



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

APR 4 1995

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP# 9F03796. Glyphosate-trimesium (formerly known as Sulfosate) in or on in/on Corn and Animal RACs. Amendments of 6/16/94 & 11/7/94. MRID#s 432981-01, -02 & 432736-01 to -11. Barcodes D205472, D209331, D209332 & D209333. CBTS#s 13993, 14726, 14727 & 15174.

FROM: G.F. Kramer, Ph.D., Chemist
Tolerance Petition Section III *[Signature]*
Chemistry Branch I, Tolerance Support
Health Effects Division (7509C)

THRU: R.B. