CONFIDENTIAL

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP# 3G04272. ID# 00279-EUP-RGR. New Chemical-Sulfentrazone (FMC 97285, F6285) in or on soybeans. Evaluation of residue data and analytical methods for a temporary tolerance. MRID#s 419116-01, -02 & -03; 429321-07 to -16. Barcodes D198702 & D198407. CBTS#s 13118 & 13103.

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4/25/94

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FMC is proposing temporary tolerances for hydroxymethyl-sulfentrazone (N-[2,4-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-hydroxymethyl-5-oxo-1H-1,2,4-triazol-1-yl]phenyl]methanesulfonamide), the major metabolite of sulfentrazone (2-(2,4-dichloro-5-methylsulfonylamidophenyl)-4-difluoromethyl-2,4-dihydro-5-methyl-3H-1,2,4-triazol-3-one). The ANSI approved systemic name for sulfentrazone is "N-[2,4-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]phenyl]methanesulfonamide." The registrant has proposed the following tolerance for hydroxymethyl-sulfentrazone:

Soybeans -- 0.025 ppm

This petition represents the first food use for sulfentrazone.

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BACKGROUND

Sulfentrazone is the a.i. in a new soil herbicide developed by FMC for use on soybeans to control broadleaf weeds and some grasses. The registrant is currently conducting an experimental use program for sulfentrazone on soybeans with a crop-destruct clause (000279-EUP-129).

CONCLUSIONS

1. The product chemistry is adequate for this EUP only. For the permanent tolerance petition, the registrant must: **a)** for GLN § 61-1: The CSF for the TGAI lists 2.9% as "unknown." Inspection of the chromatographic analysis of the TGAI submitted in conjunction with § 62-3 reveals the presence of at least three significant (>0.1%) impurities which were not identified. Any impurities in the unknown material found at a level above 0.1% must be identified and included in the CSF. Also, the a.i. is not listed under its ANSI systemic name. A revised CSF for the TGAI is thus required. **b)** for GLN § 61-3, the registrant should identify any impurities in the "unknown" component of the TGAI and discuss their formation, discuss the formation of impurities that might hypothetically occur but were not found in the TGAI, discuss possible degradation products of the TGAI and discuss the potential for starting materials to carry over to the TGAI. **c)** for GLN § 62-1: The registrant has submitted data from the analysis of only one batch of the TGAI produced by the pilot plant. The registrant should report the results of five batch analyses of sulfentrazone TGAI once it goes into market production. The CSF may need to be revised if the results of the new batch analyses differ from that done previously. **d)** for GLN § 62-2, the registrant should provide a CSF for the TGAI in which all impurities >0.1% are identified and the certified limits are based on the analysis of at least five independent batches. **e)** for GLN § 62-3, the registrant should demonstrate the repeatability (precision) of the analytical method for the a.i. by reporting the results of at least five determinations of a single sample of the TGAI, and the accuracy of the method performing at least five determinations of the sulfentrazone analytical grade standard. **f)** for GLN § 62-3: The reported precision for one impurity which has a nominal concentration in the 1.0-10.0% range was 24.9%. As the maximum acceptable precision for an impurity in this concentration range is 5%, CBTS concludes that this method is not adequate to enforce the certified limits of the known impurities in the TGAI. The registrant should develop an acceptable analytical method for the identified impurities and demonstrate the repeatability (precision) of the method by reporting the results of at least five determinations of a single sample of the TGAI. The accuracy of the method should also be determined by performing at least five determinations of the analytical grade standards. If other impurities are found at levels >0.1% in the "unknown" component of

the TGAI, then validated analytical methods will be required for all such impurities. **g)** for GLN § 63-5, submit data on the melting point of the TGAI. **h)** for GLN § 63-8, submit data on the solubility of the TGAI in nonpolar solvents. **g)** for GLN § 63-13, submit data on the sensitivity of the TGAI to metals, metal ions, elevated temperature and sunlight.

2a. The label contains the following restrictions: 1) Do not allow livestock to graze on treated plants or feed treated plants or plant trash to livestock. 2) The first rotational crop following application on soybeans is to be destroyed. Do not rotate to cotton or sugar beets.

2b. The directions for use are adequate with the following exceptions: 1) the crop rotation restriction should be changed to "Do not rotate to any crop except soybeans." 2) the ANSI systemic name for the sulfentrazone should be included on the label. **A revised Section B is required.**

2c. For the permanent tolerance petition, the restrictions against the feeding of soybean forage and hay to animals will probably need to be removed as such prohibitions will likely be considered impractical on a large scale in the upcoming revision of Table II of Subdivision O.

2d. This EUP program covers a period of one year beginning on 1/1/95. The area involved is 4000 acres or 0.007% of the total U.S. soybean acreage in 1991 (*Agricultural Statistics*, 1992). A maximum of 2000 lbs. a.i. will be applied.

3. No rotational crop studies were submitted with this petition. For the purposes of this EUP, crop rotation may be restricted by a label amendment (see above). However, for the permanent tolerance the registrant must submit a confined crop rotation study. The results of this study will be used to determine the appropriate crop rotation restrictions and/or the need for limited field trials.

4a. The nature of the residue in soybeans is understood for the purposes of this EUP only. The metabolites of sulfentrazone which were identified (sulfentrazone carboxylic acid, hydroxymethyl-sulfentrazone, desmethyl-sulfentrazone and des-methylsulfonyl sulfentrazone) comprised 52-65% of the TRR in forage; 40-50% of the TRR in hay; and 36-40%, in seed. Significant amounts of these metabolites were found as conjugates. Unidentified polar metabolites comprised 10-18% of the TRR in forage; 22-26% of the TRR in hay; and 15-24%, in seed. Uncharacterized polar compounds comprised 10-16% of the TRR in forage; 1-8% of the TRR in hay; and 9-22%, in seed.

4b. For the permanent tolerance petition, the petitioner must address the following deficiencies in the soybean metabolism study:

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i) The storage stability of the samples in this study has not been demonstrated. The registrant should report the actual dates of extraction and chromatography. If the samples were stored longer than 6 months prior to analysis, then the registrant must show that the nature of the residue in the samples has not changed during storage by presenting representative chromatographic separations performed early in the study and at the conclusion of the study. If such data do not exist or if significant changes in the metabolite profile occurred during storage, the registrant may be required to repeat this metabolism study. **ii)** Unknown metabolites 2 (0.065-0.077 ppm in hay and 0.061-0.076 ppm in forage), 3 (0.105-0.110 in hay and 0.023-0.088 in forage), 5 (0.045-0.050 ppm in hay and 6 (up to 13.1% of the TRR in seed) accounted for significant portions of the TRR in soybean RACs. The registrant should identify these compounds. **iii)** Significant portions of the TRR in forage and grain were found to be extractable but were not characterized by HPLC (polar metabolites). The registrant should characterize any of these fractions which contain >0.05 ppm or >10% of the TRR (polar extracts of forage, triazole-labelled polar extract of hay and triazole-labelled polar extract of seed). **iv)** Significant portions of the bound residues of hay and forage remained uncharacterized after enzymatic digestions. The registrant should further characterize these bound residues.

4c. We recommend that the registrant resolve these deficiencies as soon as possible so that a decision on which metabolites need to be regulated can be reached prior to the analysis and submission of the field residue data for the permanent tolerance petition.

