [b] The current maximum dietary burden is based on established tolerances; whereas, the proposed maximum dietary burden includes the proposed 0.1 ppm tolerance for residues in/on alfalfa.

On test days 1, 4, 7, 10, 14, 17, 21, 24, 28, and 31, milk samples were collected in the morning and were refrigerated (7 C) prior to compositing with the PM milk samples. The composited samples were frozen (-7 to -20 C), shipped to Rohm and Haas, and then shipped to Biodevelopment Laboratories, Inc. for residue analysis. Within 24 hours of the final dose, three cows from each test group were sacrificed and muscle (pectoral), liver, kidney, and peritoneal fat samples were collected and frozen (-7 to -20 C). The remaining cow from each test group was sacrificed after three days of depuration. All tissue samples were shipped frozen, under dry ice, to Rohm and Haas, and then shipped to Centre Analytical Laboratories, Inc. for analysis. Milk and tissue samples were analyzed for residues of oxyfluorfen and its three isomers using the GLC Methods TR 34-93-17 and TR 34-93-72. The results of the dairy cattle feeding study are summarized in Table 8. All control samples bore nondetectable (<0.003 ppm) residues.

Table 8. Residues of oxyfluorfen and its isomers in milk and tissues of lactating cows dosed at 0.278 ppm (4x), 0.834 ppm (13x), and 2.78 ppm (43x) oxyfluorfen for 28 days.

Matrix	Dose Level (ppm)		
	0.278	0.834	2.78
	---------- Total Residue (ppm) [a] ----------		
Milk [b]	<0.003	<0.003	<0.003-0.009
Liver [c]	<0.003	<0.003	<0.003
Fat [c]	<0.003-0.007	0.009-0.016	0.075-0.102
Muscle [c]	<0.003	<0.003	<0.003-0.011
Kidney [c]	<0.003	<0.003	0.003-0.006

[a] Total residue is the sum of oxyfluorfen (RH-2915) and its three isomers RH-0671, RH-2382, and RH-4672. Results were not corrected for method recoveries. [b] Results represent analyses of quadruplicate milk samples collected from test days 1, 4, 7, 10, 14, 17, 21, 24, and 28. [c] Quadruplicate samples (day-28) of each tissue were analyzed.

Oxyfluorfen residues were nondetectable (<0.003 ppm) in control samples and liver samples from all dose groups, and in milk, muscle, and kidney samples from cows dosed at 4x and 13x. Residues were ≤0.01 ppm (LOQ) in milk, muscle, and kidney samples from the high dose (43x) group. The data indicate that milk residues plateaued by day-4 (0.006-0.009 ppm) as in the ruminant metabolism study. As in the poultry and ruminant metabolism studies, residues were highest in fat. Oxyfluorfen residues were detected in fat samples from each dosing level, but were <0.01 ppm in the low dose group (4x).

The dairy cattle feeding study is adequate pending submission of acceptable storage stability data. Except for fat, oxyfluorfen residues were below the established tolerances (0.05 ppm for milk, meat, and meat by-products) following oral dosing of dairy cows with oxyfluorfen at 0.278 (4x), 0.834 (13x), and 2.78 ppm (43x). Residues of oxyfluorfen in fat exceeded the established tolerance only after treatment at 43x the maximum dietary intake. Pending the submission of the required storage stability data, the available data indicate that a tolerance of 0.01 ppm (LOQ) would be appropriate for residues of oxyfluorfen in milk, fat, and ruminant tissues.

Poultry. Tolerances of 0.05 ppm have been established for residues of oxyfluorfen in eggs and the meat, fat, and meat by-products of poultry (40 CFR §180.381[a]).

Rohm and Haas submitted (1994; MRID 43152202) data depicting the magnitude of the residue of oxyfluorfen and its isomers in eggs and tissues from laying hens. Bio-Life Associates, Ltd conducted the in-life portion of the feeding study in which 30 laying hens (ten hens per dose group) were dosed daily with technical grade oxyfluorfen (71.7% purity) via capsule for 28 days at dietary levels of 0.086, 0.345, or 1.21 ppm, based on a feed consumption of 185 grams/bird. Ten additional hens served as controls. Calculations for

deriving the daily dose of oxyfluorfen as well as information pertaining to feed consumption, egg production, and general health of the test animals were submitted.

The maximum reasonable dietary intake of residues of oxyfluorfen by poultry is 0.05 ppm, based on a diet consisting of soybean seed, soybean meal, and corn grain each with an established tolerance of 0.05 ppm. Therefore, the administered doses of 0.086 ppm, 0.345 ppm, and 1.21 ppm are equivalent to approximately 2x, 7x, and 24x, respectively, the maximum dietary burden for poultry.

Eggs were collected twice daily and pooled from three to four hens within each treatment group on test days 1, 3, 7, 10, 14, 17, 21, 24, and 28. The hens were sacrificed within 24 hours of the final dose and muscle (breast and thigh), fat (abdominal and subcutaneous), and liver samples from three to four hens of each test group were collected and pooled. All samples were frozen (-18 C) and shipped on dry ice to Rohm and Haas, and were then subsequently shipped to Centre Analytical Laboratories, Inc. where they were stored frozen (-4 C) until processing and analysis. Egg and tissue samples were analyzed for oxyfluorfen and its isomers using the GLC Methods described above. The results are summarized in Table 9. All control samples bore nondetectable residues (<0.003 ppm), except for one egg control sample (day-28) that bore residues of RH-2382 (0.004 ppm), one fat control sample (0.003 ppm of RH-2382), and two liver control samples (0.004 and 0.005 ppm of RH-0671).

