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

APR 14 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#2F4036 (CBTS #'s 10708, 10846/10914, 11054, 11055; DP Barcode #'s D183274, D184405/D184530, D185716, and D185720). Flumetsulam (DE-498) on Soybeans and Corn. Amendments dated 9/25/92, 10/8/92, 11/30/92, and 12/7/92 (MRID #'s 42489001, 42513501 and -02, 42573801 and -02, and 42580601 through -08).

FROM: Nancy Dodd, Chemist
Tolerance Petition Section II
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THROUGH: Debra Edwards, Ph.D., Chief
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4/14/93

TO: Joanne Miller, PM#23
Fungicide-Herbicide Branch
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and

Albin Kocialski, Section Head
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Chemical Coordination Branch (H7509C)

Attached is a review of Product Chemistry and Residue Chemistry for flumetsulam (DE-498; N-(2,6-difluorophenyl)-5-methyl-1,2,4-triazolo-[1,5a]-pyrimidine-2-sulfonamide). The data were submitted to support a new registration. The review was prepared by Acurex Environmental Corporation under supervision of Chemistry Branch I (CBTS). This review has undergone secondary review and revision in CBTS and reflects current Branch policies.

Data gaps listed in the enclosed report must be satisfied before permanent tolerances can be established. The remaining data gaps for soybeans and corn involve the nature of the

residue (i.e., deferral to the HED Metabolism Committee regarding which residues are of concern), analytical methods, storage stability, residue data for the raw agricultural commodities and processed commodities, and the Section F.

If you need additional input, please advise.

Attachment 1: Residue Chemistry Review
Attachment 2: Molecular Structures of Flumetsulam and Metabolites in Plants
Attachment 3: Proposed Metabolic Pathway for Flumetsulam in Soybeans
Attachment 4: Proposed Metabolic Pathway for Flumetsulam in Corn
Attachment 5: Confidential Appendix (Product Chemistry)

cc with all attachments: N. Dodd (CBTS), E. Haeberer (CBTS), PP#2F4036, PM#23, A. Kocialski (CCB), Acurex Environmental Corporation

cc with attachments 1, 2, 3, and 4: Circu, RF

RDI:E. Haeberer:04/12/93:R. Loranger:04/13/93
H7509C:CM#2:Rm804F:305:5861:N. Dodd:nd:04/14/93

FLUMETSULAM
(Chemical Code 129016)
(CBTS Nos. 10708, 10846/10914, 11054, 11055;
DP Barcodes D183274, D184405/D184530, D185716, D185720)

MRID Nos. 42489001, 42513501 and -02, 42573801 and -02, 42580601 through -08

TASK 4

PP#2F4036. DE-498 (Flumetsulam) on Soybeans and Corn. Amendments dated 9/25/92, 10/8/92, 11/30/92, and 12/7/92

March 25, 1993

Contract No. 68-DO-0142

Submitted to:

U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:

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FLUMETSULAM (Chemical Code 129016)

CBTS Nos. 10708, 10846/10914, 11054, 11055

(DP Barcodes D183274, D184405/D184530, D185716, D185720)

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Task 4

PP#2F4036. DE-498 (Flumetsulam) on Soybeans and Corn. Amendments dated 9/25/92, 10/8/92, 11/30/92, and 12/7/92

BACKGROUND

DowElanco has proposed permanent tolerances of 0.05 ppm for residues of the herbicide N-(2,6-difluorophenyl)-5-methyl-1,2,4-triazolo-[1,5a]-pyrimidine-2-sulfonamide (flumetsulam; DE-498) in or on corn fodder, forage, and grain and soybeans. Previously, the petitioner submitted data for temporary tolerances in or on soybeans (PP#1G4006) and field corn (PP#1G4006, amended by PP#2G4149). The review of the petition for permanent tolerances (N. Dodd, CBTS Nos. 10486 through 10489, 9/30/92) recommended against the proposed permanent tolerances owing to deficiencies cited in previous CBTS reviews of PP#1G4006 for soybeans (N. Dodd, CBTS No. 9845, dated 8/20/92) and corn (N. Dodd, CBTS Nos. 8400 and 8646, 3/27/92).

In response to data requirements specified for permanent tolerances the petitioner has submitted the following amendments: amendment dated 9/25/92 (CBTS No. 10708) including Section F and a revised Section B [proposed revised labeling for XRM-5019 (EPA Reg. No. 62719-EEU) and XRM-5313 (EPA Reg. No. 62719-EEE)]; amendment dated 10/8/92 (CBTS No. 10846/10914) containing soybean metabolism data (MRIDs 42513501 and -02); amendment dated 11/30/92 (CBTS No. 11054) containing corn metabolism data (MRIDs 42573801 and -02); and amendment dated 12/7/92 (CBTS No. 11055) containing product chemistry data, data on residue analytical methodology, and storage stability data (MRIDs 42580601 through -08).

No permanent tolerances for flumetsulam (DE-498) have been established. A crop destruct Experimental Use Permit (62719-EUP-13) for XRM-5019 (an end-use product containing flumetsulam) was issued by EPA on 3/8/91. CBTS has recommended for temporary tolerances for flumetsulam on soybeans at 0.05 ppm (PP#1G04006, N. Dodd, 8/20/92). CBTS has also recommended for a temporary tolerance for flumetsulam on field corn at 0.05 ppm provided a revised Section F was submitted (PP#2G04149, N. Dodd, 12/23/92). The temporary tolerances on soybeans and field corn have been established (phone conversation between N. Dodd, CBTS, and Steve Robbins, RD, on 4/13/93).

CONCLUSIONS

(Numbering follows that of the deficiencies identified in the 3/27/92 review by N. Dodd of PP#1G4006.)

PRODUCT CHEMISTRY

All deficiencies regarding product chemistry data requirements for a permanent tolerance are resolved (refer to the Confidential Appendix).

RESIDUE CHEMISTRY

Proposed Use

12a. The revised Section B, including revised labels for 62719-EEU (XRM-5019) and 62719-EEE (XRM-5313) is adequate. No additional label revisions are required.

12b. The petitioner should submit an revised Section F listing the field corn commodities as follows:

commodity	ppm
corn, field, grain	0.05
corn, field, fodder	0.05
corn, field, forage	0.05
soybeans	0.05

Nature of the Residue

Soybeans:

13b. The nature of the residue in soybeans is adequately understood. The major residues in soybean forage are parent and the metabolite N-(2,6-difluorophenyl)-5-((3-hydroxy-1-methylpropyl)amino)-1,2,4-triazole-3-sulfonamide and its conjugates. The major residues in soybean beans are parent and DFATSA (N-(2,6-difluorophenyl)-5-amino-1H-1,2,4-triazole-3-sulfonamide). The residues of concern in soybeans will be determined by the HED Metabolism Committee.

If residues other than parent are determined to be of concern in soybeans, analytical methods would be needed for those residues of concern. Independent laboratory validations and EPA laboratory validations would be needed for those methods. Extractability of the aged residues by the solvent used in the proposed enforcement method would have to be determined.

Corn:

14b. The nature of the residue in corn is adequately understood. The major residues in corn are parent, the free and conjugated 5-CH_2OH metabolite (N-(2,6-difluorophenyl)-5-hydroxymethyl-1,2,4-triazolo(1,5a)pyrimidine-2-sulfonamide), and the free and conjugated 4-OH metabolite (N-(2,6-difluoro-4-hydroxyphenyl)-5-methyl-1,2,4-triazolo(1,5a)pyrimidine-2-sulfonamide). The residues of concern in corn will be determined by the HED Metabolism Committee.

If residues other than parent are determined to be of concern in corn, analytical methods would be needed for those residues of concern. Independent laboratory validations and possibly EPA validations would be needed for those methods. Use of an extraction solvent which would extract more of the aged residues may be desired.

The metabolic pathway for flumetsulam metabolism in corn is different from that in soybeans. Therefore, if the petitioner seeks to register uses on additional species (i.e., plants in crop groups other than those containing corn and soybeans) in the future, additional metabolism studies on those new species may be required.

Animals:

15. The nature of the residue in animals is adequately defined for this proposed use provided that no detectable or very low residues are found in feed items. The residue of concern in ruminants is flumetsulam per se. The residues of concern in poultry are flumetsulam per se and the 5-hydroxy metabolite.

For uses that may result in detectable residues in feed items, additional animal metabolism data on ruminants and poultry may be required.

Analytical Methods

Plants:

16g. The requirement for an interference study is resolved. None of the 77 pesticides tested presented interference concerns with respect to Method ACR 91.6.

16i. The issues raised by ACS concerning the EPA method validation of ACR 91.6 on soybean grain and ACR 91.6.1S on corn grain and corn fodder have been satisfactorily addressed by the petitioner. Adequate enforcement methods (revised analytical methods ACR 91.6R on soybeans and ACR 91.6.S1R on field corn, both dated 4/7/93) are available for flumetsulam per se on soybeans and field corn. However, if additional residues besides parent are determined to be of concern, enforcement methods for those residues would be needed.

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Animals:

18. No analytical methods have been submitted for animal commodities. Analytical methods for animal commodities will not be required provided that no detectable or very low residues are found in feed items and no detectable residues are expected to occur in animal commodities as a result of the proposed use.

Storage Stability Data

20. The final frozen storage stability report on corn (summarized in Appendix C in MRID #424890-01) will be needed for review to support a permanent tolerance.

Residue Data

Corn:

21a. Adequate geographic representation is not provided for field corn. Additional residue data should be obtained from TX, CA, MD, and WA.

21d. References to crop oil concentrate have been deleted from the revised label for XRM-5019 on field corn dated 9/17/92.

21g. The final frozen storage stability report on corn (summarized in Appendix C in MRID #424890-01) will be needed for review to support a permanent tolerance. (Conclusion 21g is the same as Conclusion 20 above.)

Corn Processing Data:

22b. For the permanent tolerance, a processing study is needed and food additive tolerances may be needed for processed fractions of corn grain. The theoretical concentration factor from corn grain to corn oil is 28X. However, the petitioner should apply the maximum practical exaggerated foliar application rate, which would be considered to be 5X or less if phytotoxicity occurs at 5X. Even if no detectable residues were found in corn grain after postemergence treatment at 5X, the corn grain should be processed. If no detectable residues are found in the processed products, then no food additive tolerance would be required. Processed commodities from field corn are starch, crude oil and refined oil from wet milling; and grits, flour, meal, crude oil and refined oil from dry milling. Grain dust residue data are not required for this use on corn since applications are preplant incorporated, preemergence, and early postemergence. "The grain dust data are needed only in those cases in which detectable, primarily surface residues are found on the grain." (Overview of Residue Chemistry Guidelines", R.D. Schmitt, 10/10/89).

Soybeans:

23f. References to crop oil concentrates and non-ionic surfactants have been deleted from the revised label for XRM-5019 on soybeans dated 9/17/92.

