PP# 4407
9-19-95

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

SEP 19 1995

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP# 4F04407. Sulfentrazone (Authority 75 DF Herbicide) for Use on Soybeans. Amendment of 5/17/95. MRID#s 436510-10 thru -16 & 436565-01. Barcode D217390. CBTS# 15851.

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And

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FMC has submitted an application for permanent tolerances for the combined residues of the herbicide 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 its major metabolite 3-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 end use product, Authority 75DF Herbicide, is to be registered for use on soybeans. To cover use on the primary crop, the petitioner has proposed the following tolerances (expressed as parent plus the metabolite 3-hydroxymethyl sulfentrazone):

Soybean Seed	--	0.05 ppm
Aspirated Grain Fractions	--	0.05 ppm

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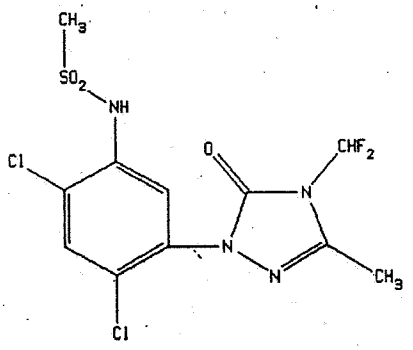
For residues in rotational crops, the petitioner has proposed the following tolerances (expressed as parent plus the metabolites 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone [N-[2,4-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-5-oxo-1H-1,2,4-triazol-1-yl]phenyl]methanesulfonamide]):

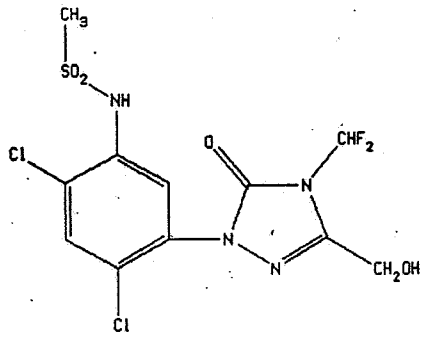
Wheat Forage	--	0.10 ppm
Wheat Straw	--	0.10 ppm
Wheat Grain	--	0.10 ppm
Corn Fodder	--	0.10 ppm
Corn Silage	--	0.10 ppm
Corn Grain	--	0.10 ppm

The current amendment addresses deficiencies pertaining to the magnitude of the residue in rotational crops, the nature of the residue in soybeans and analytical methodology for rotational crops which were identified in CBTS's previous review (Memo, G. Kramer 4/3/95).

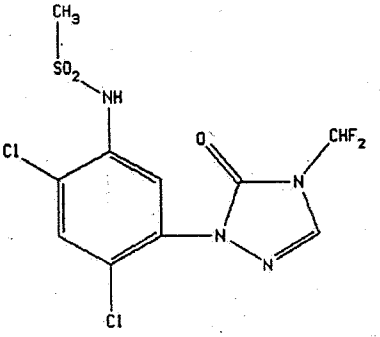
The structures of sulfentrazone and its metabolites are shown below:



Sulfentrazone



3-Hydroxymethyl Sulfentrazone



3-Desmethyl Sulfentrazone

RECOMMENDATIONS

CBTS recommends against the proposed tolerances for residues of sulfentrazone and 3-hydroxymethyl sulfentrazone on soybeans and for residues of sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone on corn and wheat RACs for reasons detailed in conclusions 1b, 1c, 2b, 2c, 3c, 4b, 5b, 5d, 5f, 5g and 6b below and conclusions 1a-f, 2a-d, 3c, 10b, 10d, 11, 12c, 14b, 14c and 15 of Memo, G. Kramer 4/3/95.

CONCLUSIONS

1a. Together with the residue data submitted with this amendment and that submitted previously, the registrant has provided the results of nine rotational wheat residue trials, conducted in Regions 2 (3 trials), 4 (2 trials), and 5 (4 trials). The total of sulfentrazone and its metabolites was a maximum of 0.088 ppm in forage and 0.097 ppm in straw. No residues were detected in grain.

1b. Rotational crop tolerances are required for wheat. The required number of field trials required to set rotational crop tolerances is the same as that required to establish primary crop tolerances (i.e., 20 for wheat- see *EPA Guidance on Number and Location of Domestic Crop Field Trials for Establishment of Pesticide Residue Tolerances, 6/2/94).*

1c. CBTS is unable to comment on the adequacy of the proposed wheat tolerances until receipt and review of the requested residue data. If the wheat field residue data submitted with this petition are to be used for setting rotational crop tolerances, then the registrant must demonstrate the stability of sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone in wheat RACs (conclusion 12c of Memo, G. Kramer 4/3/95).

2a. Together with the residue data submitted with this amendment and that submitted previously, the registrant has provided the results of 13 rotational field corn residue trials, conducted in Regions 2 (2 trials), 4 (3 trials), and 5 (8 trials). The total of sulfentrazone and its metabolites was a maximum of 0.060 ppm in forage and 0.028 ppm in fodder. No residues were detected in grain.