5. Metabolism studies for sulfentrazone in ruminants and poultry have not been reported. This data will not be required for this EUP due to the label restrictions against the feeding of treated RACs to livestock and the limited number of acres involved. However, acceptable metabolism studies in ruminants and poultry will be required for the permanent tolerance petition. These studies should utilize sulfentrazone labelled in both rings or separate studies should be performed using [^{14}C]phenyl- and [^{14}C]triazole-labelled sulfentrazone. If there are significant sulfentrazone metabolites (exocons) formed in soybean which are not also formed in animals, then CBTS may also require metabolism studies using any such metabolites.

6a. The registrant has submitted a proposed enforcement method which simultaneously measures both sulfentrazone and hydroxymethyl-sulfentrazone. The method was validated with sulfentrazone and hydroxymethyl-sulfentrazone in soybean seed at the reported LOQ, 0.025 ppm. No method validation using soybean forage and hay was reported. The LOD was reported to be 0.005 ppm. No independent laboratory validation (ILV) of this method was submitted.

6b. This method is not adequate for the purposes of this EUP.

CBTS will not recommend in favor of this EUP until we receive an ILV of the proposed enforcement method. Once we receive the ILV report, the method will be sent to ACL for the Agency's petition method validation (PMV).

6c. For the permanent tolerance petition, the registrant must also: **i)** Develop enforcement methodology which measures all residues of concern in all RACs (seed, forage and hay) and processed fractions for which a tolerance is required; **ii)** Obtain an ILV for this method(s) if significantly different from the current method; **iii)** Provide radiovalidation of the method(s) using samples from the metabolism study; **iv)** Submit the results of Multiresidue Testing of all residues of regulatory concern. The acceptability of all analytical enforcement methodology is contingent on a successful outcome of the PMV.

7a. The registrant has demonstrated sulfentrazone *per se* to be stable in seed for 6 months and in processed fractions for 90 days of frozen storage.

7b. These storage stability studies are adequate for the purposes of this EUP application only. For the permanent tolerance petition, the registrant must demonstrate storage stability of sulfentrazone, hydroxymethyl-sulfentrazone and any other metabolite determined to be of regulatory concern in all soybean RACs (seed, hay and forage) and processed fractions (hulls, meal, oil and soapstock).

8a. The registrant has reported the results of seven field trials in which seed samples were analyzed using methodology which measures both sulfentrazone and hydroxymethyl-sulfentrazone. Residues of sulfentrazone were below the LOD (0.005 ppm) and residues of hydroxymethyl-sulfentrazone were below the LOQ (0.025 ppm) in all samples. Detectable residues of hydroxymethyl-sulfentrazone were observed in three trials.

8b. These field trials are adequate to support this EUP application only. For the permanent tolerance petition, the registrant should submit the results of at least 20 field trials in which forage, hay (note conclusion 2c) and seed samples are analyzed with methodology which measures sulfentrazone and all metabolites determined to be of regulatory concern. These trials should include adequate geographic representation using the maximum application rate, minimum PHI and minimum application volume (10 gal/A).

8c. The Section F submitted by the registrant is not adequate for this EUP. As written, the parent compound is not included. The tolerance expression must be revised to include both sulfentrazone and hydroxymethyl-sulfentrazone. The common name of the parent compound and the preferred systemic names of sulfentrazone and hydroxymethyl-sulfentrazone should be included. Also, the level of

the tolerance should be at least the sum of the LOQ of all compounds included. In this case, the LOQ for sulfentrazone and hydroxymethyl-sulfentrazone is 0.025 ppm each, for a total of 0.050 ppm. **A revised Section F is required.**

8d. For the permanent tolerance petition, Section F will have to be revised to include all metabolites determined to be of regulatory concern and to include proposed tolerances for hay and forage (see conclusion 2c).

9a. For the processing study, soybeans were treated with sulfentrazone 4F at a rate of 3X. Mature soybean seeds were harvested and analyzed using Method P-2689M, which measures only sulfentrazone *per se*. Residues were below the LOD (0.005 ppm) in all samples. Seeds were processed and analyzed with Method P-2718M, which measures only sulfentrazone *per se*. Residues were below the LOD (0.005 ppm) in all samples.

9b. This processing study is not adequate to support this EUP application. The need for feed/food additive tolerances can not be determined because the samples were not analyzed for the sulfentrazone metabolite included in the tolerance expression (hydroxymethyl-sulfentrazone). As this metabolite is organosoluble and was detected in seed samples from the field trials, it is likely that significant residues would be present in the oil fractions. **For this EUP, the registrant should repeat this processing study and analyze the samples with Method P-2811M which measures both sulfentrazone and hydroxymethyl-sulfentrazone.** Alternatively, the samples from this study could be reanalyzed using this method provided some evidence of storage stability could be provided. If residues are found to concentrate, then the appropriate temporary feed/food additive tolerances should be proposed.

9c. For the permanent tolerance petition, the registrant must submit the results of processing studies in which the samples were analyzed methodology which measures sulfentrazone and all metabolites determined to be of regulatory concern and, if necessary, propose the appropriate feed/food additive tolerances.

10. The magnitude of the residue in animals has not been reported. This data will not be required for this EUP due to the label restrictions against the feeding of treated RACs to livestock and the limited number of acres involved. However, acceptable magnitude of the residue studies in ruminants and poultry will be required for the permanent tolerance petition. If there are significant sulfentrazone metabolites formed in soybean RACs which are not also formed in animals, then CBTS may also require feeding studies using any such metabolites.

11. There is no Codex proposal, nor Canadian or Mexican limits for residues of sulfentrazone or hydroxymethyl-sulfentrazone in

soybeans. Therefore, a compatibility issue is not relevant to the proposed tolerance. A copy of the IRLS is attached to the memorandum.

RECOMMENDATIONS

CBTS recommends against the proposed temporary tolerances for hydroxymethyl-sulfentrazone on soybeans for reasons detailed in conclusions 2b, 6b, 8c and 9b.

For the permanent tolerance petition, the registrant must: **1)** satisfactorily resolve all deficiencies in the product chemistry (conclusion 1), soybean metabolism study (conclusion 4b) and the analytical methodology (conclusion 6c); **2)** submit acceptable nature and magnitude of the residue in animals (conclusions 5 and 10), rotational crop (conclusion 3) and storage stability studies (conclusion 7b); **3)** submit acceptable magnitude of the residue studies in soybean RACs (conclusion 8b) and processed fractions (conclusion 9c); **4)** propose tolerances for hay, forage and any processed fraction in which residues concentrate (conclusions 8d and 9c); and, if necessary, **5)** propose tolerances for animal RACs and develop appropriate analytical enforcement methodology.

DETAILED CONSIDERATIONS

Product Chemistry

§ 61-1 Product Identity and Disclosure of Ingredients

The active ingredient (a.i.) in F6285 4F Herbicide is sulfentrazone or 1-(2,4-dichloro-5-methylsulfonylamidophenyl)-4-difluoromethyl-4,5-dihydro-3-methyl-1H-1,2,4-triazol-5-one. The chemical structure is shown in figure 1 (copied from p. 43 of MRID# 429321-07). Other identifying characteristics are:

Empirical Formula:	$C_{11}H_{10}Cl_2N_4O_3F_2S$
Molecular Weight:	387.2
CAS Registration No.:	122836-35-5
Common Name:	Sulfentrazone

The registrant has submitted a CSF for both the TGAI and end use product. Nominal concentrations were provided for all inerts and

impurities. However, the CSF for the TGAI lists 2.9% as "unknown." Inspection of the chromatographic analysis of the TGAI submitted in conjunction with § 62-3 reveals the presence of at least three impurities (>0.1%) which were not identified. Any impurities in the unknown material found at a level above 0.1% must be identified and included in the CSF. Also, the ANSI approved systemic name for sulfentrazone is "N-[2,4-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]phenyl]methanesulfonamide." The CSF should list the a.i. (and impurities) using this nomenclature. A revised CSF for the TGAI thus is required. **The requirements for GLN § 61-1 are fulfilled for the purposes of this EUP only.** For the permanent tolerance petition, the registrant should characterize the unknown components and submit a revised CSF for the TGAI which includes all impurities and ANSI systemic names.