23i. The deficiency regarding storage stability of soybean residue samples has been resolved. Flumetsulam is stable in or on soybeans stored for 30 months at ≤-15 °C. CBTS will accept storage stability data for 30 months to support residue data on soybeans stored up to 32 1/2 months. Adequate storage stability data on soybeans are available for purposes of the permanent tolerance.

Meat, Milk, Poultry, and Eggs

26. For the purposes of the permanent tolerances on soybeans and corn, CBTS must reserve its conclusion regarding the need for animal feeding studies until questions regarding the nature of the residue, analytical methods, storage stability, and residue data are resolved. If no detectable residues are found in feed items, no animal feeding studies and no tolerances for animal commodities will be required.

RECOMMENDATIONS

CBTS recommends against the proposed tolerances for the use of flumetsulam on corn and soybeans for reasons given in Conclusions 12b, 15, 16i, 18, 20, 21a, 21g, 22b, and 26 above. As noted in Conclusions 13b and 14b, the residues of concern in plants will be determined by the HED Metabolism Committee.

The metabolic pathway for flumetsulam metabolism in corn is different from that in soybeans. Therefore, if the petitioner seeks to register uses on additional species (i.e., plants in crop groups other than those containing corn and soybeans) in the future, additional metabolism studies on those new species may be required.

CBTS recommends that a copy of this entire review be sent to the petitioner.

DETAILED CONSIDERATIONS

Outstanding CBTS data deficiencies from N. Dodd reviews of PP#1G04006 dated 3/27/92, 3/10/92, 8/20/92, and 12/9/92; and PP#2G04149 dated 12/23/92 are listed below, followed by the petitioner's responses and CBTS's discussions/conclusions.

PRODUCT CHEMISTRY

Refer to the Confidential Appendix (Attachment 5).

RESIDUE CHEMISTRY

Proposed Use

CBTS's Deficiency #12a

The petitioner should submit a revised Section B/label with the following additional information: the maximum number of applications, the maximum pounds ai/A/yr for postemergence uses, the maximum pounds ai/A/yr for all uses combined (preplant incorporated, preemergence, and postemergence), the minimum interval between applications, the minimum interval between the last application and harvest (preharvest interval), and the application rate also expressed in terms of pounds of active ingredient per acre (lbs ai/A).

Petitioner's Response to Deficiency #12a

The petitioner submitted a revised Section B including EPA Reg. No. 62719-EEU (XRM-5019), printed 9/17/92, bearing uses for soybeans and field corn; and 62719-EEE (XRM-5313), printed 7/24/92, for use on soybeans only.

CBTS's Discussion re: Deficiency #12a

In the review of PP#1G04006 for temporary tolerances (N. Dodd, 3/27/92) revisions to the proposed labelling were required. A revised Section B (label for XRM-5019; EPA Reg. No. 62719-EEU dated 7/24/92) was reviewed for the proposed temporary tolerance on soybeans (N. Dodd; 8/20/92) and found adequate to resolve the previous deficiencies. A revised Section B (label for XRM-5019) dated 9/17/92 was reviewed for the proposed temporary tolerance on field corn (N. Dodd, 12/23/92) and found adequate to resolve the previous deficiencies. With the current amendment, the petitioner submitted a revised Section B including EPA Reg. No. 62719-EEU (XRM-5019), printed 9/17/92, bearing uses for soybeans and field corn; and 62719-EEE (XRM-5313), printed 7/24/92, for use on soybeans only. The revisions for soybeans and field corn on 62719-EEU (XRM-5019) are the same as those discussed in the 8/20/92 and 12/23/92 reviews. The revised XRM-5313 label dated 7/24/92, for use on soybeans only, was reviewed in PP#1G04006 (N. Dodd, 8/20/92). The XRM-5313 label dated 7/24/92 bears the following revisions under "General Use Precautions:

> "Do not exceed a total application rate of 2.25 pints per acre (0.07 lb ai Broadstrike + 0.96 lb ai Treflan) in a single crop year.
>
> Preharvest Interval: An interval of at least 85 days is required between application of Broadstrike + Treflan and soybean harvest."

CBTS's Conclusion #12a

The revised Section B, including revised labels for 62719-EEU (XRM-5019) and 62719-EEE (XRM-5313) is adequate. No additional label revisions are required.

CBTS's Deficiency #12b

The petitioner should submit an revised Section F listing the field corn commodities as follows:

commodity	ppm
corn, field, grain	0.05
corn, field, fodder	0.05
corn, field, forage	0.05
soybeans	0.05

Petitioner's Response to Deficiency #12b

This amendment includes a Section F dated 9/25/92. This is identical to the Section F reviewed for PP#2G04149 for a temporary tolerance for flumetsulam on corn (N. Dodd; 12/23/92). That review requested a revised Section F as stated above, which was submitted for the temporary tolerance.

CBTS's Conclusion #12b

Deficiency #12b as stated above remains outstanding.

Nature of the Residue

Soybeans:

CBTS's Deficiency #13b

For a permanent tolerance, additional soybean metabolism data will be required. In the submitted studies on soybeans, residues were not adequately characterized in any plant part. Residue components accounting for $\geq$10% of the residue after exhaustive extraction should be identified, preferably by two techniques (eg. TLC, HPLC, MS). Such components may include components A2 and B1 which were present in the 12-day and 28-day forage samples from ^{14}C-phenyl-labelled DE-498 treated soybeans. Analysis should also include determination of the presence of 2,6-difluoroaniline (possibly present as a product of hydrolysis of the sulfonamide linkage of ^{14}C-phenyl-labelled DE-498) and 5-methyl-(1,2,4)triazolo-(1,5a)pyrimidine-2-sulfonic acid [possibly present as a product of the

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hydrolysis of the sulfonamide linkage of (5-^{14}C) pyridine-labelled DE-498] at all sampling times by use of authentic standards.

Extractability of the residue into solvents used in the proposed analytical enforcement method should be determined. Most of the radioactivity should be extracted, or exhaustive attempts using acid, base, and/or enzymes should be made to do so. The petitioner should use the radiolabelled samples to determine what percentage of the total recovered radioactivity is determined by the proposed enforcement methodology.

The identity of the residues in all plant parts of the raw agricultural commodity which could be used for food or feed (seed, forage, and hay) should be determined. Samples should be either analyzed or frozen immediately after harvest.

The additional work needed for soybeans treated with phenyl labelled DE-498 may be done using reserve forage samples (12 and 28 day samples) provided they have been kept frozen. For the pyridine labelled DE-498, CBTS recommends a new study be conducted at the maximum rate that does not result in significant phytotoxicity. The green plant should be analyzed at intervals similar to those in the previous phenyl labelled study.

Petitioner's Response to Deficiency #13b

DowElanco has submitted amendments to PP#4F4036 dated 10/8/92 containing soybean metabolism data.

Soybeans. Reanalysis of 1990 Postemergence-treatment Samples. In response to requirements for data to support a permanent tolerance, DowElanco (1992; MRID 42513501) submitted data from the reanalysis of stored soybean and forage samples reserved from the earlier study (1990; MRID 41931713). In the original study, [phenyl-^{14}C]flumetsulam (specific activity 5.9 μCi/μmole; radiochemical purity 99%) was applied to soybeans 42 days after planting at a rate equivalent to 0.015 lb ai/A (5x). Forage was sampled 0, 12, and 28 days posttreatment, and beans were harvested 120 days after treatment. After the initial study, the samples were stored frozen for approximately 1 year prior to the new analyses.

Total Radioactive Residues (TRR)

Total radioactive residues in 28-day posttreatment forage (pre-bloom stage) and beans (at maturity) were determined by combustion and subsequent liquid scintillation spectrometry (LSS). The results of three to five combustion replicates of each tissue indicated that the TRRs after storage were the same as the initial determinations: 0.021 ppm in beans and 1.7 ppm in pre-bloom forage.

Extraction

The distributions of radioactivity in soluble and insoluble ^{14}C-residues from 28-day forage and beans (120 days) are shown in Table 1. The table also indicates which fractions were subjected to further analysis for residue characterization and identification.

Forage. Residues in forage were extracted sequentially with hexane, chloroform, acetone, acetonitrile (ACN), and water. The aqueous fraction (46% of the TRR) was concentrated and analyzed by HPLC yielding four fractions that were further analyzed as described below under "Characterization of Residues." The other soluble fractions each contained 0.1-2% of the TRR and were not analyzed further.

The insoluble residues, accounting for 38% of the TRR, were hydrolyzed with 1 N HCl for 1 hour at 100 °C. The resulting hydrolysate (13% of the TRR) was partitioned into 50% aqueous acetone and radioassayed. The remaining solids were treated with $KMnO_4$ yielding a cellulose fraction (2% of the TRR) and a filtrate (12%). None of these fractions derived from the initial insoluble fraction underwent additional analyses.

Beans. Residues in soybeans were extracted sequentially with hexane, acetone, 90% acetone, and water. The hexane fraction was not analyzed further. The aqueous fraction (24% of TRR; 0.005 ppm) was treated with 10% TCA, resulting in a protein precipitate (5% of the TRR) and the remaining aqueous residues (19% of the TRR); neither fraction was analyzed further.

The acetone/aqueous acetone fractions were combined (50% of the TRR), the acetone was removed and the residues were concentrated and partitioned with hexane. The aqueous fraction (49% of the TRR) was analyzed by HPLC and subjected to additional analyses for residue characterization as explained in the following section.

The insoluble residues (22% of the TRR) were treated with $KMnO_4$ yielding a cellulose fraction (7% of the TRR) and a filtrate. In addition, the insoluble fraction was extracted with 0.05 M sodium phosphate containing 5% NaCl at pH 7.5 and then hydrolyzed in 1 N HCl at 100 °C for 2-3 hours. The hydrolyzed residues were treated with 10% TCA to precipitate protein (3% of the TRR), leaving 7% of the TRR in solution. The acid hydrolyzed residues were partitioned into 50% acetone (6% of TRR). The remaining insoluble residues accounted for 9% of the TRR.

Table 1. Distribution of ^{14}C-residues in soybean samples: reanalysis of 1-year stored samples originally described in MRID 41931713. Current data are from MRID 42513501.

Substrate	Fraction	% TRR	ppm	Characterization/Identification
Forage (1.7 ppm)	Hexane	0.1	0.002	None
	$CHCl_3$	1.0	0.02	None
	Acetone	2.0	0.04	None
	Acetonitrile	1.0	0.02	None
	Aqueous	46.0	0.78	HPLC analysis; acid & enzyme hydrolysis of isolated residues and subsequent HPLC identification of 38% of TRR
	Solids	38.0	0.63	N/A
	Acid hydrolysate	13.0	0.23	No further analysis
	Pellet	Not reported	Not reported	$KMNO_4$ oxidation yielded 0.04 ppm cellulose; 0.2 ppm (12%) remained in solution
Beans (0.021 ppm)	Hexane	4.0	0.001	None
	Acetone/90% acetone	50.0	0.011	HPLC analysis identified 37% of TRR as A2, B1, C(Cl), D2 present after acid hydrolysis. C1 confirmed as DFATSA by GC/MS.
	Aqueous	24.0	0.005	TCA precipitated 0.001 ppm (protein); 0.004 ppm remained in solution
	Solids	22.0	0.005	$KMNO_4$ oxidation yielded 0.001 ppm (cellulose)
	Buffer/salt	10.0	0.002	TCA precipitated 0.001 ppm (protein); 0.001 ppm remained in solution
	Acid hydrolysate	6.0	0.001	No further analysis
	Pellet	9.0	0.002	No further analysis
	Hexane	1.0	<0.001	None
	Aqueous	49.0	0.01	HPLC analysis identified 37% of the TRR as A2, B1, Cl(DFATSA), D2

Characterization of Residues

Forage. Reverse phase HPLC analysis of the concentrated aqueous extract (46% of the TRR; 0.78 ppm) detected components A2, B1, and fraction GHD-3129-48e. No 2,6-difluoroaniline (DFA) was detected. The isolated components were characterized by mild and stringent acid hydrolysis and β-glucosidase digestion and subsequent HPLC analysis.

The fraction containing metabolite A2 received the following treatments: (i) 10.5 hours in 1 N HCl at 37 °C; (ii) 5 hours in 1 N HCl at 98 °C followed by 19 hours in 1 N HCl at 98 °C; and (iii) 3 hours in β-glucosidase in sodium acetate buffer at pH 5 and 30 °C. HPLC analysis indicated that metabolite A2 was intact following the hot water and mild acid treatments, whereas the harsher acid treatments resulted in the conversion or complete conversion of A2 to metabolite D2 and other minor components. A2 remained intact following enzyme hydrolysis.

In fraction B1, metabolite B1 was converted to metabolite D2 after either a 24-hour incubation in 100 °C acid or a 3.5-hour β-glucosidase hydrolysis at 37 °C. The identity of D2 as the de-glucosylated moiety was confirmed by further purification, acetylation, and analysis by GC/MS.

HPLC analysis detected metabolites C2, C3, D2, F, and parent in fraction GHD-3129-48e. C2 and C3 were partially converted to B1 following 4.5 hours in 37 °C acid and were completely converted to D2 after further acid hydrolysis. Enzyme hydrolysis partially converted C2 and C3 to metabolite D2. D2 remained unchanged following separate treatments with mild acid, NaCNBH3, Lucas reagent, iodoform, and enzyme. Metabolite F was described by the petitioner as multi-component and as a strongly retained material.

An accounting of the residue characterization results is presented in Table 2. The most abundant residues were B1 (16%) and A2 (9%). Flumetsulam and isolated metabolites accounted for 38% of the TRR in forage. Acid extractable residues from the initial extracted solids comprised 13% of the TRR and, although these were not analyzed in the present study, the original work showed parent (1% of the TRR), B metabolites (6%), and D metabolites (1%) in this fraction. The cellulose fraction accounted for 2% of the TRR. Approximately 12% of the TRR was in the filtrate after cellulose precipitation and an additional 11% was left unaccounted for in the analysis of the insolubles. Some of this unidentified 23% of the TRR could have been associated with lignin, as in 1990 analysis where 19% of the TRR was in the lignin fraction.

Table 2. Metabolite identification from reanalysis of [phenyl-^{14}C]flumetsulam postemergence soybean forage.

Metabolite/fraction[a]	%TRR	ppm
A1	3	0.06
A2	9	0.15
B1	16	0.26
C[b]	4	0.07
D2	4	0.06
DE-498	1	0.02
F[c]	5	0.08
Identified residues	38	0.7
Acid hydrolysate of solids	13	0.22
Cellulose	2	0.04
Unanalyzed extractables	16[d]	0.27
Unaccounted		
from solids	11	0.19
from aqueous	5	0.09
Total	85	1.51

[a]See Attachment 1 for chemical names and molecular structures of flumetsulam and metabolites.

[b]Component C includes metabolites C1, C2, and C3.

[c]Component F is strongly retained material and may be multi-component.

[d]Includes 4% from organo-solubles and 12% in aqueous filtrate following $KMnO_4$ oxidation to isolate cellulose.

Beans. The combined acetone and 90% acetone extracts (50% of the TRR) were analyzed for residue characterization. The acetone was evaporated and the residues were cleaned up by partitioning with hexane. A portion of the aqueous fraction (49% of the TRR) was analyzed by HPLC and components A2 (4%; 0.0008 ppm), B1 (5%; 0.001 ppm), and C1 (26%; 0.005 ppm) were isolated. Following acid hydrolysis, metabolite D2 (2% of TRR) was observed as a component of the aqueous extract. The identity of metabolite C1 was confirmed by partitioning C1 into EtOAc, derivatizing with diazomethane, and identifying methyl-C1 by GC/MS. An accounting of residue characterization in beans is presented in Table 5. Identified or characterized components accounted for 52% of the TRR. The 48% of the TRR remaining unidentified amounted to only 0.01 ppm.

In summary, metabolites A2, B1, C2, C3, and D2 from forage were characterized by acid and enzyme hydrolysis and HPLC analysis. Metabolite B1 was characterized as a glucoside of D2, metabolites A2, C2, and C3 as conjugates of D2, and D2 as hydroxybutyl DFATSA. In bean, C was the major component composed primarily of C1, which was identified as DFATSA by HPLC and GC/MS. 2,6-DFA was not detected.

Soybeans. Preplant-incorporated Application of [Phenyl-^{14}C] and [5-Pyrimidine-^{14}C]Flumetsulam]. In response to requirements for data to support a permanent tolerance, DowElanco (1992; MRID 42513502) submitted data reflecting pre-plant incorporated application of [^{14}C]flumetsulam. [Phenyl-^{14}C]flumetsulam (39,400 dpm/μg; radiochemical purity 98.8%) was applied to four plots at a nominal rate of 0.25 lb ai/A (3.5x the maximum preplant rate); subsequent soil analysis reported for one plot indicated that the actual rate was 0.33 lb ai/A (5x). [5-Pyrimidine-^{14}C]flumetsulam (39,300 dpm/μg; radiochemical purity 97.9%) was applied to one plot at 0.24 lb ai/A (3.4x), confirmed by soil analysis. Two hours after application, the plots were seeded. Plants were sampled at 22, 42, and 63 days after application. The remaining plants were harvested 139 days posttreatment and beans were separated from the desiccated pods and vines (trash). Samples were stored frozen at -20 to -10 °C within 2 hours of collection. The frozen plant samples were processed by blending with dry ice or liquid nitrogen 1-12 days later and combined into a single sample for each radioisotope/posttreatment interval, and returned to frozen storage.

Total Radioactive Residues (TRR)

Three aliquots of each composited sample were radioassayed by combustion/LSS 3-20 days after harvest. The limit of detection of the radioassay was 0.001 ppm. The averaged results are presented in Table 3.

Table 3. Total radioactive residues in soybean samples following pre-plant incorporated application of [^{14}C]flumetsulam at 3.5x.

Matrix	TRR (ppm)	
	[phenyl ^{14}C]	[5-pyrimidine ^{14}C]
22-Day thinnings	3.1	2.2
42-Day forage	1.4	0.73
63 Day bloom forage	0.15	0.047
139 day beans	0.043	0.020
139 day trash	0.32	0.20

Extraction

The results of residue extraction are presented in Table 4 along with brief descriptions of further analysis of fractions. ^{14}C-Residues in plant thinnings and forage samples were extracted into 50% acetone (56-78% of the TRR), concentrated and analyzed by HPLC. Unextracted residues in the 63-day forage were treated with 1 N HCl at 100 °C for 3 hours and the hydrolyzed residues (5-8% of the TRR) were extracted into 50% acetone. The remaining solids were analyzed for lignin (6-14% of the TRR) and cellulose (1-3% of the TRR).

Residues in 139-day soybeans were extracted sequentially with hexane, acetone, 90% acetone, and water. The aqueous fraction was treated with TCA, resulting in a protein precipitate (3-8% of the TRR) and the remaining aqueous residues; neither fraction was analyzed further. The acetone/aqueous acetone fractions were combined (22-43% of the TRR), the acetone was removed and the residues were concentrated and partitioned with hexane. The resulting aqueous fractions (17-34% of the TRR) were analyzed by HPLC and were subjected to additional analyses for residue characterization as explained in the following section. The insoluble residues (30-49% of the TRR) were treated with $KMnO_4$ yielding a cellulose fraction (10-22% of the TRR) and a filtrate. In addition, the insoluble residues were extracted with 0.05 M sodium phosphate containing 5% NaCl at pH 7.5 and then hydrolyzed in 1 N HCl at 100 °C for 2-3 hours. The hydrolyzed residues in buffer were treated with 10% TCA to precipitate protein. The acid hydrolyzed residues were partitioned into 50% acetone (9-16%). The remaining insoluble residues accounted for 14-23% of the TRR.

Table 4. Distribution of ^{14}C-residues in soybean matrices from plants treated with [phenyl-^{14}C] or [5-pyrimidine-^{14}C]flumetsulam.

Substrate	Fraction	%TRR[a]	ppm[a]	Characterization/Identification
Thinnings (22 days)	50% acetone	83 86	1.8 2.7	N/A
	Concentrated	73 76	1.6 2.4	HPLC; A2, B1/B2, C1/C2/C3, D, F and parent
	Solids	13 15	0.28 0.48	No further analysis
Forage (42 days)	50% acetone	72 79	0.52 1.1	N/A
	Concentrated	71 77	0.52 1.1	HPLC; A1, A2, B1/B2, C1/C2/C3, D2, F and parent
	Solids	28 21	0.21 0.30	No further analysis
Forage (63 days)	50% acetone	56 78	0.026 0.12	N/A
	Concentrated	55 71	0.026 0.11	HPLC: A1, A2, B, C, D, F peaks
	Solids	35 19	0.016 0.030	Acid hydrolyzed
	Acid soluble	8 5	0.004 0.008	No further analysis
	Solids			Analyzed for natural cellular constituents
	Lignin	14 6	0.006 0.010	
	Cellulose	3 1	0.001 0.001	
Beans (139 days)	Hexane	3 1	0.001 0.001	No further analysis
	Acetone/90% acetone	22 43	0.004 0.018	HPLC;A1, A2, B1/B2, C1, D2, F, and parent
	Aqueous	18 21	0.004 0.009	TCA to precipitate protein
	Protein	8 3	0.002 0.001	Lowry reagent confirmed
	Aqueous	10 16	0.002 0.007	No further analysis
	Solids	49 30	0.010 0.013	$KMnO_4$ to isolate cellulose
	Cellulose	22 10	0.005 0.004	Hydrolyzed, confirmed by MS
	Buffer			TCA to precipitate protein
	Protein	6 2	0.001 0.001	Lowry reagent confirmed
	Aqueous	3 4	0.001 0.002	No further analysis
	Acid	16 9	0.004 0.005	No further analysis
	Solids	23 14	0.006 0.006	No further analysis

[a]Values not shaded are from [5-pyrimidine-^{14}C]-treated plants and shaded values are from [phenyl-^{14}C]-treated plants.