2b. Rotational crop tolerances are required for field corn. The required number of field trials required to set rotational crop tolerances is the same as that required to establish primary crop tolerances (i.e., 20 for field corn- see *EPA Guidance on Number and Location of Domestic Crop Field Trials for Establishment of Pesticide Residue Tolerances, 6/2/94).*

2c. CBTS is unable to comment on the adequacy of the proposed corn tolerances until receipt and review of the requested residue data. If the field corn residue data submitted with this petition are to be used for setting rotational crop tolerances, then the registrant must demonstrate the stability of sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone in corn RACs (conclusion 12c of Memo, G. Kramer 4/3/95).

3a. The registrant has provided the results of four rotational rice field trials conducted in Region 4. The total of sulfentrazone and its metabolites was a maximum of 0.073 ppm in straw and 0.032 ppm in grain. Rotational crop tolerances are thus required for rice. The required number of field trials required to set rotational crop tolerances is the same as that required to establish primary crop tolerances (i.e., 16 for rice- see *EPA Guidance on Number and Location of Domestic Crop Field Trials for Establishment of Pesticide Residue Tolerances, 6/2/94)*.

3b. If the rice residue data submitted with this petition are to be used for setting rotational crop tolerances, then the registrant must demonstrate the stability of sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone in corn and wheat RACs (conclusion 12c of Memo, G. Kramer 4/3/95). The corn and wheat data can be translated to rice RACs.

3c. Based on the results of this study, rotational crop residue trials will also be required to support the proposed interval for barley. Until the required data for rotational barley, rice and peanuts are submitted, all plantback intervals of 1 year or less should be removed from the sulfentrazone label, except for soybeans, wheat and corn.

4a. The nature of the residue in soybeans is now considered to be understood. The major metabolites are 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone, accounting for 38-50% and 13% of the TRR in forage, 9-23% and 26-27% of the TRR in hay and 30-35% and 4% of the TRR in seed, respectively. Other metabolites identified include sulfentrazone carboxylic acid, desmethylsulfonyl sulfentrazone, desdifluoromethyl desmethyl sulfentrazone, desdifluoromethyl sulfentrazone and methyl triazole.

4b. CBTS will refer to the Metabolism Committee on the toxicological significance of the sulfentrazone metabolites. A decision by CBTS concerning which residues to regulate will then follow. A tolerance based on the parent and 3-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.

5a. The registrant has submitted Method P-2982M for wheat (MRID# 436510-14). The limit of detection (LOD) was reported to be 0.005 ppm for sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-

desmethyl sulfentrazone. The limit of quantitation (LOQ) was reported to be 0.025 ppm for sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone.

5b. An ILV of this method was performed by North Coast Laboratories. Acceptable recoveries were obtained by the laboratory for all analytes. The method and ILV have been sent to Beltsville for PMV (Memo, G. Kramer 8/30/95). CBTS will withhold a final conclusion on the adequacy of this method as an analytical enforcement method pending receipt of the PMV report.

5c. Reports on Multiresidue testing for both desdifluoromethyl desmethyl sulfentrazone and 3-desmethyl sulfentrazone (MRID# 436510-13) have been received and forwarded to FDA (Memo, G. Kramer 8/30/95). Neither compound was recovered by any of the protocols.

5d. Radiovalidation should be performed by running the entire method on barley samples from the confined rotational crop study.

5e. The registrant has included conditions for use of a MSD detector in order to confirm the identity of the analytes. A specificity study will not be required since the confirmatory method is specific for the analytes (MS).

5f. The registrant employed a different analytical method for each corn RAC. These methods closely resembled either the proposed enforcement methods for soybeans or wheat RACs with the exception that sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone are measured in a <u>single</u> GC run. Due to the similarity to these other methods, CBTS does not feel that an ILV is necessary for the corn methods. The registrant should submit the complete protocol for the corn methodology so that a PMV can be requested.

5g. The method employed for rice grain was the same as the corn grain method. The method employed for sulfentrazone and 3-desmethyl sulfentrazone in rice straw was the same as the corn forage method with the exception that only two analytes were determined. The method employed for 3-hydroxymethyl sulfentrazone in straw was very similar to the wheat method for 3-hydroxymethyl sulfentrazone. As the rice methods closely resemble those employed for wheat and corn, CBTS will not require that they be validated (ILV and PMV). The registrant should, however, include the rice procedures in the requested protocol for the corn methodology.

6a. The corn grain samples from five of the 1993 limited field trials were composited and shipped to TX A&M for processing. The bulk grain samples were processed into grits, meal, flour, crude oil and refined oil by dry milling; and into starch, crude oil and refined oil by wet milling. The maximum storage interval was 3 months. Samples were analyzed by the corn grain method. No residues of sulfentrazone or its metabolites were detectable in

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grain or any processed fraction.