Oxyfluorfen residues were detected in eggs from each dose group. Residues in eggs plateaued by day-10 at 0.01-0.024 ppm in the 2x dose group, by day-21 at 0.042-0.057 ppm in the 7x dose group, and by day-24 at 0.14-0.213 ppm in the 24x dose group. To determine appropriate tolerances, residues of oxyfluorfen *per se* detected in the 2x group were used. Residues in egg, fat, and muscle samples from the 2x group consisted of oxyfluorfen *per se*; liver samples bore residues of oxyflurofen *per se*, RH-0671, and RH-2382.

The poultry feeding study is adequate pending submission of acceptable storage stability data. Except for fat, residues of oxyfluorfen *per se* were below established tolerances (0.05 ppm for eggs, meat, and meat by-products) following oral dosing of laying hens with oxyfluorfen at 0.086 ppm (2x). Residues of oxyfluorfen *per se* in fat exceeded the tolerance level of 0.05 ppm after treatment with oxyfluorfen at 0.086 ppm. The available data indicate that the following tolerances for oxyfluorfen *per se* would be appropriate for poultry commodities: 0.03 ppm for eggs, 0.01 ppm for meat and meat by-products, and 0.2 ppm for fat.

Table 9. Uncorrected residues of oxyfluorfen and its isomers in eggs and tissues of laying hens dosed at 0.086 ppm (2x), 0.345 ppm (7x), and 1.21 ppm (24x) oxyfluorfen for 28 days.

		Residues in 2x Dose Group (ppm)		
Matrix	RH-0671	RH-2382	RH-4672	Oxyfluorfen
Eggs [a]	<0.003	<0.003	<0.003	<0.003-0.024
Liver [b]	0.004-0.005	<0.003-0.012	<0.003	<0.003-0.006
Fat [b]	<0.003	<0.003	<0.003	0.084-0.163
Muscle [b]	<0.003	<0.003	<0.003	<0.003-0.004
		Residues in 7x Dose Group (ppm)		
	RH-0671	RH-2382	RH-4672	Oxyflurfen
Eggs	<0.003	<0.003	<0.003	<0.003-0.057
Liver	<0.003	<0.003	<0.003	0.018-0.025
Fat	<0.003	0.008-0.009	<0.003	0.487-0.620
Muscle	<0.003	<0.003	<0.003	0.011-0.022
		Residues in 24x Dose Group (ppm)		
	RH-0671	RH-2382	RH-4672	Oxyflurfen
Egg	<0.003	<0.003-0.213	<0.003	<0.003-0.217
Liver	0.003-0.005	<0.003	<0.003	0.049-0.066
Fat	<0.003	0.025-0.031	0.007-0.009	1.35-1.73
Muscle	<0.003	<0.003	<0.003	0.047-0.055

[a] Results represent analyses of triplicate egg samples collected on days 1, 3, 7, 10, 14, 17, 21, and 28.
[b] Triplicate samples (day-28) of each tissue were analyzed.

MASTER RECORD IDENTIFICATION NUMBERS

The citations for the MRID documents used in this review are presented below.

43152201 Zhang, Q.; Martin, D. (1994) Oxyfluorfen (Goal Herbicide) Cow Feeding Study; Magnitude of Residue in Lactating Dairy Cows: Technical Report No. 34-93-114. Unpublished study prepared by Biodevelopment Laboratories, Inc., Centre Analytical Laboratories, Inc., Bio-Life Associates, Ltd., and Enviro-Bio-Tech, Ltd. 715 p.

43152202 Zhang, Q.; Martin, D. (1994) Oxyfluorfen (Goal Herbicide) Hen Feeding Study; Magnitude of Residue in Chickens in Full Lay: Technical Report No. 34-93-115. Unpublished study prepared by Rohm and Haas Co., Centre Analytical Laboratories, Inc., Bio-Life Associates, Ltd., and Enviro-Bio-Tech, Ltd. 587 p.

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AGENCY MEMORANDA CITED IN THIS DOCUMENT

CBRS No: 11303
DP Barcode: D187615
Subject: Oxyfluorfen. Guideline 171-4(b) Nature of the Residue in Poultry.
From: S. Knizner
To: B. Sidwell
Date: 6/10/93
MRID(s): 42634701

CBRS No: 11526
DP Barcode: D188906
Subject: Oxyfluorfen. Guideline 171-4(b) Nature of the Residue in Ruminants.
From: S. Knizner
To: B. Sidwell
Date: 6/16/93
MRID(s): 42670601

CBRS Nos: 12522, 13212, 12513, and 13338
DP Barcodes: D194785, D199266, D194789, and D200012
Subject: Oxyfluorfen. Nature of the Residue in Tomatoes, Onions, Stone Fruit, and Alfalfa.
From: S. Knizner
To: B. Sidwell
Date: 4/8/94
MRID(s): 42865001, 42913201, 42873301, and 92136114