Characterization of Residues

The soluble residues from the 22-day plants, 63-day forage, and mature beans were fractionated by reverse phase HPLC. The isolated components were further purified and characterized by acid and enzyme hydrolysis and subsequent HPLC analysis using the same schemes described above for reanalysis of stored samples.

Components A1 and A2 were characterized as conjugates after yielding metabolite D2 (hydroxybutyl DFATSA) following acid hydrolysis. B1 was shown to be a glucose conjugate of D2, by enzyme and acid hydrolysis. Component C was found to consist of a mixture of C1, C2, and C3 components. Purified component C1 co-eluted with radioactive DFATSA. In addition, methylated C1 and methyl-DFATSA gave comparable GC/MS spectra. In beans, component C was the major component and this peak co-chromatographed with the purified C1 from thinnings, which had been identified and confirmed to be DFATSA. After enzyme and acid hydrolysis, C2 and C3 from plant and forage extracts were characterized as conjugates of B1. Component D was separated into two components, D1 and D2. The structure of D1 was elucidated by UV analysis to show reduction of the pyrimidine ring; by acid hydrolysis to parent, indicating an intact sulfonamide bond, the presence of the pyrimidine ring, and the methyl group on the number 5 carbon; by HPLC elution patterns indicating a hydroxylated ring; and by chemical test results showing the hydroxyl at either the number 6 or 7 carbon. The structure of D2 was determined similarly, based on UV absorbance, hydrolysis patterns, HPLC elution, mass spectral analysis, and chemical tests.

A1, A2, B1, and D1 were detected in both phenyl- and pyrimidine-labeled tissues, indicating that both the phenyl and pyrimidine moieties are present in these metabolites and that the sulfonamide linkage remained intact. 2,6-DFA was not detected by HPLC analyses.

In beans, cellulose and protein fractions together accounted for up to 36% of the TRR. The TCA precipitated solids from beans was accounted for as protein using a modified Lowry procedure. To confirm the identity of the cellulose, the permanganate-insoluble residues were hydrolyzed using cellulase and the hydrolysate was acetylated and analyzed by GC/MS. The spectrum was similar to that of standard glucose penta-acetate.

Table 5. Summary of residue characterization/identification in soybean raw agricultural commodities; %TRR in isolated metabolites[a] and natural constituents.

Treatment/ Substrate	A1	A2	B	C	D2	F	Flumetsulam	Cellulose	Lignin	Protein
Postemergence (reanalysis)										
[phenyl ^{14}C]										
28-day forage (bloom)	3(1)[b]	9(17)	16(14)	4(3)	4(4)	5	1(2)	2	(19)	--
120-day bean	--	4	5	26	2	--	--	7	--	8
Pre-plant incorporated										
22-day thinnings										
[phenyl ^{14}C]	--	14	32	5	18	4	2	--	--	--
[5-^{14}C]	--	14	25	2	20	1	1	--	--	--
42-day forage										
[phenyl ^{14}C]	10	5	35	4	8	5	3	--	--	--
[5-^{14}C]	9	11	23	8	9	5	1	--	--	--
63-day forage (bloom)										
[phenyl ^{14}C]	1	38	9	7	5	2	2	1	6	--
[5-^{14}C]	5	12	12	3	10	3	2	3	14	--
139-day bean										
[phenyl ^{14}C]	4	2	2	17	3	2	1	10	--	5
[5-^{14}C]	4	5	3	--	1	--	0	22	--	14

[a]The names and molecular structures of flumetsulam and its metabolites are presented in Attachment 2. [b]The values presented for the postemergence study are from the reanalysis of samples stored for 1 year. The values in parentheses are from the first analyses reported in the original study (MRID 41931713).

Summary of Flumetsulam Metabolism in Soybeans

The available metabolism data on soybeans are summarized in Table 5. DFATSA (metabolite C1) was the predominant residue in beans. In forage, hydroxybutyl-DFATSA (D2) and the conjugated metabolites A2 and B1 were the most abundant. Flumetsulam was present at low levels (<3%). DFATSA accounted for 17% of the TRR in beans from the new preplant incorporated study and 26% of the TRR in samples stored for 1 year. The available data adequately address the deficiencies cited previously for soybean metabolism. The stability of the sulfonamide bond and the absence of 2,6-DFA as a metabolite have been demonstrated. The structures of metabolites D1, D2, and C1 have been elucidated and B1, A1, A2, C2, and C3 have been characterized as conjugates. The data from postemergence and pre-plant (using two radioisotopes) support the petitioner's proposed metabolic pathway for soybeans (depicted in Attachment 3).

CBTS's Conclusion #13b

The nature of the residue in soybeans is adequately understood. The major residues in soybean forage are parent and the metabolite N-(2,6-difluorophenyl)-5-((3-hydroxy-1-methylpropyl)amino)-1,2,4-triazole-3-sulfonamide and its conjugates. The major residues in soybean beans are parent and DFATSA (N-(2,6-difluorophenyl)-5-amino-1H-1,2,4-triazole-3-sulfonamide). The residues of concern in soybeans will be determined by the HED Metabolism Committee.

If residues other than parent are determined to be of concern in soybeans, analytical methods would be needed for those residues of concern. Independent laboratory validations and EPA laboratory validations would be needed for those methods. Extractability of the aged residues by the solvent used in the proposed enforcement method would have to be determined.

Corn:

CBTS's Deficiency #14b

For a permanent tolerance, additional metabolism data will be required. In the submitted studies on corn, residues were not adequately characterized in any plant part. Residue components accounting for $\geq$10% of the residue after exhaustive extraction should be identified, preferably by two techniques (eg. TLC, HPLC, MS). Analysis should also include determination of the presence of 2,6-difluoroaniline (possibly present as a product of hydrolysis of the sulfonamide linkage of ^{14}C-phenyl-labelled DE-498) and 5-methyl-(1,2,4)triazolo-(1,5a)pyrimidine-2-sulfonic acid [possibly present as a product of the hydrolysis of the sulfonamide linkage of (5-^{14}C) pyridine-labelled DE-498] at all sampling times by use of authentic standards.

Extractability of the residue into solvents used in the proposed analytical enforcement method should be determined. Most of the radioactivity should be extracted, or exhaustive attempts using acid, base, and/or enzymes should be made to do so. The petitioner should use the radiolabelled samples to determine what percentage of the total recovered radioactivity is determined by the proposed enforcement methodology.

The identity of the residues in all plant parts of the raw agricultural commodity which could be used for food or feed (grain, forage, silage, and fodder) should be determined. Concerning the (5-^{14}C)pyridine-labelled DE-498 corn study, CBTS further recommends that a new study be conducted using a higher rate (ie. the maximum rate not resulting in significant phytotoxicity) and examining plant parts at intervals similar to those used in the ^{14}C-phenyl-labelled DE-498 study. Samples should be either analyzed or frozen immediately after harvest. The additional work (eg. looking for the presence of 2,6-difluoroaniline) needed for corn treated with phenyl labelled DE-498 may be done using reserve samples provided they have been kept frozen.

Petitioner's Response to Deficiency #14b

DowElanco has submitted amendments to PP#4F4036 dated 11/30/92 containing corn metabolism data. A summary of the corn metabolism data was also provided with the amendment dated 9/25/92 (MRID 42489001).

[Phenyl-^{14}C] and [2-Pyrimidine-^{14}C]Flumetsulam Metabolism in Corn Forage. DowElanco submitted data (1992; MRID 42573802) from two studies reflecting simulated postemergence foliar application of [^{14}C]flumetsulam. [Phenyl-^{14}C]flumetsulam (specific activity 5.1 μCi/μmol; radiochemical purity 99%) and [2-pyrimidine-^{14}C]flumetsulam (specific activity 6.1 μCi/μmol; radiochemical purity 99%) were, respectively, pipetted onto the upper surfaces of greenhouse-grown corn plants in the five- to six-leaf stage. The applications were equivalent to 0.196 lb ai/A (3.3x the maximum postemergence rate of 0.06 lb ai/A). Forage samples were collected 0, 1, 3, 6, 10, and 14 days posttreatment and rinsed with methanol, and the methanol rinses were radioassayed by LSS. The percentage of applied radioactivity recovered in the methanol rinses ranged from 100% in the 0-day samples to approximately 80% in the 10- and 14-day samples. Total radioactive residues (TRR) were not determined by combustion/LSS prior to extraction. The TRRs listed in Table 6 are the sum of extractable and unextractable residues.

Extraction/Characterization of Residues

The procedures for extracting and characterizing residues from corn forage are summarized in Table 6. ^{14}C-Residues were extracted from 3- and 14-day posttreatment samples with acetonitrile (ACN):water (1:1, v/v) and the extracts and solids were radioassayed. The extracts of 14-day samples were concentrated and partitioned with methylene chloride, and the organic and aqueous extracts were analyzed by HPLC. The distribution of the two radioisotopes was very similar.

HPLC of the organic extracts resolved three peaks that were the same in both [phenyl-^{14}C] and [2-pyrimidine-^{14}C] labeled samples. There was one quantitative difference, however, in the peak designated M-3, which accounted for 5.6% of the TRR (0.022 ppm) in the phenyl-labeled sample and 12% of the TRR (0.048 ppm) in the 2-labeled sample. These components did not cochromatograph with DFA and were not further characterized.

Residues in aqueous fractions were separated into four fractions by solid-phase extraction (SPE) through C18 Sep-Pak eluted successively with water, 20% ACN, 50% ACN, and ACN, each containing 0.5% acetic acid. The 100% water and ACN eluants each accounted for $\leq$3% of the TRR and were not further analyzed. Residues in the 20% and 50% ACN fractions were further separated by HPLC. The 20% ACN fractions contained (i) Component 2, which was separated by TLC into DFATSA and a component which yielded the 4-hydroxy metabolite following β-glucosidase digestion; (ii) Component 5, which TLC analysis indicated consists principally of the 5-CH_2OH metabolite; and (iii) at least five minor components that were not identified. The 50% ACN fraction was resolved by HPLC into flumetsulam and a second component which was further separated into five minor components.

The analyses of extracts and isolated components from [phenyl-^{14}C] and [2-pyrimidine-^{14}C] treated 14-day forage are summarized in Table 6. The percentages of the TRR in identified compounds and in characterized but unidentified components are summarized in Table 7. Results from both radioisotopes were very similar. Flumetsulam and identified metabolites comprised 38-45.2% of the TRR. With the exception of the organosoluble MC-3 (12% TRR) component from the 2-^{14}C forage sample, none of the unidentified soluble components accounted for >6.4% (0.025 ppm). Insoluble residues accounted for 12% of the TRR (0.048 ppm) from the phenyl-^{14}C forage sample and 2.9% of the TRR (0.012 ppm) from the 2-pyrimidine-^{14}C forage sample.