§ 61-2 Beginning Materials and Manufacturing Process

The registrant has submitted the names and addresses of the suppliers and the specifications of the starting materials. Copies of the Material Safety Data Sheets for the starting materials were also included.

Included in the report are the chemical equations for each reaction of each step in the process, the amounts of each starting material, the equipment used, the parameters controlled and the steps at which analytical methods were used to make quality control measurements. Details of each step are given in the confidential appendix. **The requirements for GLN § 61-2 are fulfilled.**

§ 61-3 Discussion of the Formation of Impurities

The registrant has provided a discussion of the formation of the two identified impurities that were found at >0.1% in the TGAI. The registrant has failed to include discussions of impurities that might hypothetically occur but were not found in the TGAI, possible degradation products and the potential for starting materials to carry over to the TGAI. Details are provided in the confidential appendix. **The requirements for GLN § 61-3 are fulfilled for the purposes of this EUP only.** For the permanent tolerance petition, the registrant should identify any impurities in the "unknown" component of the TGAI and discuss their formation, discuss the formation of impurities that might hypothetically occur but were not found in the TGAI, discuss possible degradation products of the TGAI and discuss the potential for starting materials to carry over to the TGAI.

§ 62-1 Preliminary Analysis of Product Samples

The registrant has submitted data from the analysis of one batch of the TGAI produced by the pilot plant. **The requirements for GLN § 62-1 are fulfilled for the purposes of this EUP only.** For the permanent tolerance petition, the registrant should report the results of at least five batch analyses of sulfentrazone TGAI once it goes into market production. The CSF may need to be revised if the results of the results of the new batch analyses differ from that done previously.

§ 62-2 Certified Limits

The registrant has submitted data and a CSF dated 5/7/91 which establishes certified limits for the a.i. and all impurities present at a level >0.1% (see the confidential appendix). The upper limits for the impurities were approximately 2X the levels observed in the batch analysis. However, 2.9% of the TGAI is "unknown" and appears to contain impurities which have not been identified. **The requirements for GLN § 62-2 are fulfilled for the purposes of this EUP only.** To satisfy GLN § 62-2 for the permanent tolerance petition, the registrant should provide a CSF for the TGAI in which all impurities >0.1% are identified and the certified limits are based on the analysis of at least five independent batches.

§ 62-3 Analytical Methods to Verify Certified Limits

The registrant has submitted a non-confidential method (Test Method AGC No. 174, MRID# 419116-01) for determination of the a.i. in the TGAI. The method involves HPLC using gradient elution from an ODS column with UV detection at 232 nm. The registrant has not included a validation of this method. **CBTS concludes that this method is adequate to enforce the certified limits of the a.i. in the TGAI for this EUP only.** For the permanent tolerance petition, the registrant should demonstrate the repeatability (precision) of the method by reporting the results of at least five determinations of a single sample of the TGAI, and the accuracy of the method by performing at least five determinations of the sulfentrazone analytical grade standard.

The registrant has also submitted a confidential method (Test Method AGC No. 174, MRID# 419116-02) for determination of FMC97267 and FMC97283 in the TGAI. Details of the method are found in the confidential appendix. The reported precision for one impurity which has a nominal concentration in the 1.0-10.0% range was 24.9%. As the maximum acceptable precision for an impurity in this concentration range is 5%, **CBTS concludes that this method is not adequate to enforce the certified limits of the known impurities in the TGAI.** For the permanent tolerance petition, the registrant should develop an acceptable analytical method for the identified impurities and demonstrate the repeatability (precision) of the

method by reporting the results of at least five determinations using a single sample of the TGAI. The accuracy of the method should also be determined by performing at least five determinations using the sulfentrazone analytical grade standard. If other impurities are found at levels >0.1% in the "unknown" component of the TGAI, then validated analytical methods will be required for all such impurities.

§ 63 Physical and Chemical Characteristics of the TGAI

§ 63-2 Color: Visual inspection and the Munsell system was used to determine that the color of the TGAI was tan. These data fulfill the requirements for GLN § 63-2.

§ 63-3 Physical State: The TGAI was observed to be a solid. These data fulfill the requirements for GLN § 63-3.

§ 63-4 Odor: The TGAI was observed to have a faint sulfur-like odor. These data fulfill the requirements for GLN § 63-4.

§ 63-5 Melting Point: The melting point of the analytical standard of sulfentrazone was determined using a Fisher-Jones Melting Point Apparatus to be 126.5 °C. **These data do not fulfill the requirements for GLN § 63-5 as the melting point of the TGAI has not been reported.** This data should be reported in the permanent tolerance request.

§ 63-7 Density: The bulk density relative was determined to be 0.53 g/cm^3. These data fulfill the requirements for GLN § 63-7.

§ 63-8 Solubility: The solubility in distilled water and aqueous buffers was determined by equilibration.

Solvent	Solubility, µg/g
Distilled Water	4.0×10^2
Buffer, pH 6	4.9×10^2
Buffer, pH 7	1.8×10^3
Buffer, pH 7.5	2.0×10^3

These data do not fulfill the requirements for GLN § 63-8 as the registrant has not reported on the solubility of the TGAI in nonpolar solvents. This data should be reported in the permanent tolerance request.

§ 63-9 Vapor Pressure: Using the gas saturation method, the vapor pressure of analytical grade sulfentrazone was found to be 8×10^{-10}

mm Hg at 25 °C. These data fulfill the requirements for GLN § 63-9.

§ 63-10 Dissociation Constant: Using the UV spectrophotometric method, the dissociation constant of analytical grade sulfentrazone was found to be: pKa = 6.56 at 20 °C. These data fulfill the requirements for GLN § 63-10.

§ 63-11 Octanol/Water Partition Coefficient ($P_{o/w}$)

The $P_{o/w}$ of analytical grade fipronil (99.7% pure) was determined by the shake flask method in aqueous buffers. The observed $P_{o/w}$ values were:

pH	$P_{o/w}$	$\log P_{o/w}$
5	31.1	1.49
7	9.8	0.99
9	0.27	-0.57

These data fulfill the requirements for GLN § 63-11.

§ 63-12 pH

The pH of a 1% w/w aqueous mixture of the TGAI was found to be 4.78 at 23 °C. These data fulfill the requirements for GLN § 63-12.

§ 63-13 Stability

The stability at room temperature during 3 months of storage was investigated. No degradation of the TGAI was observed. No data on the stability of the TGAI at elevated temperatures or to metals, metal ions or sunlight was submitted. **The requirements for GLN § 63-13 are not fulfilled.** To satisfy GLN § 63-13 for the permanent tolerance petition, the registrant must submit data on the stability of the TGAI at elevated temperatures and to metals, metal ions and sunlight.

The product chemistry status is summarized in Table 1.