6b. Provided that the storage stability of sulfentrazone and its metabolites can be demonstrated in corn grain and processed fractions, CBTS concludes that food/feed additive tolerances will not be required for rotational corn.

DETAILED CONSIDERATIONS

Rotational Crop Studies: GLN § 165-2

The sulfentrazone label contains the following rotational crop restrictions: winter wheat, 4 months; spring wheat, 9 months; field corn, 10 months; barley, peanuts, rice and tobacco, 12 months; canola, corn (pop, seed and sweet), cotton and sorghum, 18 months; all other crops, 24 months.

Deficiency - Conclusion 4a (from Memo, G. Kramer 4/3/95)

4a. The registrant has submitted the results of five limited field rotational trials for corn and six for winter wheat. No quantifiable residues were observed in field corn so that rotational crop tolerances are not required for corn with a 10 month or greater plantback interval. However, quantifiable residues of 3-hydroxymethyl sulfentrazone were observed in winter wheat forage so that rotational crop tolerances are required for wheat. The required number of field trials required to set rotational crop tolerances is the same as that required to establish primary crop tolerances (i.e., 20 for wheat).

Petitioner's Response: Submission of:

> Magnitude of the Residue of Sulfentrazone and its Metabolites in/on Winter Wheat as a Rotated Crop Following Soybeans which were Treated with F6285 75DF at 0.375 Pounds Active per Acre. MRID# 436510-10
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> Magnitude of the Residue of Sulfentrazone and its Metabolites in/on Field Corn as a Rotated Crop Following Soybeans which were Treated with F6285 75DF at 0.375 Pounds Active per Acre. MRID# 436510-11

Wheat: Four limited field trials were conducted in the states of GA (2), OH and MS in 1993. Sulfentrazone 75 DF was applied at a rate of 0.375 lbs. ai/A (1X). Preplant soil incorporation (PPI) was employed in two trials and preemergence application was used in two trials. Soybeans were planted, grown and harvested. Rotational winter wheat was planted 100-125 days after sulfentrazone application. Wheat forage was harvested 60-192 days after planting; wheat grain and straw, 233-296 days after planting. After harvest, samples were stored frozen until analysis using

method P-2982M. The maximum storage interval was 13 months for forage and 7 months for straw and grain. The method was validated in wheat forage, straw and grain over a range of 0.025-0.10 ppm. The average recovery for sulfentrazone was 87 ± 11% (n=16); for 3-desmethyl sulfentrazone, 88 ± 14% (n=16); for 3-hydroxymethyl sulfentrazone, 74 ± 7% (n=14); and for desmethyl desdifluoromethyl sulfentrazone, 109 ± 17% (n=6). Analysis of the treated samples showed that the total of sulfentrazone and its metabolites was a maximum of 0.088 ppm in forage and 0.097 ppm in straw (Table 1). No residues were detected in grain.

Table 1- Results of limited field trials for winter wheat in which Sulfentrazone 75DF was applied to the primary crop at a rate of 0.375 lbs. ai/A. Values of 0.005-0.025 ppm are above the LOD, but below the LOQ.

Location	DAT[1]	RAC	Crop Age (Days)	Maximum Residue (ppm)				
				Sulfent.	DMS	HMS	DDS	Total
OH[3]	100	Forage	61	ND	ND	0.023	0.01	0.033
		Grain	296	ND	ND	ND	NA	ND
		Straw	296	0.005	ND	0.006	NA	0.011
GA[3]	126	Forage	63	ND	0.008	0.011	0.01	0.029
		Grain	233	ND	ND	ND	NA	ND
		Straw	233	0.024	0.035	0.023	NA	0.082
GA[2]	125	Forage	61	0.007	0.029	0.052	ND	**0.088**
		Grain	266	ND	ND	ND	NA	ND
		Straw	266	0.068	0.011	0.011	NA	0.090
MS[2]	123	Forage	192	0.016	0.046	0.009	0.01	0.081
		Grain	247	ND	ND	ND	NA	ND
		Straw	247	0.038	0.030	0.029	NA	**0.097**

[1]Days after treatment of soil with sulfentrazone when wheat was planted
[2]Sulfentrazone applied by preplant incorporation, [3]Sulfentrazone applied preemergence
ND = Not Detected; i.e., below the LOD (0.005 ppm for sulfentrazone, HMS and DMS; 0.01 ppm for DDS).
HMS = Hydroxy Methyl Sulfentrazone
DMS = Des-Methyl Sulfentrazone
DDS = Desmethyl Des(difluoromethyl) Sulfentrazone

Conclusions: The registrant previously submitted the results of five rotational wheat trials (Memo G. Kramer 4/3/95). Together with the residue data submitted with this amendment, the registrant has provided the results of nine wheat trials, conducted in Regions 2 (3 trials), 4 (2 trials), and 5 (4 trials). The total of sulfentrazone and its metabolites was a maximum of 0.088 ppm in

forage and 0.097 ppm in straw. No residues were detected in grain.

Rotational crop tolerances are required for wheat. The required number of field trials required to set rotational crop tolerances is the same as that required to establish primary crop tolerances (i.e., 20 for wheat- see *EPA Guidance on Number and Location of Domestic Crop Field Trials for Establishment of Pesticide Residue Tolerances, 6/2/94).*

CBTS is unable to comment on the adequacy of the proposed wheat tolerances until receipt and review of the requested residue data. If the wheat field residue data submitted with this petition are to be used for setting rotational crop tolerances, then the registrant must demonstrate the stability of sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone in wheat RACs (conclusion 12c of Memo, G. Kramer 4/3/95).

Corn: Seven limited field trials were conducted in the states of IA (2), LA (2), OH, NE and IL in 1993. Sulfentrazone 75 DF was applied at a rate of 0.375 lbs. ai/A (1X). Preplant soil incorporation (PPI) was employed in four trials and preemergence application was used in three trials. Soybeans were planted, grown and harvested. Rotational field corn was planted 10-11 months after sulfentrazone application. Corn forage was harvested 91-134 days after planting; corn grain and fodder, 144-173 days after planting. After harvest, samples were stored frozen until analysis. The maximum storage interval was 8 months. Samples were analyzed by extraction in acetone/0.25 N HCl (75/25, v/v) with refluxing. After filtration, the grain samples were cleaned-up using a C-8 SPE column. The samples were then derivatized with N,O-bis-(trimethylsilyl)-trifluoroacetamide (BSTFA), cleaned-up using a silica SPE column and analyzed by GC-ECD. Samples of forage were cleaned-up using solvent partitioning with dichloromethane. The samples were then derivatized with BSTFA, cleaned-up using a silica SPE column and analyzed by GC-ECD. Samples of fodder were cleaned-up using C-8 and silica SPE columns. The samples were then derivatized with BSTFA, cleaned-up using a silica SPE column and analyzed by GC-ECD. All three analytes were quantified in a single GC run. The LOD was reported to be 0.005 ppm and the LOQ was reported to be 0.025 ppm. These methods were validated in corn silage, fodder and grain at 0.025-0.125 ppm. The average recovery for sulfentrazone was 89 ± 17% (n=19); for 3-desmethyl sulfentrazone, 102 ± 14% (n=19); and for 3-hydroxymethyl sulfentrazone, 89 ± 15% (n=19). Analysis of the treated samples showed that the total of sulfentrazone and its metabolites was a maximum of 0.060 ppm in forage and 0.028 ppm in fodder (Table 2). No residues were detected in grain.

Table 2- Results of limited field trials for field corn in which Sulfentrazone 75DF was applied to the primary crop at a rate of 0.375 lbs. ai/A. Values of 0.005-0.025 ppm are above the LOD, but below the LOQ.

Location	MAT[1]	RAC	Crop Age (Days)	Maximum Residue (ppm)			
				Sulfent.	DMS	HMS	Total
IA[3]	10	Forage	134	0.019	0.012	ND	0.031
		Grain	166	ND	ND	ND	ND
		Fodder	166	ND	ND	ND	ND
IA[2]	10	Forage	134	0.012	0.031	ND	0.043
		Grain	166	ND	ND	ND	ND
		Fodder	166	ND	ND	ND	ND
NE[3]	11	Forage	119	ND	0.017	0,007	0.024
		Grain	153	ND	ND	ND	ND
		Fodder	153	ND	ND	ND	ND
IL[2]	11	Forage	114	0.006	0.054	ND	**0.060**
		Grain	144	ND	ND	ND	ND
		Fodder	144	ND	ND	ND	ND
LA[3]	9	Forage	91	ND	ND	ND	ND
		Grain	147	ND	ND	ND	ND
		Fodder	147	ND	0.016	ND	0.016
LA[2]	9	Forage	91	0.005	ND	ND	0.005
		Grain	147	ND	ND	ND	ND
		Fodder	147	ND	0.028	ND	**0.028**
OH[2]	10	Forage	134	0.008	0.019	ND	0.027
		Grain	173	ND	ND	ND	ND
		Fodder	173	ND	ND	ND	ND

[1]Months after treatment of soil with sulfentrazone when wheat was planted
[2]Sulfentrazone applied by preplant incorporation, [3]Sulfentrazone applied preemergence
ND = Not Detected; i.e., below the LOD (0.005 ppm).
HMS = Hydroxy Methyl Sulfentrazone
DMS = Des-Methyl Sulfentrazone

Conclusions: The registrant previously submitted the results of six rotational field corn trials (Memo G. Kramer 4/3/95). Together with the residue data submitted with this amendment, the registrant has provided the results of 13 field corn trials, conducted in Regions 2 (2 trials), 4 (3 trials), and 5 (8 trials). The total of sulfentrazone and its metabolites was a maximum of 0.060 ppm in

forage and 0.028 ppm in fodder. No residues were detected in grain.

Rotational crop tolerances are required for field corn. The required number of field trials required to set rotational crop tolerances is the same as that required to establish primary crop tolerances (i.e., 20 for field corn- see *EPA Guidance on Number and Location of Domestic Crop Field Trials for Establishment of Pesticide Residue Tolerances, 6/2/94)*.

CBTS is unable to comment on the adequacy of the proposed corn tolerances until receipt and review of the requested residue data. If the field corn residue data submitted with this petition are to be used for setting rotational crop tolerances, then the registrant must demonstrate the stability of sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone in corn RACs (conclusion 12c of Memo, G. Kramer 4/3/95).

Deficiency - Conclusion 4b (from Memo, G. Kramer 4/3/95)

4b. The sulfentrazone label allows rotational barley, peanuts and rice to be planted at 12 months. However, limited field trials are required for these crops in order to determine whether rotational crop tolerances are required. If two limited trials are performed with barley or rice and no quantifiable residues are observed, then it will be concluded that rotational crop tolerances are not required for either crop. Until the required data for rotational barley, rice and peanuts are submitted, all plantback intervals of 1 year or less should be removed from the sulfentrazone label, except for soybeans, wheat and corn.

Petitioner's Response: Submission of:

> Magnitude of the Residue of Sulfentrazone and its Metabolites in/on Rice as a Rotated Crop Following Harvest of Soybeans which were Treated with F6285 75DF at 0.375 Pounds Active per Acre. MRID# 436510-12

Rice: Four limited field trials were conducted in the states of AR (2) and MS (2) in 1993. Sulfentrazone 75 DF was applied at a rate of 0.375 lbs. ai/A (1X). Preplant soil incorporation (PPI) was employed in two trials and preemergence application was used in two trials. Soybeans were planted, grown and harvested. Rotational rice was planted 200-302 days after sulfentrazone application. Rice grain and straw was harvested 91-134 days after planting. After harvest, samples were stored frozen until analysis. The maximum storage interval was 7 months for grain and 8 months for straw. Rice grain samples were analyzed for sulfentrazone, 3-desmethyl sulfentrazone and 3-desmethyl sulfentrazone by extraction in acetone/0.25 N HCl (70/30, v/v) with refluxing. After filtration, the samples were cleaned-up using a silica SPE column. The samples were then derivatized with BSTFA, cleaned-up using a silica SPE column and analyzed by GC-ECD in a single run. Rice

straw samples were analyzed for sulfentrazone and 3-desmethyl sulfentrazone by extraction in acetone/0.25 N HCl (3/1, v/v) with refluxing. After filtration, the samples were cleaned-up using solvent partitioning with dichloromethane. The samples were then derivatized with BSTFA, cleaned-up using a silica SPE column and analyzed by GC-ECD. Rice straw samples were analyzed for 3-hydroxymethyl sulfentrazone by extraction in acetone/0.25 N HCl (3/1, v/v) with refluxing. After filtration, the samples were cleaned-up using a hexane wash and solvent partitioning with dichloromethane. The samples were then derivatized with BSTFA, cleaned-up using a silica SPE cclumn and analyzed by GC-ECD. The LOD was reported to be 0.005 ppm for grain and 0.01 ppm for straw. The LOQ was reported to be 0.025 ppm for grain and 0.05 ppm for straw. However, based on the similarity of these methods to those submitted for wheat straw and corn fodder and on the submitted chromatograms, CBTS concludes that 0.025 ppm is the appropriate LOQ for rice straw. Analysis of the treated samples showed that the total of sulfentrazone and its metabolites was a maximum of 0.073 ppm in straw and 0.032 ppm in grain (Table 3).

Table 3- Results of limited field trials for rice in which Sulfentrazone 75DF was applied to the primary crop at a rate of 0.375 lbs. ai/A. Values of 0.005-0.025 ppm are above the LOD, but below the LOQ.

Location	DAT[1]	RAC	Crop Age (Days)	Maximum Residue (ppm)			
				Sulfent.	DMS	HMS	Total
AR[3]	302	Straw	150	ND	0.013	ND	0.013
		Grain	150	ND	ND	ND	ND
AR[2]	301	Straw	151	ND	0.017	0.012	0.029
		Grain	166	ND	ND	0.007	0.007
MS[3]	300	Straw	174	ND	0.036	0.037	**0.073**
		Grain	174	ND	0.012	0.016	0.028
MS[2]	300	Straw	174	ND	0.045	0.021	0.066
		Grain	174	ND	0.012	0.020	**0.032**

[1]Days after treatment of soil with sulfentrazone when wheat was planted
[2]Sulfentrazone applied by preplant incorporation, [3]Sulfentrazone applied preemergence
ND = Not Detected; i.e., below the LOD (0.005 ppm).
HMS = Hydroxy Methyl Sulfentrazone
DMS = Des-Methyl Sulfentrazone

Conclusions: The registrant has provided the results of four rotational rice field trials conducted in Region 4. The total of sulfentrazone and its metabolites was a maximum of 0.073 ppm in straw and 0.032 ppm in grain. Rotational crop tolerances are thus

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required for rice. The required number of field trials required to set rotational crop tolerances is the same as that required to establish primary crop tolerances (i.e., 16 for rice- see *EPA Guidance on Number and Location of Domestic Crop Field Trials for Establishment of Pesticide Residue Tolerances, 6/2/94)*. If the rice residue data submitted with this petition are to be used for setting rotational crop tolerances, then the registrant must demonstrate the stability of sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone in corn and wheat RACs (conclusion 12c of Memo, G. Kramer 4/3/95). The corn and wheat storage stability data can be translated to rice RACs.

Based on the results of this study, rotational crop residue trials will also be required to support the proposed interval for barley. Until the required data for rotational barley, rice and peanuts are submitted, all plantback intervals of 1 year or less should be removed from the sulfentrazone label, except for soybeans, wheat and corn.

Nature of Residue- Plants

The structures of the sulfentrazone metabolites which have been identified in soybean RACs are shown in figure 1.

Deficiency - Conclusion 5 (from Memo, G. Kramer 4/3/95)

5. The petitioner must address the following deficiencies in the soybean metabolism study: 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.

Petitioner's Response: Submission of:

Nature of the Residue in Plants: Soybean Metabolism of ^{14}C-F6285. MRID# 436565-01

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i) The dates of extraction and analysis were provided. All samples were analyzed within 6 months of harvest.

ii) Using HPLC co-chromatography with synthetic standards and GC/MS, Unknowns 2, 3, 5 and 6 were identified as desdifluoromethyl desmethyl sulfentrazone (2); desdifluoromethyl sulfentrazone (3) and sulfentrazone *per se* (5 and 6). The revised summary of metabolite identification is shown in Table 4.

iii) The uncharacterized polar fraction of the triazole-labelled samples was separated into four peaks by HPLC. The major peak coeluted with a synthetic standard of methyl triazole. None of the other peaks accounted for more than 0.05 ppm.

iv) The uncharacterized bound residues were treated sequentially with a 6 N HCl reflux, 4.3 N KOH and 38% H_2SO_4. The remaining bound residues were <10% of the TRR in all samples. No single fraction of the released residue exceeded 10% of the TRR in any sample.

Table 4- 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
Sulfentrazone	0.012	1.2	0.011	1.1	0.050	4.7	0.045	4.5	0.012	13.8	0.004	2.5
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
DDS	0.061	5.8	0.076	7.4	0.065	6.0	0.076	7.6	0.005	5.9	0.009	5.2
DFMS	0.023	2.1	0.088	8.6	0.105	9.8	0.110	10.9	0.001	0.7	0.007	4.0
Methyl Triazole	ND	-	0.112	10.9	ND	-	0.029	2.9	ND	-	0.019	11.2
Bound	0.157	14.9	0.133	13.0	0.288	26.8	0.260	25.8	0.026	30.8	0.039	22.9
Total Identified	**0.780**	**73.7**	**0.827**	**80.4**	**0.751**	**70.0**	**0.664**	**66.0**	**0.049**	**56.2**	**0.107**	**62.6**

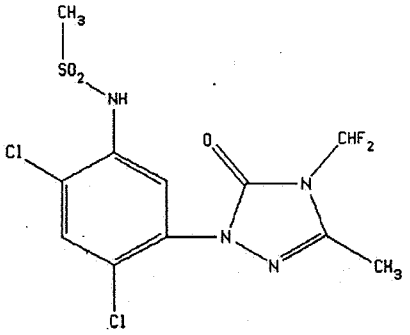
SCA = Sulfentrazone Carboxylic Acid
HMS = Hydroxy Methyl Sulfentrazone
DMS = Des-Methyl Sulfentrazone
DMSS = Des-MethylSulfonyl Sulfentrazone
DDS = Des-Difluoromethyl-Des-Methyl Sulfentrazone
DFMS = Des-difluoromethyl Sulfentrazone

CBTS's Conclusions: The nature of the residue in soybeans is now considered to be understood. The major metabolites are 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone, accounting for 38-50% and 13% of the TRR in forage, 9-23% and 26-27% of the TRR in hay and 30-35% and 4% of the TRR in seed, respectively. Other metabolites identified include sulfentrazone

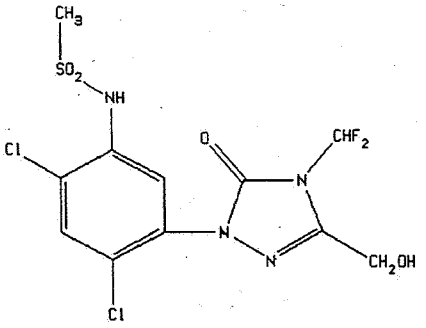
carboxylic acid, desmethylsulfonyl sulfentrazone, desdifluoromethyl desmethyl sulfentrazone, desdifluoromethyl sulfentrazone and methyl triazole. Sulfentrazone is thus metabolized via four different pathways: 1) Oxidation of the 3-methyl group to form 3-hydroxymethyl sulfentrazone, followed by further oxidation to form sulfentrazone carboxylic acid which is decarboxylated to 3-desmethyl sulfentrazone. 2) Hydrolysis of the trifluoromethyl group to form desdifluoromethyl sulfentrazone which is oxidized and decarboxylated to form desdifluoromethyl desmethyl sulfentrazone. 3) Hydrolysis of the sulfonamide group to form desmethylsulfonyl sulfentrazone. and 4) Scission of the phenyl and triazole rings to produce methyl triazole. The corresponding phenyl metabolites are believed to remain bound. These pathways are shown in figure 2 (copied from p. 270 of MRID# 436565-01).

CBTS will refer to the Metabolism Committee on the toxicological significance of the sulfentrazone metabolites. A decision by CBTS concerning which residues to regulate will then follow. A tolerance based on the parent and 3-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.

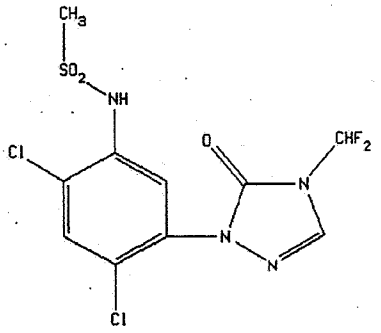
Figure 1- Structures of Sulfentrazone Metabolites Identified in Soybeans.



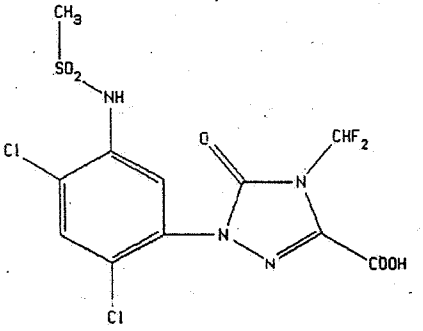
Sulfentrazone



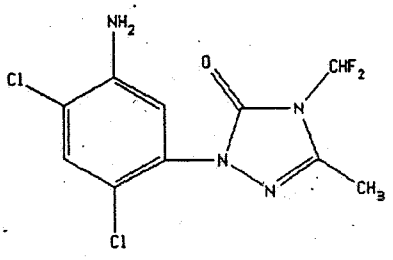
3-Hydroxymethyl Sulfentrazone



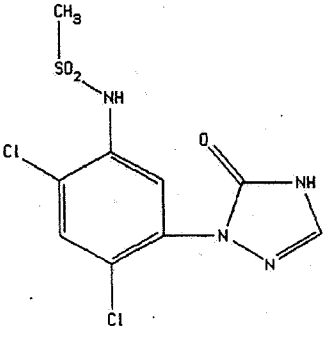
3-Desmethyl Sulfentrazone



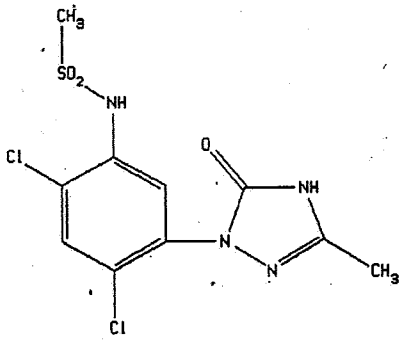
Sulfentrazone Carboxylic Acid



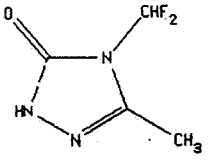
Desmethylsulfonyl Sulfentrazone



Desdifluoromethyl Desmethyl Sulfentrazone



Desdifluoromethyl Sulfentrazone



Methyl Triazole

Analytical Methodology- Rotational Crops

Deficiency - Conclusion 10g (from Memo, G. Kramer 4/3/95)

10g. The analytical methods used for rotational wheat RACs differed significantly from the proposed enforcement method for soybeans. CBTS thus requests that these methods be validated by an independent laboratory. Once we receive the ILV, the method will be forwarded to ACL for Agency validation.

Petitioner's Response: Submission of Method P-2982M for Wheat (MRID# 436510-14).

Procedure: Samples were analyzed for sulfentrazone and 3-desmethyl sulfentrazone by extraction in acetone/0.25 N HCl (70/30, v/v) with refluxing. After filtration, the samples were cleaned-up using C-8 and silica SPE columns. The samples were then analyzed by GC-ECD. Samples were analyzed for 3-hydroxymethyl sulfentrazone by extraction in acetone/0.25 N HCl (3/1, v/v) with refluxing. After filtration, the samples were cleaned-up using solvent partitioning with dichloromethane followed by silica SPE column chromatography of the organic phase. The samples were then derivatized with BSTFA, cleaned-up using a silica SPE column and analyzed by GC-ECD. Samples of forage were analyzed for desmethyl desdifluoromethyl sulfentrazone by extraction in acetone/0.25 N HCl (3/1, v/v) with refluxing. After filtration, the samples were cleaned-up using C-18 SPE column chromatography. The samples were then derivatized with iodomethane, cleaned-up using a silica SPE column and analyzed by GC-ECD. The limit of detection (LOD) was reported to be 0.005 ppm for sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone and 0.01 ppm for desmethyl desdifluoromethyl sulfentrazone. The limit of quantitation (LOQ) was reported to be 0.025 ppm for sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone and 0.05 ppm for desmethyl desdifluoromethyl sulfentrazone.

Results: The method was validated in wheat forage, straw and grain over a range of 0.025-0.10 ppm. The average recovery for sulfentrazone was 87 ± 11% (n=16); for 3-desmethyl sulfentrazone, 88 ± 14% (n=16); for 3-hydroxymethyl sulfentrazone, 74 ± 7% (n=14); and for desmethyl desdifluoromethyl sulfentrazone, 109 ± 17% (n=6).

ILV: An ILV of this method was performed by North Coast Laboratories. Acceptable recoveries were obtained by the laboratory for all analytes. The method and ILV have been sent to Beltsville for PMV (Memo, G. Kramer 8/30/95). CBTS will withhold a final conclusion on the adequacy of this method as an analytical enforcement method pending receipt of the PMV report.

Multiresidue Method Testing: Reports on Multiresidue testing for both desdifluoromethyl desmethyl sulfentrazone and 3-desmethyl

sulfentrazone (MRID# 436510-13) have been received and forwarded to FDA (Memo, G. Kramer 8/30/95). Neither compound was recovered by any of the protocols.

Radiovalidation: Radiovalidation should be performed by running the entire method on barley samples from the confined rotational crop study.

Confirmatory Method: The registrant has included conditions for use of a MSD detector in order to confirm the identity of the analytes.

Specificity: A specificity study will not be required since the confirmatory method is specific for the analytes (MS).

Corn: The registrant employed a different analytical method for each corn RAC. These methods closely resembled either the proposed enforcement methods for soybeans or wheat RACs with the exception that sulfentrazone, 3-hydroxymethyl sulfentrazone and 3-desmethyl sulfentrazone are measured in a single GC run. Due to the similarity to these other methods, CBTS does not feel that an ILV is necessary for the corn methods. The registrant should submit the complete protocol for the corn methodology so that a PMV can be requested.

RICE: The method employed for rice grain was the same as the corn grain method. The method employed in rice straw for sulfentrazone and 3-desmethyl sulfentrazone was the same as the corn forage method with the exception that only two analytes were determined. The method employed for 3-hydroxymethyl sulfentrazone in straw was very similar to the wheat method for 3-hydroxymethyl sulfentrazone. As the rice methods closely resemble those employed for wheat and corn, CBTS will not require that they be validated (ILV and PMV). The registrant should, however, include the rice procedures in the requested protocol for the corn methodology.

Magnitude of the Residue- Processed Fractions

Submitted with this amendment:

> Magnitude of the Residue of Sulfentrazone and its Metabolites in/on Processed Parts of Corn as a Rotated Crop Following Harvest of Soybeans Treated with F6285 75DF at 0.375 Pounds Active per Acre. MRID# 436510-16

The corn grain samples from five of the 1993 limited field trials (IA, OH, NE and IL) were composited and shipped to TX A&M for processing. The bulk grain samples were processed into grits, meal, flour, crude oil and refined oil by dry milling; and into

starch, crude oil and refined oil by wet milling. After processing, samples were stored frozen until analysis. The maximum storage interval was 3 months. Samples were analyzed by the corn grain method. These methods were validated in corn processed fractions at 0.025-0.10 ppm. The average recovery for sulfentrazone was 91 ± 15% (n=12); for 3-desmethyl sulfentrazone, 102 ± 15% (n=12); and for 3-hydroxymethyl sulfentrazone, 89 ± 16% (n=12). Analysis of the treated samples showed that no residues of sulfentrazone or its metabolites were detectable in grain or any processed fraction.

Conclusion: Provided that the storage stability of sulfentrazone and its metabolites can be demonstrated in corn grain and processed fractions, CBTS concludes that food/feed additive tolerances will not be required for rotational corn.

cc: PP#4F4407, Kramer, Circ., R.F.
RDI: F.B. Suhre (9/8/95), R.A. Loranger (9/18/95), M.S. Metzger (9/19/95)
G.F. Kramer:804V:CM#2:(703)305-5079:7509C:CBTS

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