Table 6. Distribution of ^{14}C-residues in early forage of corn plants following postemergence foliar treatment with [^{14}C]flumetsulam.

Substrate	Fraction	% TRR	ppm	Characterization/Identification
3-day forage [phenyl-^{14}C] (0.73 ppm)	ACN/H_2O Insoluble	96.1 3.9	0.70 0.028	Not further analyzed
3-day forage [2-^{14}C] (0.6 ppm)	ACN/H_2O Insoluble	94.8 5.2	0.57 0.031	Not further analyzed
14-day forage [phenyl-^{14}C] (0.39 ppm)	ACN/H_2O	88.3	0.34	Partitioned with methylene chloride
	Organic	8.6	0.034	HPLC: three peaks each at 0.1-5.6%
	Aqueous	79.0	0.31	SepPak C18 separation; HPLC of fractions
	20% ACN eluant	56	0.22	HPLC yielded Components 2 and 5, analyzed by TLC
	Component 2	11	0.043	TLC: 2b identified as DFATSA (02.2%); 2a yields 4-OH (8%) after ß-glucosidase digestion
	Component 5	26	0.099	TLC: 5b identified as 5-OH methyl (24%); 5a not identified (2.1%)
	50% ACN eluant	22	0.088	HPLC yielded parent (11%) and five minor components each at 1.5-3.6%
	Insoluble residues	12	0.048	Not further analyzed
14-day forage [2-^{14}C] (0.41 ppm)	ACN/H_2O	96.9	0.40	Partitioned with methylene chloride
	Organic	15.0	0.062	HPLC: one peak at 12% (0.048 ppm), two minor peaks; none identified
	Aqueous	82.0	0.34	SepPak C18 separation; HPLC of fractions
	20% ACN eluant	57.0	0.23	HPLC yielded Components 2 and 5, analyzed by TLC
	Component 2	9.4	0.039	TLC: 2b identified as DFATSA (2.3%); 2a yields 4-OH (6.7%) after ß-glucosidase digestion
	Component 5	22.0	0.089	TLC: 5b identified as 5-OH methyl (18%); 5a not identified (3.3%)
	50% ACN eluant	22.0	0.092	HPLC yielded parent (11%) and five minor components each at 1.4-3.2%
	Insoluble residues	2.9	0.012	Not further analyzed

Table 7. Identified metabolites and isolated components in postemergence-treated corn forage (14 days posttreatment).

Metabolite/Component	Phenyl-^{14}C-isotope		2-^{14}C-isotope	
	%TRR	ppm	%TRR	ppm
Identified Compounds				
Flumetsulam	11.0	0.042	11.0	0.043
DFATSA	2.2	0.009	2.3	0.009
4-OH	8.0	0.031	6.7	0.027
5-CH_2OH	24.0	0.093	18.0	0.075
	45.2	0.175	38.0	0.154
Organic unidentified				
MC-1	0.1	<0.001	0.2	<0.001
MC-2	2.9	0.011	2.8	0.012
MC-3	5.6	0.022	12.0	0.048
	8.6	0.034	15.0	0.061
Aqueous Unidentified Components	26.3[a]	0.102	26.9[b]	0.111
Unextracted	12.0	0.048	2.9	0.012
Total	92.1	0.359	82.8	0.338

[a]Ten components each accounting for ≤6.4% of the TRR (0.025 ppm). [b]Ten components each accounting for ≤5.7% of the TRR (0.023 ppm).

Reanalysis of [Phenyl-^{14}C]Flumetsulam Postemergence-treated Corn. DowElanco submitted supplemental data (1992; MRID 42573801) to their original corn metabolism study (1990; MRID 41931715), which was reviewed for PP#1G04006 (N. Dodd; CBTS Nos. 8400 and 8646; 3/27/92). In brief, corn plants at the V5 to V6 stage were sprayed with [^{14}C]flumetsulam at 0.18 lb ai/A (3x the maximum proposed postemergence rate). TRRs were 21.8 ppm in 0-day plants, 0.38 ppm in 14-day forage, 0.02 ppm in silage-stage forage, 0.04 ppm in fodder, and <0.005 ppm (nondetectable) in grain and cob samples. Residues in forage and fodder were extracted with ACN:water (1:1) and analyses were attempted with HPLC. The parent compound accounted for 97-98% of the TRR in 0-day plants, but was not found in analyses of older forage or fodder samples. Only one component was tentatively identified in 14-day forage, the 5-CH_2OH metabolite (6.8% TRR).

In the current submission (1992; MRID 42573801), samples of 14-day forage, silage-stage forage (81-day), and mature fodder (131-day) were reanalyzed after approximately 2 years in frozen storage (≤10 °C). Levels of TRRs determined by combustion/LSS were 0.38, 0.021, and 0.047 ppm, respectively. ^{14}C-Residues were extracted from these three matrices

with ACN:water (1:1) and the extracts were analyzed by HPLC for comparison with the original results; the old and new metabolite profiles were qualitatively similar.

Extraction/Characterization of Residues

For the current analyses, the ACN was removed from the ACN:water extract and the residues were partitioned with methylene chloride. The aqueous residues were further separated by SPE on SepPak C18, eluted successively with water, 20% ACN, 50% ACN, and ACN, each containing 0.5% acetic acid. The water, 50% ACN, and ACN eluant fractions each accounted for ≤9.3% of the TRR and were not further analyzed. The 20% ACN fractions were subjected to further analysis.

Residues in the 20% ACN eluant fraction (73% TRR) from 14-day forage were separated by TLC into "Component G," which co-chromatographed with the 5-CH_2OH metabolite (18% TRR), and a second fraction that remained at the TLC origin (55% TRR). Digestion of the TLC origin material with ß-glucosidase and subsequent HPLC and TLC analyses isolated the 4-OH metabolite (45% TRR) and several minor components that totaled 9.8% of the TRR.

Residues in the 20% ACN eluant fraction (60% TRR) from silage-stage forage were hydrolyzed with 1 N HCl prior to HPLC and TLC analyses. HPLC analysis revealed an unidentified component (H-1; 19% TRR) and a component (H-2; 15% TRR) that co-chromatographed with the 4-OH metabolite. The identity of the 4-OH metabolite was confirmed by TLC.

Residues in the 20% ACN eluant fraction (34% TRR) from mature fodder were also hydrolyzed with 1 N HCl prior to HPLC and TLC analyses. HPLC analysis revealed an unidentified component (H-3; 10% TRR) and a component (H-4; 8.8% TRR) that co-chromatographed with the 4-OH metabolite. The identity of the 4-OH metabolite was confirmed by TLC.

Aliquots of insoluble fractions from silage-stage forage (34% TRR) and mature fodder (43% TRR) were further analyzed by (i) acid hydrolysis (1N HCl), (ii) hydrolysis in hot concentrated (72%) sulfuric acid to isolate a lignin fraction, (iii) $KMnO_4$ oxidation to isolate a cellulose fraction, and (iv) dimethylsulfoxide (DMSO) extraction to isolate starch.

The analyses of extracts and isolated components from [phenyl-^{14}C] treated forage and fodder are summarized in Table 8. The percentages of the TRR in identified compounds and in characterized but unidentified components are summarized in Table 9.

Table 8. Distribution of ^{14}C-residues in corn forage and fodder: reanalysis of samples originally described in MRID 41931715 after 2 years of frozen storage.

Substrate	Fraction	% TRR	ppm	Characterization/Identification
Forage 14-day (0.38 ppm)	ACN/H_2O	81.8	0.31	Analyzed by HPLC. Partitioned with methylene chloride
	Organic	3.6	0.014	
	Aqueous	78	0.30	SepPak C18 separation
	Aqueous eluant	3.5	0.013	Not further analyzed
	20% ACN eluant	73	0.28	TLC
	Component G	18	0.07	HPLC: co-chromatographed with 5-CH_2OH metabolite (18%)
	TLC origin	55	0.21	ß-glucosidase: yielded an aglycone co-chromatographing with 4-OH metabolite (45%), confirmed by TLC. Minor components totalling 9.8%.
	50% ACN eluant	2	<0.01	Not further analyzed
	Insoluble residues	11	0.043	Not further analyzed
Silage-stage forage 81-day (0.021 ppm)	ACN/H2O	76	0.016	Analyzed by HPLC. Partitioned with methylene chloride
	Organic	3.3	<0.001	
	Aqueous	73	0.015	SepPak C18 separation
	Aqueous eluant	6.4	0.001	Not further analyzed
	20% ACN eluant	60	0.012	1N HCl hydrolysis, HPLC. Components H-1 and H-2. Minor peaks totalling 26% (0.005 ppm).
	Component H-1	19	0.004	Unidentified; not further analyzed
	Component H-2	15	0.003	HPLC: co-chromatographed with 4-OH metabolite (15%, 0.003 ppm); confirmed by TLC
	50% ACN eluant	7	0.001	Not further analyzed
	Insoluble	34	0.007	Acid hydrolyzed and analyzed for natural cell constituents
	Acid soluble (1N HCl)	16	0.003	Not further analyzed
	Lignin fraction	14	0.003	Insoluble in 72% H_2SO_4
	Cellulose fraction	2.9	0.001	Residue remaining after $KMnO_4$ oxidation
	Starch fraction	1.3	<0.001	Extracted in DMSO, and precipitated by ethanol

Substrate	Fraction	% TRR	ppm	Characterization/Identification
Mature Fodder 131-day (0.047 ppm)	ACN/H2O	48	0.023	Concentrated and partitioned with methylene chloride
	Organic	2.2	0.001	
	Aqueous	46	0.022	SepPak C18 separation; HPLC of fractions
	Aqueous eluant	9.3	0.004	Not further analyzed
	20% ACN eluant	34	0.016	1N HCl hydrolysis, HPLC. Components H-3 and H-4. Minor peaks totalling 15% (0.007 ppm).
	Component H-3	10	0.005	Not further analyzed
	Component H-4	8.8	0.004	HPLC: Co-chromatographed with 4-OH metabolite; confirmed by TLC
	50% ACN eluant	2.4	0.001	Not further analyzed
	Insoluble residues	43	0.020	Acid hydrolyzed and analyzed for natural cell constituents
	Acid soluble (1N HCl)	17	0.008	Not further analyzed
	Lignin fraction	22	0.011	Insoluble in 72% H_2SO_4
	Cellulose fraction	1.6	0.001	Residue remaining after $KMnO_4$ oxidation

Table 9. Summary of metabolite identification in [^{14}C-phenyl]flumetsulam-treated corn forage and fodder; reanalysis of samples originally described in MRID 41931715 after 2 years of frozen storage. Current data from MRID 42573801.