Table 1- PRODUCT CHEMISTRY DATA SUMMARY
Chemical No. 129081
Product: Sulfentrazone TGAI

Guideline Number	Requirement	Are Data Requirements Fulfilled?[a]	MRID Number
61-1	Product Identity and Disclosure of Ingredients	N[b]	419116-01
61-2	Beginning Materials and Manufacturing Process	Y	419116-01
61-3	Discussion of Formation of Impurities	N[c]	419116-01
62-1	Preliminary Analysis	N[d]	419116-02
62-2	Certification of Ingredient Limits	N[e]	419116-02
62-3	Analytical Methods to Verify the Certified Limits	N[f]	419116-02
63-2	Color	Y	419116-03
63-3	Physical State	Y	419116-03
63-4	Odor	Y	419116-03
63-5	Melting Point	N[g]	419116-03
63-6	Boiling Point	N/A	
63-7	Density, Bulk Density or Specific Gravity	Y	419116-03
63-8	Solubility	N[h]	419116-03
63-9	Vapor Pressure	Y	419116-03
63-10	Dissociation Constant	Y	419116-03
63-11	Octanol/Water Partition Coefficient	Y	419116-03
63-12	pH	Y	419116-03
63-13	Stability	N[i]	419116-03

[a] Y = Yes; N = No; N/A = Not Applicable.
[b] Identification of additional impurities and revised CSF required.
[c] Discussion incomplete.
[d] Only one batch of the TGAI was analyzed.
[e] CSF for the TGAI in which all impurities >0.1% are identified and the certified limits are based on the analysis of at least five independent batches is required.
[f] Validation data for a.i. method and more precise method for impurities required.
[g] Data required for TGAI.
[h] Data required for nonpolar solvents.
[i] Data required on the sensitivity of the TGAI to metals, metal ions, elevated temperature and sunlight.

Formulation: Sulfentrazone is formulated as F6285 4F Herbicide, containing 39.6% a.i. by weight and 4 lbs. a.i./gal.

Proposed Use

Sulfentrazone is applied preemergence or preplant soil incorporated (PPI) by ground equipment in a volume of 10-40 gal/A. The application rate is 0.25-0.50 lbs. ai/A and only one application may be made per season.

The label contains the following restrictions: 1) Do not allow livestock to graze on treated plants or feed treated plants or plant trash to livestock. 2) The first rotational crop following application on soybeans is to be destroyed. Do not rotate to cotton or sugar beets.

The directions for use are adequate with the following exceptions: 1) the crop rotation restriction should be changed to "Do not rotate to any crop except soybeans." 2) the ANSI systemic name for the sulfentrazone (N-[2,4-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]phenyl]methanesulfonamide) should be included on the label. **A revised Section B is required.** For the permanent tolerance petition, the restrictions against the feeding of soybean forage and hay to animals will probably need to be removed as such prohibitions will likely be considered impractical on a large scale in the upcoming revision of Table II of Subdivision O.

This EUP program covers a period of one year beginning on 1/1/95. The area involved is 4000 acres or 0.007% of the total U.S. soybean acreage in 1991 (*Agricultural Statistics*, 1992). A maximum of 2000 lbs. a.i. will be applied.

Rotational Crop Studies

No studies were submitted with this petition.

For the purposes of this EUP, crop rotation may be restricted by a label amendment (see above). However, for the permanent tolerance the registrant must submit a confined crop rotation study. The results of this study will be used to determine the appropriate crop rotation restrictions and/or the need for limited field trials.

Nature of Residue- Plants

Submitted with this petition:

> Nature of the Residue in Plants: Soybean Metabolism of ^{14}C-F6285. MRID# 429321-07

In Life Phase: Sulfentrazone, radiochemically labelled in the aromatic ring (phenyl-UL-^{14}C) or in the triazole ring (carbonyl-^{14}C), was diluted to a specific activity of 3.50 mci/mmol and applied to outdoor plots in a single preemergence broadcast application at a rate of 0.5 lbs. ai/A (1X). A second set of soybeans was planted after poor germination of the first set. Both sets of plants were grown to maturity and harvested for seed and hay. Immature plants were also harvested for forage.

TRR: The tissues were ground to a powder and the TRR in both sets of plants was determined by combustion (Table 2). The highest TRR from both trials was taken as the worst case and used as a base value for quantifying residues. The maximum residues observed in forage were 1.057 ppm; in hay, 1.073 ppm; and in seed, 0.171 ppm.

Table 2- TRR in soybean RACs as a result of application of phenyl- or triazole-labelled sulfentrazone at a rate of 0.5 lbs. ai/A.

RAC	PHI (days)	Label	TRR (ppm)
First Trial			
Forage	98	Phenyl	0.279
		Triazole	0.457
Hay	145	Phenyl	0.444
		Triazole	1.001
Seed	145	Phenyl	0.084
		Triazole	0.171
Second Trial			
Forage	63	Phenyl	1.057
		Triazole	1.028
Hay	114	Phenyl	1.073
		Triazole	1.006
Seed	114	Phenyl	0.064
		Triazole	0.079

Extraction and Fractionation: Tissues were ground in methanol/water and the debris removed by centrifugation. The debris was reextracted at least twice using the same solvent. The methanol/water fraction was partitioned three times with methylene chloride. Non-conjugated polar metabolites were partitioned into the organic phase while polar metabolites and conjugates remained in the organic phase. The results of this procedure is shown in Table 3. The polar fraction was generally greater than the non-polar fraction and bound residues accounted for 13-31% of the TRR.

Table 3- Extraction and fractionation of TRR in soybean RACs.

RAC	Label	Extractable				Bound	
		Nonpolar		Polar			
		ppm	% TRR	ppm	% TRR	ppm	% TRR
Forage	Phenyl	0.385	36.4	0.515	48.7	0.157	14.9
	Triazole	0.349	33.9	0.546	53.1	0.133	13.0
Hay	Phenyl	0.287	26.8	0.498	46.4	0.287	26.8
	Triazole	0.170	16.9	0.577	57.3	0.260	25.8
Seed	Phenyl	0.029	34.3	0.029	34.9	0.026	30.8
	Triazole	0.040	23.3	0.092	53.8	0.039	22.9

Conjugated polar residues were released by hydrolysis of the methanol/water fraction with cellulase and HCl. The majority of the radioactivity in this fraction was released by this procedure (Table 4). The remaining polar metabolites accounted for 1-22% of the TRR. The triazole-labelled samples had a greater percentage of polar metabolites than did the phenyl-labelled samples.

Table 4- Fractionation of polar residues after hydrolysis (cellulase, HCl).

RAC	Label	Nonpolar		Polar	
		ppm	% TRR	ppm	% TRR
Forage	Phenyl	0.406	38.4	0.109	10.3
	Triazole	0.377	36.6	0.169	16.5
Hay	Phenyl	0.483	45.0	0.015	1.4
	Triazole	0.499	49.5	0.078	7.8
Seed	Phenyl	0.022	26.1	0.007	8.8
	Triazole	0.054	31.7	0.038	22.1

Bound Residues: The bound residues were further characterized by enzymatic digestion. The residue was treated sequentially with the following procedures: 1) Extraction of cellulose- The residue was treated with cellulase. 2) Extraction of starch- The residues were treated with α-amylase. 3) Extraction of pectins- The residue was treated with pectinase. 4) Extraction of proteins- The residue was treated with pronase. 5) Extraction of pectins- The residue from the EGTA step was treated with EGTA, sonicated and heated. 5) Extraction of lignins- The residue was treated with dioxane, sonicated and heated. These procedures together released 6-20% of the TRR while 5-13% of the TRR remained bound (Table 5).