Matrix	Metabolite/component	%	(ppm)
14-Day Forage (0.38 ppm)	Identified components		
	4-OH conjugate	45.0	0.17
	5-CH_2OH	18.0	0.07
	Unidentified components		
	Organic	3.6	0.014
	Aqueous[a]	15.3	0.06
	Insoluble	11.0	0.043
	Total	92.6	0.36
Silage-Stage Forage (0.021 ppm)	Identified components		
	4-OH conjugate	15.0	0.003
	Characterized components		
	Lignin	16.0	0.003
	Cellulose	2.9	0.001
	Starch	1.3	<0.001
	Unidentified components		
	Organic	3.3	0.001
	Aqueous[a]	58.4	0.011
	Acid soluble	16.0	0.003
	Total	112.9	0.024
Mature Fodder (0.047)	Identified component		
	4-OH conjugate	8.8	0.004
	Characterized components		
	Lignin	22.0	0.011
	Cellulose	1.6	0.001
	Unidentified components		
	Organic	2.2	0.001
	Aqueous[a]	36.7	0.017
	Acid soluble	17.0	0.008
	Total	88.3	0.041

[a]Includes aqueous, 50% ACN, and ACN eluant fractions from SPE that were not analyzed and unknown components detected following acid or enzyme digestion of residues in the 20% ACN eluant from SPE.

Extractability of the ^{14}C residues from corn silage and fodder with the extraction solvent used in the proposed enforcement method (90% acetone/10% 0.1 N HCl) was less than that obtained using acetonitrile/water (1:1) as shown in the following table:

crop	total ^{14}C(ppm)	Percent Extracted	
		acetonitrile/water (1:)	acetone/1 N HCl (9:1)
14-day forage	0.28	82	56
silage-stage forage	0.021	70	58
fodder	0.047	48	32

Summary of flumetsulam metabolism in corn: These data adequately address the deficiencies noted in previous corn metabolism reviews. The data indicate that the sulfonamide linkage of the parent molecule was not cleaved. If any 2,6-DFA did occur, it would be expected to be found in an organic fraction, which contained low percentages of the residue ($\leq$3.6% TRR). Both studies support the petitioner's proposed metabolic pathway (see Attachment 4) wherein flumetsulam is hydroxylated either at the methyl side group of the pyrimidine ring producing the 5-CH_2OH metabolite or at the 4-position of the benzene ring. The 4-hydroxy metabolite is conjugated with glucose. Flumetsulam accounted for 11% of the total radioactive residue (TRR) in 14-day posttreatment forage analyzed from the new postemergence treatment study; the most prevalent residue was the 5-hydroxymethyl metabolite at 24% of the TRR. In early forage samples from an earlier study the 5-hydroxymethyl metabolite accounted for 18% of the TRR, whereas 45% was comprised of the glucose conjugate of the 4-hydroxy metabolite. The 4-hydroxy metabolite accounted for 15 and 8.8% of the TRR in silage-stage forage and mature fodder, respectively. Approximately 20% of the TRR in these older samples was characterized as lignin and cellulose.

Extractability of the ^{14}C residues from corn silage and fodder with the extraction solvent used in the proposed enforcement method (90% acetone/10% 0.1 N HCl) was less than that obtained using acetonitrile/water (1:1).

The nature of the residue in corn grain has not been determined because no radioactivity (<0.005 ppm) was found in corn grain after postemergence treatment at a 3X rate.

The metabolic pathway for flumetsulam metabolism in corn is different from that in soybeans. Therefore, if the petitioner seeks to register uses on additional species (i.e., plants in crop groups other than those containing corn and soybeans) in the future, additional metabolism studies on those new species may be required.

CBTS's Conclusion #14b

The nature of the residue in corn is adequately understood. The major residues in corn are parent, the free and conjugated 5-CH_2OH metabolite (N-(2,6-difluorophenyl)-5-hydroxymethyl-1,2,4-triazolo(1,5a)pyrimidine-2-sulfonamide), and the free and conjugated 4-OH metabolite (N-(2,6-difluoro-4-hydroxyphenyl)-5-methyl-1,2,4-triazolo(1,5a)pyrimidine-2-sulfonamide). The residues of concern in corn will be determined by the HED Metabolism Committee.

If residues other than parent are determined to be of concern in corn, analytical methods would be needed for those residues of concern. Independent laboratory validations and EPA validations would be needed for those methods. Use of an extraction solvent which would extract more of the aged residues may be desired.

The metabolic pathway for flumetsulam metabolism in corn is different from that in soybeans. Therefore, if the petitioner seeks to register uses on additional species (i.e., plants in crop groups other than those containing corn and soybeans) in the future, additional metabolism studies on those new species may be required.

Animals:

CBTS's Deficiency #15

The nature of the residue in animals is adequately defined for this proposed use provided that no detectable or very low residues are found in feed items. The residue of concern in ruminants is flumetsulam per se. The residues of concern in poultry are flumetsulam per se and the 5-hydroxy metabolite.

For uses that may result in detectable residues in feed items, additional animal metabolism data on ruminants and poultry may be required.

Petitioner's Response to Deficiency #15

None.

CBTS's Conclusion #15

Deficiency #15 as stated above remains outstanding.

Analytical Methods

Plants:

CBTS's Deficiency #16g

An interference study should be conducted to determine if other pesticides registered on corn and soybeans would interfere with the method. This specificity study is needed for enforcement purposes.

Petitioner's Response to Deficiency #16g

DowElanco submitted data from an interference/specificity study (1992; MRID 42580607) required for enforcement purposes, as well as method (ACR 91.6) modifications along with storage stability data on soybeans (1992; MRID 42580608). Method ACR 91.6 was described in detail in a previous Agency review (N. Dodd, CB Nos. 8400 and 8646, 3/27/92).

Seventy-seven pesticides were analyzed by gas chromatography with mass selective detection. The petitioner submitted mass chromatograms from the 77 pesticides that indicated that interference with the flumetsulam peak of interest is not likely under the method (ACR 91.6) conditions. Of these 77 pesticides 71 are listed in Table 10.

Table 10. Pesticides for which mass chromatograms were submitted indicating that interference with the flumetsulam peak of interest is not likely under the method (ACR 91.6) (Continued on next page)

Alachlor	Diazinon	Pentachlorophenol
Aldicarb	Dicamba	Phorate
Aldrin	Dichlobenil	Phosalone
Aspon	1,4-Dichlorobenzene	Picloram Methyl Ester
Atrazine	Dichlorovos	Prometryne
Azinphos Methyl	Dieldrin	Prometon
Benfluralin	Dimethoate	Propanil
Bentazon	Disulfoton	Propazine
Benzene Hexachloride (3 isomers)	Diuron	Prophos
β-Benzene Hexachloride	Endrin	Propoxur
Bromoxynil	Endosulfan (2 isomers)	Rotenone
Chlordane (2 isomers)	Ethion	Simazine
Chlorimuron Ethyl	Fenthion	Strobane
Chloropicrin	Fensulfothion	2,4,5-T Methyl Ester
Chlorpropham	Glyphosate	2,4,5-TP Methy Ester
Chlorthal	Heptachlor	Tebuthiuron

Coumaphos	Malathion	Tetraphenfos
Cyanazine	Methomyl	Tralomethrin
2,4-D Methyl Ester	Methoxyclor	S,S,S-Tributylphosphorotrithioate
p,p'-DDD (2 isomers)	Methyl Parathion	Trifluralin
p,p'-DDE	Metolachlor	Toxaphene
S-Ethyl Dipropylthiocarbamate	Metribuzin	
p,p'-DDT	Mevinphos	
cis-Deltamethrin	Oxydemeton-Methyl	
trans-Deltamethrin	Pendimethalin	

The other chemicals tested were DowElanco chemicals under development and are not shown here.

The petitioner stated that modifications to method ACR 91.6 were employed to allow for shorter analysis time, and to enable the use of automated sample preparation equipment. The modifications involved substitution of the SPE cleanup with liquid/liquid partition into diethyl ether, and substitution of methyl derivatization with methyl iodide to methylation with diazomethane. Method recoveries determined concurrently with storage stability analyses (Table 11) indicate adequate recovery (77-106%) of flumetsulam from fortified (1.0-1.3 ppm) soybean samples using the modified method.

CBTS's Conclusion #16g

Deficiency #16g is resolved by submission of the interference study. None of the 77 pesticides tested presented interference concerns with respect to Method ACR 91.6.

CBTS's Deficiency #16i

EPA's Analytical Chemistry Laboratory (ACS, ACB, BEAD) reported the results of their method trial of ACR 91.6 on soybean grain and ACR 91.6.1S on corn grain and corn fodder (PP#2F4036, Everett Greer, Jr., 3/19/93). CBTS cannot approve the enforcement methods for flumetsulam on soybeans and field corn until issues raised by ACS in the 3/19/93 memo are addressed (PP#2F4036, N. Dodd, 3/29/93). More specifically, ACS's comments #1, 2, 3, 4, and 8 in Attachment 1 should be addressed by the petitioner. Revised analytical methods should be submitted which incorporate ACS's comments #1, 2, 3, and 4. Concerning comment #8, the petitioner should assure that RTP has an uncontaminated deuterated DE-498 standard.

Petitioner's Response to Deficiency #16i

The petitioner submitted a letter dated 4/8/93 with a response dated 4/7/93 in which ACS's comments were addressed. Revised analytical methods ACR 91.6R and ACR 91.6.S1R, both dated 4/7/93, were also submitted.

ACS's comments are repeated below, followed by the petitioner's responses and CBTS's discussions/conclusions:

ACS's Comment #1

"The method uses a deuterated internal standard and the response ratio between the analyte standard and the internal standard (m/z 134/145) is taken for quantitation. Analytical standards are derivatized along with each set of samples. During the course of the method validation it was noted that this ratio was consistently close to 3, but occasionally the ratio turned out to be approximately 2 or less. Standards that gave low response ratios would give high sample recoveries and therefore were not used. Another aliquot of the standard solution was derivatized and the sample set was reinjected into the GC/MS in order to obtain more accurate values. Changing the amount of derivatizing reagent from 10 microliters as stated in the method to 5 and 20 microliters did not seem to have an effect on the analytical standard response. The derivatized internal standard was prepared in sufficient quantity at the beginning of the validation and aliquots of this same solution were used throughout the analysis. An analyst should be aware of any changes in the m/z 134/145 response ratio so that corrections can be made in order to achieve reliable results."

Petitioner's Response to Comment #1

"On 4/5/93, the author of the Analytical Methods, Mr. Edward Olberding, contacted Mr. Everett Greer of the Analytical Chemistry Section to clarify the above point. In this discussion, Mr. Greer indicated that the intent of the above comment was not to require a formal response, but rather to document his observations during the TMV. Mr. Greer attributed the above observation to variation in instrument performance, although another possibility suggested by Mr. Olberding was that some variation may be due to the instrument parameters used to integrate the chromatographic peak. Both scientists concluded, however, that the chemistry of the derivatization was not in question. As a result, no changes in the methods are warranted."