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Table 5- Fractioantion of bound residues.

RAC	Label	Cellulose		Starch		Pectin		Protein		Lignin		Remainder Bound	
		ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR
Forage	Phenyl	0.014	1.4	0.005	0.5	0.015	1.4	0.010	0.9	0.018	1.7	0.095	9.0
	Triazole	0.020	2.0	0.010	1.0	0.016	1.5	0.009	0.9	0.016	1.6	0.062	6.0
Hay	Phenyl	0.026	2.4	0.018	1.7	0.027	2.4	0.031	2.9	0.049	4.6	0.137	12.8
	Triazole	0.028	2.8	0.015	1.5	0.028	2.8	0.024	2.3	0.043	4.2	0.123	12.2
Seed	Phenyl	0.008	9.0	0.004	5.0	0.003	3.2	0.002	2.3	0.000	0.0	0.010	11.4
	Triazole	0.013	7.8	0.005	3.2	0.005	3.3	0.007	4.1	0.000	0.0	0.008	4.6

Metabolite Identification: Polar metabolites were resolved on HPLC and compared with reference standards of sulfentrazone and six possible metabolites (fig. 1). The non-conjugated polar metabolites and the conjugated polar residues released by hydrolysis were analyzed separately. The identity of all metabolites found in these samples was confirmed by TLC, GC/MS and F-NMR.

Nature of the Residue in Forage: The primary non-conjugated metabolite was found to be hydroxymethyl-sulfentrazone, accounting for 26-33% of the TRR (Table 6).

Table 6- HPLC identification of non-conjugated (nonpolar) residues in forage.

Metabolite	Phenyl-Labelled		Triazole-Labelled	
	ppm	% TRR	ppm	% TRR
Polar	0.000	0.0	0.002	0.2
SCA	0.000	0.0	0.002	0.2
Unknown 1	0.000	0.0	0.000	0.0
Unknown 2	0.001	0.1	0.001	0.1
Unknown 3	0.009	0.8	0.046	4.5
HMS	0.348	32.9	0.268	26.0
Unknown 4	0.008	0.7	0.008	0.8
DMS	0.005	0.5	0.008	0.8
Unknown 5	0.007	0.7	0.008	0.8
DMSS	0.006	0.6	0.006	0.5

SCA = Sulfentrazone Carboxylic Acid
HMS = Hydroxy Methyl Sulfentrazone
DMS = Des-Methyl Sulfentrazone
DMSS = Des-MethylSulfonyl Sulfentrazone

In the conjugated fraction, both hydroxymethyl-sulfentrazone (12-18% of the TRR) and desmethyl-sulfentrazone (12-13% of the TRR) were identified (Table 7). A significant amount (0.060-0.075 ppm) of an unknown compound, Unknown 2, was also observed in the conjugated fraction. Unknown 3 was observed in both fractions, with a total level of 0.023-0.088 ppm.

Table 7- HPLC identification of conjugated nonpolar residues (released by hydrolysis) in forage.

	Phenyl-Labelled		Triazole-Labelled	
Metabolite	ppm	% TRR	ppm	% TRR
Polar	0.001	0.1	0.000	0.0
SCA	0.002	0.1	0.005	0.5
Unknown 1	0.001	0.1	0.000	0.0
Unknown 2	0.060	5.7	0.075	7.3
Unknown 3	0.014	1.3	0.042	4.1
HMS	0.185	17.5	0.128	12.4
DMS	0.136	12.8	0.124	12.0
Unknown 4	0.005	0.5	0.003	0.3
DMSS	0.002	0.2	0.000	0.0

SCA = Sulfentrazone Carboxylic Acid
HMS = Hydroxy Methyl Sulfentrazone
DMS = Des-Methyl Sulfentrazone
DMSS = Des-MethylSulfonyl Sulfentrazone

Nature of the Residue in Hay: The primary non-conjugated metabolite was found to be hydroxymethyl-sulfentrazone, accounting for 7-20% of the TRR (Table 8).

Table 8- HPLC identification of non-conjugated (nonpolar) residues in hay.

Metabolite	Phenyl-Labelled		Triazole-Labelled	
	ppm	% TRR	ppm	% TRR
Polar	0.000	0.0	0.002	0.2
SCA	0.000	0.0	0.031	3.1
Unknown 1	0.000	0.0	0.000	0.0
Unknown 2	0.000	0.0	0.002	0.2
Unknown 3	0.025	2.3	0.018	1.8
HMS	0.215	20.0	0.072	7.2
DMS	0.004	0.4	0.004	0.4
Unknown 4	0.004	0.3	0.005	0.5
Unknown 5	0.033	3.1	0.032	3.2
DMSS	0.006	0.6	0.004	0.4

SCA = Sulfentrazone Carboxylic Acid
HMS = Hydroxy Methyl Sulfentrazone
DMS = Des-Methyl Sulfentrazone
DMSS = Des-MethylSulfonyl Sulfentrazone

In the conjugated fraction, desmethyl-sulfentrazone (25-26% of the TRR) was the primary metabolite (Table 9). A significant amount (0.065-0.074 ppm) of Unknown 2 was observed only in the conjugated fraction. Unknown 3 and Unknown 5 were observed in both fractions, with total levels of 0.105-0.110 and 0.045-0.050 ppm, respectively.

Table 9- HPLC identification of conjugated nonpolar residues (released by hydrolysis) in hay.

Metabolite	Phenyl-Labelled		Triazole-Labelled	
	ppm	% TRR	ppm	% TRR
Polar	0.000	0.0	0.000	0.0
SCA	0.000	0.0	0.000	0.0
Unknown 1	0.005	0.4	0.002	0.2
Unknown 2	0.065	6.0	0.074	7.4
Unknown 3	0.080	7.5	0.092	9.1
HMS	0.030	2.8	0.023	2.2
Unknown 4	0.010	1.0	0.026	2.5
DMS	0.271	25.3	0.265	26.3
Unknown 5	0.017	1.6	0.013	1.3
DMSS	0.005	0.4	0.005	0.5

SCA = Sulfentrazone Carboxylic Acid
HMS = Hydroxy Methyl Sulfentrazone
DMS = Des-Methyl Sulfentrazone
DMSS = Des-MethylSulfonyl Sulfentrazone

Nature of the Residue in Seed: The primary non-conjugated metabolite was found to be hydroxymethyl-sulfentrazone, accounting for 16-17% of the TRR (Table 10).

Table 10- HPLC identification of non-conjugated (nonpolar) residues in seed.

	Phenyl-Labelled		Triazole-Labelled	
Metabolite	ppm	% TRR	ppm	% TRR
Polar	0.001	0.7	0.002	1.2
SCA	0.001	0.8	0.001	0.4
Unknown 1	0.000	0.2	0.001	0.3
Unknown 2	0.000	0.2	0.001	0.4
Unknown 3	0.000	0.1	0.001	0.6
HMS	0.013	15.9	0.029	16.7
Unknown 4	0.000	0.4	0.001	0.4
DMS	0.001	0.8	0.001	0.7
Unknown 5	0.001	1.0	0.001	0.3
Unknown 6	0.011	13.1	0.003	1.8
DMSS	0.001	1.0	0.001	0.5

SCA = Sulfentrazone Carboxylic Acid
HMS = Hydroxy Methyl Sulfentrazone
DMS = Des-Methyl Sulfentrazone
DMSS = Des-MethylSulfonyl Sulfentrazone

A significant amount of Unknown 6 (up to 13% of the TRR) was also observed in this fraction. In the conjugated fraction, hydroxymethyl-sulfentrazone (14-18% of the TRR) was the primary metabolite (Table 11).

Table 11- HPLC identification of non-conjugated nonpolar residues (released by hydrolysis) in seed.

Metabolite	Phenyl-Labelled		Triazole-Labelled	
	ppm	% TRR	ppm	% TRR
Polar	0.000	0.5	0.000	0.1
Unknown 1	0.000	0.0	0.000	0.0
Unknown 2	0.000	0.0	0.001	0.6
Unknown 3	0.000	0.1	0.000	0.0
Unknown 4	0.001	0.9	0.000	0.1
SCA	0.000	0.2	0.000	0.1
Unknown 5	0.000	0.1	0.000	0.1
Unknown 6	0.005	5.7	0.008	4.8
Unknown 7	0.001	0.6	0.006	3.4
HMS	0.012	13.8	0.031	18.3
Unknown 8	0.000	0.1	0.001	0.5
DMS	0.003	3.1	0.005	2.9
Unknown 9	0.001	0.7	0.001	0.7
DMSS	0.000	0.2	0.000	0.1

SCA = Sulfentrazone Carboxylic Acid
HMS = Hydroxy Methyl Sulfentrazone
DMS = Des-Methyl Sulfentrazone
DMSS = Des-MethylSulfonyl Sulfentrazone

Storage Stability: The dates of extraction and chromatography were not provided so that the storage time of the samples can not be calculated. Based on the termination date of the study and the harvest date of the samples, the maximum storage interval was 10 months. The registrant attempted to demonstrate storage stability by spiking two samples with ^{14}C-sulfentrazone and analyzing after 5-9 months in storage. Sulfentrazone, *per se*, was shown to be stable for up to 9 months in soybean forage.

Conclusions: The nature of the residue in soybeans is understood for the purposes of this EUP only. The metabolites of sulfentrazone which were identified (sulfentrazone carboxylic acid, hydroxymethyl-sulfentrazone, desmethyl-sulfentrazone and des-methylsulfonyl sulfentrazone) comprised 52-65% of the TRR in forage; 40-50% of the TRR in hay; and 36-40%, in seed (Table 12). Significant amounts of these metabolites were found as conjugates, especially desmethyl-sulfentrazone (Table 13). Unknown polar metabolites comprised 10-18% of the TRR in forage; 22-26% of the TRR in hay; and 15-24%, in seed. Uncharacterized polar compounds comprised 10-16% of the TRR in forage; 1-8% of the TRR in hay; and 9-22%, in seed.

Table 12- Summary of metabolite identification/characterization in soybean RACs.

Metabolite/ Fraction	Forage				Hay				Seed			
	Phenyl-labelled		Triazole-labelled		Phenyl-labelled		Triazole-labelled		Phenyl-labelled		Triazole-labelled	
	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR
SCA	0.002	0.1	0.007	0.7	0.000	0.0	0.031	3.1	0.001	1.0	0.001	0.5
HMS	0.533	50.4	0.396	38.4	0.245	22.8	0.095	9.4	0.025	29.7	0.060	35.0
DMS	0.141	13.3	0.132	12.8	0.275	25.7	0.269	26.7	0.004	3.9	0.006	3.6
DMSS	0.008	0.8	0.006	0.5	0.011	1.0	0.009	0.9	0.001	1.2	0.001	0.6
Unknowns	0.106	10.0	0.185	18.1	0.239	22.2	0.266	26.4	0.021	24.4	0.027	15.3
Uncharacterized Soluble (polar)	0.109	10.3	0.169	16.5	0.015	1.4	0.078	7.8	0.007	8.8	0.038	22.1
Characterized Bound	0.062	5.9	0.071	7.0	0.151	14.0	0.138	13.6	0.017	19.5	0.030	18.4
Uncharacterized Bound	0.095	9.0	0.062	6.0	0.137	12.8	0.123	12.2	0.010	11.4	0.008	4.6
Total Identified	**0.684**	**64.6**	**0.541**	**52.4**	**0.531**	**49.5**	**0.404**	**39.8**	**0.031**	**35.8**	**0.068**	**39.7**

SCA = Sulfentrazone Carboxylic Acid
HMS = Hydroxy Methyl Sulfentrazone
DMS = Des-Methyl Sulfentrazone
DMSS = Des-MethylSulfonyl Sulfentrazone

Table 13- Proportion of polar metabolites identified in soybean metabolism study which are found as conjugates (average of phenyl- and triazole-labelled samples)

RAC	Metabolite	ppm Non-Conjugated	ppm Conjugated	Total	% Conjugated
Forage	SCA	0.001	0.004	0.005	80
	HMS	0.308	0.156	0.464	34
	DMS	0.006	0.130	0.136	96
	DMSS	0.006	0.001	0.007	14
Hay	SCA	0.016	0.000	0.016	0
	HMS	0.144	0.026	0.170	15
	DMS	0.004	0.268	0.272	99
	DMSS	0.005	0.005	0.010	50
Seed	SCA	0.001	0.000	0.001	0
	HMS	0.021	0.022	0.043	51
	DMS	0.001	0.004	0.005	80
	DMSS	0.001	0.000	0.001	0

SCA = Sulfentrazone Carboxylic Acid
HMS = Hydroxy Methyl Sulfentrazone
DMS = Des-Methyl Sulfentrazone
DMSS = Des-MethylSulfonyl Sulfentrazone

For the permanent tolerance petition, the petitioner must address the following deficiencies in the soybean metabolism study: **a)** The storage stability of the samples in this study has not been demonstrated. The data that was presented by the registrant indicated only that sulfentrazone *per se* was stable during storage in forage for 9 months. The registrant should report the actual dates of extraction and chromatography. If the samples were stored longer than 6 months prior to analysis, then the registrant must show that the nature of the residue in the samples has not changed during storage by presenting representative chromatographic separations performed early in the study and at the conclusion of the study. If such data do not exist or if significant changes in the metabolite profile occurred during storage, the registrant may be required to repeat this metabolism study. **b)** Unknown metabolites 2 (0.065-077 ppm in hay and 0.061-0.076 ppm in forage), 3 (0.105-0.110 in hay and 0.023-0.088 in forage), 5 (0.045-0.050 ppm in hay and 6 (up to 13.1% of the TRR in seed) accounted for significant portions of the TRR in soybean RACs. The registrant should identify these compounds. **c)** Significant portions of the TRR in forage and grain were found to be extractable but were not characterized by HPLC (polar metabolites). The registrant should characterize any of these fractions which contain >0.05 ppm or >10% of the TRR (polar extracts of forage, triazole-labelled polar extract of hay and triazole-labelled polar extract of seed). **d)** Significant portions of the bound residues of hay and forage remained uncharacterized after enzymatic digestions. The registrant should further characterize these bound residues.

CBTS will refer to the Metabolism Committee on the toxicological significance of metabolites once the deficiencies associated with plant metabolism have been addressed. A decision by CBTS concerning which residues to regulate will then follow. A tolerance which includes only metabolite hydroxymethyl-sulfentrazone may not be appropriate; in such an instance a revised Section F and additional field studies, analytical methodology, and storage stability data may be needed.

We recommend that the registrant resolve these deficiencies as soon as possible so that a decision on which metabolites need to be regulated can be reached prior to the analysis and submission of the field residue data for the permanent tolerance petition.