CBTS's Conclusion re. Comment #1

Comment #1 is resolved, based on the above discussion.

ACS's Comment #2

"The method states that an elution profile should be obtained for both the C_{18} and alumina SPE columns, but no specific instructions are given for running these calibrations."

Petitioner's Response to Comment #2

Parts 15 c and d of the analytical methods have been revised to include instructions for obtaining elution profiles.

CBTS's Conclusion re. Comment #2

Comment #2 is resolved by submission of the revised analytical methods.

ACS's Comment #3

"The method uses a recovery correction factor for calculating residue concentrations. This practice is precluded in a tolerance enforcement procedure."

Petitioner's Response to Comment #3

Sections 12 of the analytical methods have been revised by addition of the following statements:

> "For the analysis of soybean (corn) samples whose results will be used for tolerance enforcement, the DE-498 concentrations as determined in Section 11 are reported without correction. For those analyses that require correction for method recovery, the following procedure is used: ....."

CBTS's Conclusion re. Comment #3

Comment #3 is resolved by submission of the revised analytical methods.

ACS's Comment #4

"The Supelco vacuum manifold used at ACL-Beltsville to elute the solid phase extraction columns was found to be a source of interference. A GC/MS peak eluting at the same retention time as the analyte for m/z 134 was detected each time the manifold was used. The plastic fittings between the SFC cartridge and the collection tubes were found to be the cause of this contamination. A B&J manifold equipped with Teflon fittings throughout was used to eliminate this problem. This was not a specific fault of the method, but we suggest that a note be included to use only Teflon or other inert fittings for manifold equipment."

Petitioner's Response to Comment #4

Sections 15a of the analytical methods have been revised by addition of the following statements:

> "During one method validation trial, an SPE vacuum manifold manufactured by Supelco was found to be a source of chromatographic interference. The cause of this contamination was determined to be the plastic fittings that were part of the assembly. For this reason, all vacuum manifold fittings that are exposed to solvents or sample solutions should be constructed of poly(tetrafluoroethylene) or other inert material."

CBTS's Conclusion re. Comment #4

Comment #4 is resolved by submission of the revised analytical methods.

ACS's Comment #8

"The standard used for this TMV was supplied to ACL by the RTP repository. ACL derivatized an In-House deuterated DE-498 standard as per method because the deuterated standard provided by RTP appeared to have been contaminated. The commodities were supplied by the petitioner."

Petitioner's Response to Comment #8

"In 1992, approximately ten grams of the deuterated methyl DE-498 internal standard were prepared, purified, and characterized. On June 12, 1992, two grams of this standard (Notebook Number A355-31/Lot Number TSN100089) were sent to Mr. Terry Bundy at Research Triangle Park.

The DowElanco report (GH-C 2895) describing the preparation, purification, and characterization of the above standard is attached as Appendix C. This standard was determined to be 97% pure by capillary gas chromatography and high performance liquid chromatography. Because of the finding that the deuterated methyl DE-498 received by ACL may potentially have been contaminated, this same lot was recently re-analyzed (4/7/93) by capillary GC/MS to determine the presence of contaminants. From the GC/MS data shown in Appendix D, Lot Number TSN100089 does not appear to contain any contaminants. DowElanco concludes, therefore, that the material sent to the RTP repository is pure and that no further action is necessary."

CBTS's Conclusion re. Comment #8

Comment #8 is resolved since a recent reanalysis (4/7/93) of the same batch which was sent to RTP indicates that the internal standard is not contaminated.

CBTS's Conclusion #16i

The issues raised by ACS concerning the EPA method validation of ACR 91.6 on soybean grain and ACR 91.6.1S on corn grain and corn fodder have been satisfactorily addressed by the petitioner. Adequate enforcement methods (revised analytical methods ACR 91.6R on soybeans and ACR 91.6.S1R on field corn, both dated 4/7/93) are available for flumetsulam per se on soybeans and field corn. However, if additional residues besides parent are determined to be of concern, enforcement methods for those residues would be needed.

Animals:

CBTS's Deficiency #18

No analytical methods have been submitted for animal commodities. Analytical methods for animal commodities will not be required provided that no detectable or very low residues are found in feed items and no detectable residues are expected to occur in animal commodities as a result of the proposed use.

Petitioner's Response to Deficiency #18

The petitioner anticipates that analytical methods for animal commodities will not be required since DE-498 probably meets the above criteria.

CBTS's Conclusion #18

Deficiency #18 as stated above remains outstanding.

Storage Stability

CBTS's Deficiency #20

The final frozen storage stability report on corn (summarized in Appendix C in MRID #424890-01) will be needed for review to support a permanent tolerance.

Petitioner's Response to Deficiency #20

None.

CBTS's Conclusion #20

Deficiency #20 as stated above remains outstanding.

Residue Data

Corn:

Deficiency #21a

Adequate geographic representation is not provided for field corn. Additional residue data should be obtained from TX, CA, MD, and WA.

Petitioner's Response to Deficiency #21a

Magnitude of residue trials are being conducted in 1992 in the above four states. The protocol being used for the conduct of these studies is in Appendix D.

CBTS's Conclusion #21a

Deficiency #21a remains outstanding. Adequate geographic representation is not provided for field corn. Additional residue data should be obtained from TX, CA, MD, and WA.

CBTS's Deficiency #21d

References on the label to crop oil concentrate should be deleted or additional residue data should be submitted reflecting use of the crop oil concentrate.

Petitioner's Response to Deficiency #21d

The label has been revised to delete the use of a crop oil concentrate in the spray.

CBTS's Conclusion #21d

Deficiency #21d is resolved. References to crop oil concentrate have been deleted from the revised label for XRM-5019 on field corn dated 9/17/92.

CBTS's Deficiency #21g

The final frozen storage stability report on corn (summarized in Appendix C in MRID #424890-01) will be needed for review to support a permanent tolerance.

Petitioner's Response to Deficiency #21g

None.

CBTS's Conclusion #21g

Deficiency #21g as stated above remains outstanding. (This deficiency is the same as Deficiency #20.)

Corn Processing Data:

Deficiency #22b

For the permanent tolerance, a processing study is needed and food additive tolerances may be needed for processed fractions of corn grain. The theoretical concentration factor from corn grain to corn oil is 28X. However, the petitioner should apply the maximum practical exaggerated foliar application rate, which would be considered to be 5X or less if phytotoxicity occurs at 5X. Even if no detectable residues were found in corn grain after postemergence treatment at 5X, the corn grain should be processed. If no detectable residues are found in the processed products, then no food additive tolerance would be required. Processed commodities from field corn are starch, crude oil and refined oil from wet milling; and grits, flour, meal, crude oil and refined oil from dry milling. Grain dust residue data are not required for this use on corn since applications are preplant incorporated, preemergence, and early postemergence. "The grain dust data are needed only in those cases in which detectable, primarily surface residues are found on the grain." (Overview of Residue Chemistry Guidelines", R.D. Schmitt; 10/10/89).

Petitioner's Response to Deficiency #22b

Magnitude of residue trials are being conducted in 1992 in CA, MD, TX, and WA. The protocol used for the conduct of these studies is in Appendix D (MRID #424890-01). Grain samples from these studies will be processed, and the necessary processed commodities will be analyzed for DE-498. Following analysis of the samples, a final formatted report will be issued and submitted.

CBTS's Conclusion #22b

Deficiency #22b as stated above remains outstanding.

Soybeans:

CBTS's Deficiency #23f

References on the label to crop oil concentrates and non-ionic surfactants should be deleted or additional residue data should be submitted reflecting use of a crop oil concentrate and a non-ionic surfactant.

Petitioner's Response to Deficiency #23f

The label has been revised to delete the use of crop oil concentrates and non-ionic surfactants in the spray.

CBTS's Conclusion #23f

Deficiency #23f is resolved. References to crop oil concentrates and non-ionic surfactants have been deleted from the revised label for XRM-5019 on soybeans dated 9/17/92.

CBTS's Deficiency #23i

The final amended storage stability report on soybeans will be reviewed to determine adequacy of storage stability data to support a permanent tolerance.

Petitioner's Response to Deficiency #23i

DowElanco submitted supplemental 30-month (908 days) storage stability data on soybeans (1992; MRID 42580608) including method descriptions, example calculations, and representative chromatograms that are reviewed here for purposes of the permanent tolerance. The petitioner stated that the final report will contain 5-year stability data. Untreated samples of soybeans were fortified at 1 ppm with flumetsulam, and were stored at ≤-15 °C for up to 30 months.

Stability samples (day-1 through -187) were analyzed using the GC/MSD method ACR 91.6, which was described in detail in the Agency review of 3/27/92. The petitioner stated that the day-411 and -908 determinations were made using a modification to GC/MSD method ACR 91.6 that is discussed above. The results are presented in Table 11 below, along with concurrent method recoveries.

These data indicate that residues of flumetsulam are stable in frozen (≤-15 °C) soybeans for up to 30 months.

Table 11. Percent recovery from soybean samples fortified with flumetsulam and stored frozen for up to 30 months.

Storage Interval; Days	Fortification Level (ppm)	Concurrent Method Recoveries	Flumetsulam Recoveries[a]
0	1.0	88, 83	104, 106
64	1.0	101, 104	100, 105, 104
124	1.0	89, 77	94, 113
187	1.0	92, 91	100, 98
411[b]	1.3, 1.0	102, 106	83, 101, 96
908	1.0	101, 103	93, 98, 99

[a]Corrected for % recovery from method spikes for each storage interval. [b]Fortification level for concurrent method recovery was 1.3 ppm, and 1.0 ppm for storage sample.

CBTS's Conclusion #23i

Deficiency #23i regarding storage stability of soybean residue samples has been resolved. Flumetsulam is stable in or on soybeans stored for 30 months at ≤-15 °C. CBTS will accept storage stability data for 30 months to support residue data on soybeans stored up to 32 1/2 months. Adequate storage stability data on soybeans are available for purposes of the permanent tolerance.

Meat, Milk, Poultry, and Eggs

CBTS's Deficiency #26

For the purposes of the permanent tolerances on soybeans and corn, CBTS must reserve its conclusion regarding the need for animal feeding studies until questions regarding the nature of the residue, analytical methods, storage stability, and residue data are resolved. If no detectable residues are found in feed items, no animal feeding studies and no tolerances for animal commodities will be required.