Nature of Residue- Animals

No studies were submitted with this petition.

The nature of the residue in animals has not been reported. This data will not be required for this EUP due to the label restrictions against the feeding of treated RACs to livestock and the limited number of acres involved. However, acceptable nature

of the residue studies in ruminants and poultry will be required for the permanent tolerance petition. These studies should utilize sulfentrazone labelled in both rings or separate studies should be performed using [^{14}C]phenyl- and [^{14}C]triazole-labelled sulfentrazone. If there are significant sulfentrazone metabolites formed in soybean which are not also formed in animals, then CBTS may also require metabolism studies using any such metabolites.

Analytical Methodology- Plants

Submitted with this petition:

Residue Analytical Method for the Determination of FMC 97285 in/on Soybeans (Method P-2689M). MRID# 429321-08

Independent Method Validation Ruggedness Trial for FMC 97285 in Soybeans Using FMC Co. Method P-2689M, Residue Analytical Method for the Determination of FMC 97285 in/on Soybeans. MRID# 429321-11

Residue Analytical Method for the Determination of FMC 97285 and FMC 106091 in/on Soybeans Treated with F6285 4F (Method P-2811M). MRID# 429321-09

Method P-2689M

Procedure: Macerated tissue is initially refluxed in acetone/0.25 N HCl (70/30, v/v). After filtration, the acetone is removed by evaporation. The sample is then cleaned-up using C-18 and DEA cartridge columns. The sample is concentrated and analyzed on GC/EC with a Megabore column. This method measures only sulfentrazone *per se*.

Results: The method was validated with sulfentrazone in soybean seed at the reported LOQ, 0.025 ppm. The average recovery was 104 ± 6% (n = 14). The LOD was reported to be 0.005 ppm.

ILV: A successful ILV was performed by EN-CAS Analytical Labs, Winston-Salem, NC. The average recovery was 87 ± 9% (n = 6).

Conclusions: This method is not adequate to support the proposed temporary tolerance as the metabolite included in the tolerance expression, hydroxymethyl-sulfentrazone, is not measured.

Method P-2811M

Procedure: Macerated tissue is initially refluxed in acetone/0.25 N HCl (75/25, v/v). After filtration, the acetone is removed by evaporation. The sample is then cleaned-up using C-8 SPE and

silica gel cartridge columns. The sample is concentrated and derivatized with N,O-bis-(trimethylsilyl)-trifluoroacetamide, which converts hydroxymethyl-sulfentrazone to its trimethylsilyl derivative. Analysis was then performed on GC/EC with a Megabore column. This method simultaneously measures both sulfentrazone and hydroxymethyl-sulfentrazone.

Results: The method was validated with sulfentrazone and hydroxymethyl-sulfentrazone in soybean seed at the reported LOQ, 0.025 ppm. The average recovery was 113 ± 6% (n = 7) for sulfentrazone and 84 ± 12% for hydroxymethyl-sulfentrazone. No method validation using soybean forage and hay was reported. The LOD was reported to be 0.005 ppm.

ILV: No ILV of this method was submitted.

Conclusions: Method P-2811M is not adequate for the purposes of this EUP. **CBTS will not recommend in favor of this EUP until we receive an ILV of the proposed enforcement method.** Once we receive the ILV report, the method will be sent to ACL for the PMV. For the permanent tolerance petition, methodology which measures residues in forage and hay will also be required. Based on the results of the metabolism study, desmethyl-sulfentrazone is a major metabolite in forage and the primary metabolite in hay. It is thus possible that this metabolite will need to be included in the tolerance expression. CBTS will refer to the Metabolism Committee on the toxicological significance of metabolites once the deficiencies associated with plant metabolism have been addressed. A decision by CBTS concerning which residues to regulate will then follow. A tolerance which includes only the metabolite hydroxymethyl-sulfentrazone may not be appropriate; in such an instance revised analytical methodology will be needed. Also, the proposed analytical enforcement method includes a hydrolysis step, presumably to release conjugates. Efficient release of conjugated residues is necessary as a significant portion of sulfentrazone metabolites are found as conjugates (Table 13). The registrant should provide evidence that the proposed analytical enforcement methodology releases conjugated residues by performing a radiovalidation study using samples from the metabolism study.

Multiresidue Method Testing: No reports on Multiresidue testing of sulfentrazone or its metabolites have been received. For the permanent tolerance petition, the registrant must submit the results of Multiresidue testing for sulfentrazone and all of its metabolites that are determined to be of regulatory concern.

In summary, for the permanent tolerance petition, the registrant must: **a)** Develop enforcement methodology which measures all residues of concern in all RACs (seed, forage and hay) and processed fractions for which a tolerance is required; **b)** Obtain an ILV for this method(s) if substantially different from the current

method; **c)** Provide radiovalidation of the method(s) using samples from the metabolism study; **d)** Submit the results of Multiresidue Testing of all residues of regulatory concern. The acceptability of all analytical enforcement methodology is contingent on a successful outcome of the PMV.

Analytical Methodology- Animals

No analytical method has been submitted by the registrant

Since no temporary tolerances have been proposed for animal RACs, an analytical enforcement method for animals is not required for this EUP. If, however, animal metabolism/feeding studies demonstrate a potential for transfer of residues to meat, milk or eggs, then the registrant will be required to propose tolerances for these RACs and develop the appropriate analytical enforcement methodology. Any required enforcement methods for meat, milk and eggs will need successful ILVs and PMVs before being judged to be acceptable by CBTS.

Storage Stability Studies

Submitted with this petition:

> Residue Analytical Method for the Determination of FMC 97285 in/on Soybeans and the Processed Parts (Method P-2718M). MRID# 429321-10
>
> Cold Storage Stability of FMC 97285 in/on Laboratory-Fortified Soybean Seed. MRID# 429321-13
>
> Storage Stability of FMC 97285 in/on Soybean Processed Parts. MRID# 429321-12

MRID# 429321-13: Soybean seed was fortified with sulfentrazone at a level of 0.25 ppm and stored frozen (≈ -18 °C). Samples were analyzed using Method P-2689M after 0, 3 and 6 months of storage. Each assay set included a control, two freshly fortified and three stored spiked samples. The average recoveries at 0, 3 and 6 months were 104, 92 and 116%, respectively. Sulfentrazone *per se* thus appears to be stable in seed for 6 months of frozen storage.

MRID# 429321-12: Soybean meal, hulls, refined oil and soapstock was fortified with sulfentrazone at a level of 0.25 ppm and stored frozen (≈ -18 °C). Samples were analyzed using Method P-2718M after 0, 45 and 90 days of storage. This method was identical to Method P-2689M for hulls and meal. For soapstock and oil, the method was modified by replacement of the initial HCl reflux step

with hexane partitioning. The average recovery of sulfentrazone in samples spiked at the LOQ (0.025 ppm) was 87 ± 5% for crude oil, 89 ± 2% for refined oil, 79 ± 5% for soapstock, 101 ± 12% for meal and 108 ± 10% for hulls. Each assay set included a control, two freshly fortified and three stored spiked samples. The average recoveries at 0, 45 and 90 days were 100, 90 and 117%, respectively, in meal; 92, 105 and 101%, in hulls; 104, 104 and 100%, in refined oil; and 91, 108 and 111%, in soapstock. Sulfentrazone *per se* thus appears to be stable in soybean processed fractions for 90 days of frozen storage.