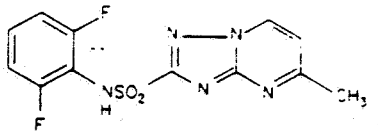
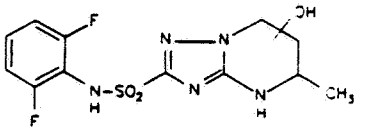
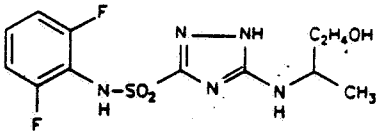
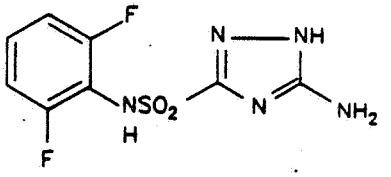
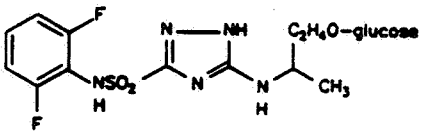
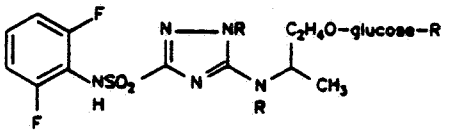
Petitioner's Response to Deficiency #26

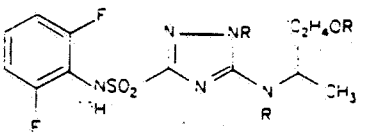
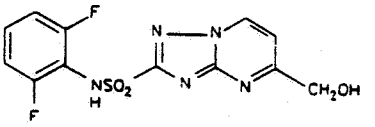
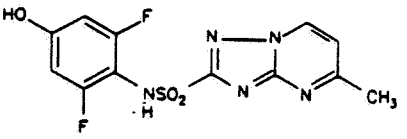
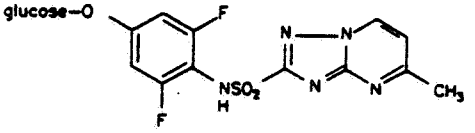
None.

CBTS's Conclusion #26

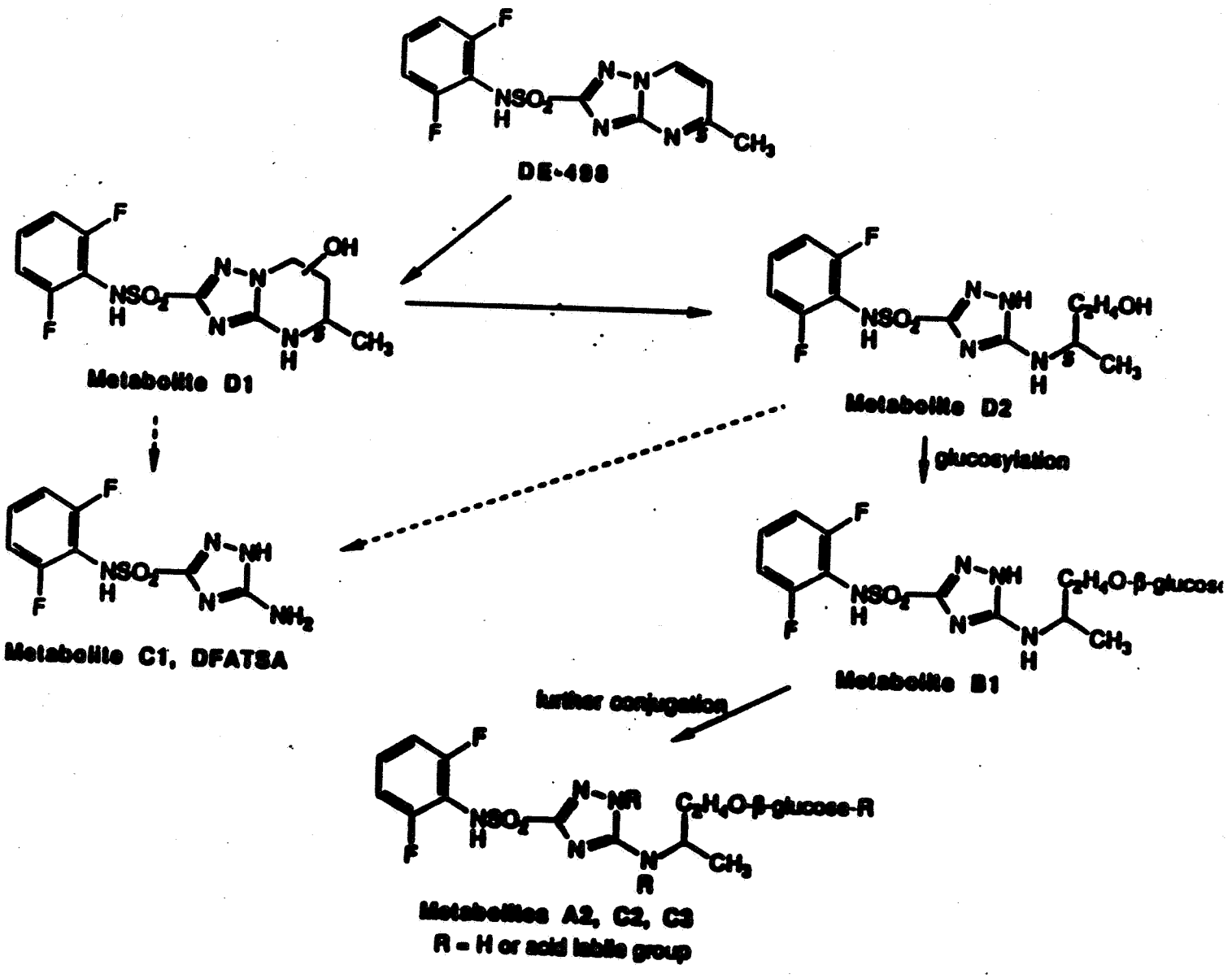
Deficiency #26 as stated above remains outstanding.

Chemical names and structures of flumetsulam and its metabolites isolated from soybeans and corn.

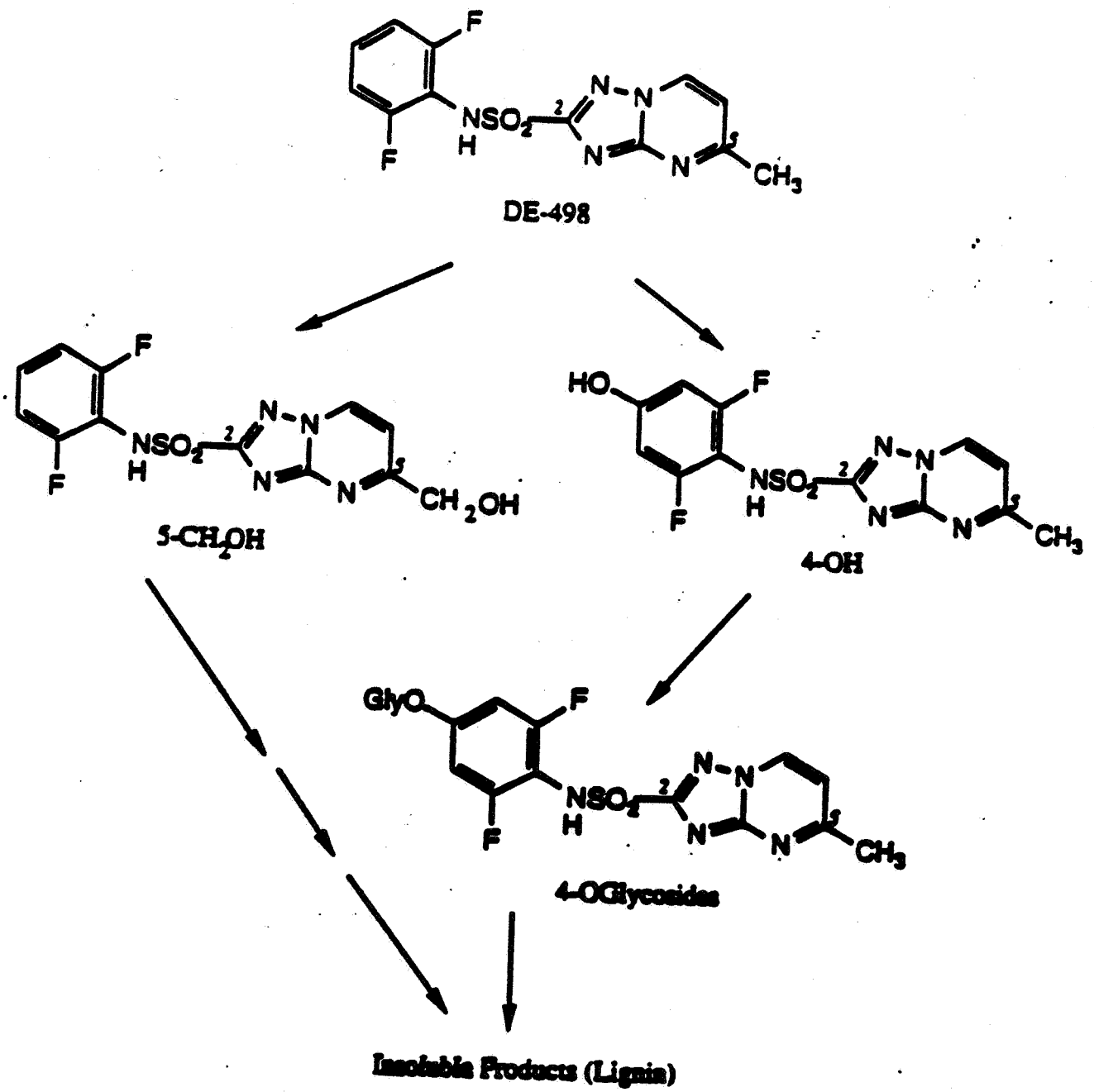
Chemical names	Chemical Structure
Flumetsulam N-(2,6-difluorophenyl)-5- methyl-1,2,4-triazolo(1,5a)pyrimidine-2-sulfonamide,	
Metabolite D1 hydroxylated-tetrahydro-flumetsulam	
Metabolite D2 N-(2,6-difluorophenyl)-5-((3-hydroxy-1 methylpropyl)amino)-1,2,4-triazole-3-sulfonamide	
DFATSA; Metabolite C1 N-(2,6-difluorophenyl)-5-amino-1H-1,2,4-triazole-3-sulfonamide	
Metabolite B1 Glycosyl-conjugate of metabolite D2	
Metabolite A2, C2, and C3	 **R=H or acid labile group**

Chemical names	Chemical Structure
Metabolite A1	 R=H or acid labile group
5-CH_2OH Metabolite N-(2,6-difluorophenyl)-5-hyroxymethyl-1,2,4-triazolo(1,5a)pyrimidine-2-sulfonamide	
4-OH Metabolite N-(2,6-difluoro-4-hydroxyphenyl)-5-methyl-1,2,4-triazolo(1,5a)pyrimidine-2-sulfonamide	
Glycosyl conjugate of 4-OH Metabolite	

PROPOSED METABOLIC PATHWAY FOR FLUMETSULAM IN SOYBEANS



PROPOSED METABOLIC PATHWAY FOR FLUMETSULAM IN CORN



RIN 7767-93

REVIEWS FOR BROADSTRIKE (FLUMETSULAM 129016)

Page_____ is not included in this copy.

Pages 46 through 51 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

✓ CONFIDENTIAL APPENDIX

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