Conclusions: These storage stability studies are adequate for the purposes of this EUP application only. For the permanent tolerance petition, the registrant must demonstrate storage stability of sulfentrazone, hydroxymethyl-sulfentrazone and any other metabolite determined to be of regulatory concern in all soybean RACs (seed, hay and forage) and processed fractions (hulls, meal, oil and soapstock).

Magnitude of Residue- Plants

Submitted with this petition:

> Magnitude of the Residue of FMC 97285 in/on Soybeans Treated with F6285 4F. MRID# 429321-14
>
> Magnitude of the Residue of FMC 97285 and FMC 106091 in/on Soybeans Treated with F6285 4F. MRID# 429321-15

MRID# 429321-14: Fourteen field trials were conducted in eight states which together represented 70% of the U.S. soybean acreage in 1991 (*Agricultural Statistics*, 1992). The application rate of sulfentrazone 4F was 0.5 lbs. ai/A (1X). Preplant incorporation was employed in seven trials and preemergence application, in six trials. In one trial, sulfentrazone was applied preplant, but not incorporated. The minimum application volume represented was 15.0 gal/A. Mature soybean seeds were harvested 121-157 days after planting. After 4-5 months in storage, seeds were analyzed using Method P-2689M, which measures only sulfentrazone *per se*. Residues were below the LOD (0.005 ppm) in all samples.

MRID# 429321-15: Seven field trials were conducted in seven states which together represented 41% of the U.S. soybean acreage in 1991 (*Agricultural Statistics*, 1992). The application rate of sulfentrazone 4F was 0.5 lbs. ai/A (1X) in four trials and 1.5 lbs. ai/A (3X) in three trials. Preplant incorporation was employed in all seven trials. The minimum application volume represented was 16 gal/A. Mature soybean seeds were harvested 101-150 days after planting. After 3-4 months in storage, seeds were analyzed using Method P-2811M, which measures both sulfentrazone and

hydroxymethyl-sulfentrazone. Residues of sulfentrazone were below the LOD (0.005 ppm) and residues of hydroxymethyl-sulfentrazone were below the LOQ (0.025 ppm) in all samples (Table 14). Detectable residues of hydroxymethyl-sulfentrazone were observed in three trials.

Table 14- Results of field residue trials for soybean seed.

Trial	Application Rate	Application Volume (Gal/A)	PHI (Days)	Maximum Residues (ppm)	
				Sulfentrazone	HMS
GA	1X	20	150	ND	ND
LA	1X	17	148	ND	ND
NE	1X	20	101	ND	<0.025
TN	1X	20	160	ND	<0.025
IL	3X	19	140	ND	ND
MN	3X	20	143	ND	ND
OH	3X	16	137	ND	<0.025

HMS = Hydroxy Methyl Sulfentrazone
ND = Not Detected (<LOD, 0.005 ppm)
<0.025 = Detectable residue below the LOQ

Conclusions: These field trials are adequate to support this EUP application only. For the permanent tolerance petition, the registrant should submit the results of at least 20 field trials in which forage, hay and seed samples are analyzed with methodology which measures sulfentrazone and all metabolites determined to be of regulatory concern. These trials should include adequate geographic representation using the maximum application rate, minimum PHI and minimum application volume (10 gal/A).

The Section F submitted by the registrant is not adequate for this EUP. As written, the parent compound is not included. The tolerance expression must be revised to include both sulfentrazone and hydroxymethyl-sulfentrazone. The common name of the parent compound and the preferred systemic names of sulfentrazone (N-[2,4-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]phenyl]methanesulfonamide)) and hydroxymethyl-sulfentrazone (N-[2,4-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-hydroxymethyl-5-oxo-1H-1,2,4-triazol-1-yl]phenyl]methanesulfonamide) should be included. Also, the level of the tolerance should be at least the sum of the LOQ of all compounds included. In this case, the LOQ for sulfentrazone and hydroxymethyl-sulfentrazone is 0.025 each, for a total of 0.050 ppm. **A revised Section F is required.** For the permanent tolerance petition, Section F will have to be revised to include all metabolites determined to be of regulatory concern and to include proposed tolerances for hay and forage.

Magnitude of the Residue- Processed Fractions

Submitted with this petition:

> Magnitude of the Residue of FMC 97285 in/on Processed Parts. MRID# 429321-16

Two soybean fields were treated with sulfentrazone 4F at a rate of 3X by preplant incorporation or preemergence application. Mature soybean seeds were harvested and analyzed using Method P-2689M, which measures only sulfentrazone *per se*. Residues were below the LOD (0.005 ppm) in all samples. Seeds were processed at Texas A & M and analyzed with Method P-2718M. Residues were below the LOD (0.005 ppm) in all samples. The maximum storage interval for the processed fractions was 46 days.

Conclusions: This processing study is not adequate to support this EUP application. The need for feed/food additive tolerances can not be determined because the samples were not analyzed for the sulfentrazone metabolite included in the tolerance expression (hydroxymethyl-sulfentrazone). As this metabolite is organosoluble and was detected in seed samples from the field trials, it is possible that significant residues would be present in the oil fractions. **For this EUP, the registrant should repeat this processing study and analyze the samples with Method P-2811M which measures both sulfentrazone and hydroxymethyl-sulfentrazone.** Alternatively, the samples from this study could be reanalyzed using this method provided some evidence of storage stability could be provided. If residues are found to concentrate, then the appropriate temporary feed/food additive tolerances should be proposed. For the permanent tolerance petition, the registrant must submit the results of processing studies in which the samples were analyzed using methodology which measures sulfentrazone and all metabolites determined to be of regulatory concern and, if necessary, propose the appropriate feed/food additive tolerances.

Magnitude of the Residue- Animals

No studies were submitted with this petition.

The magnitude of the residue in animals has not been reported. This data will not be required for this EUP due to the label restrictions against the feeding of treated RACs to livestock and the limited number of acres involved. However, acceptable magnitude of the residue studies in ruminants and poultry will be required for the permanent tolerance petition. If there are significant sulfentrazone metabolites formed in soybean RACs which are not also formed in animals, then CBTS may also require feeding studies using any such metabolites.

cc (with confidential appendix): PP#3G04272, Kramer, R.F.
cc (without confidential appendix):circ.
RDI: P.V. Errico (4/14/94), R.A. Loranger (4/19/94)
G.F. Kramer:804T:CM#2:(703)305-5079:7509C

Substantive Review

Page 30 is not included in this copy.

Pages _____ through _____ are not included in this copy.

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.

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.

Attachment:

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Sulfentrazone*

CODEX NO. _____

CODEX STATUS:

[] No Codex Proposal
Step 6 or Above

Residue (if Step 8): _____

PROPOSED U.S. TOLERANCES:

Petition No. 3G04272

CBTS Reviewer G.F. Kramer

Residue: Hydroxymethyl-
Sulfentrazone$

Crop(s)	Limit (mg/KG)

Crop(s)	Limit (mg/KG)
Soybeans	0.025

CANADIAN LIMITS:

[] No Canadian Limits

Residue: _____

Crop(s)	Limit (mg/KG)

MEXICAN LIMITS:

[] No Mexican Limits

Residue: _____

Crop(s)	Limit (mg/KG)

NOTES

*FMC 97285 (F6285, N-[2,4-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]phenyl]methanesulfonamide.

$N-[2,4-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-hydroxymethyl-5-oxo-1H-1,2,4-triazol-1-yl]phenyl]methanesulfonamide)

Received unacceptable

Page _____ is not included in this copy.

Pages 32 through 38 are not included in this copy.

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.

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.
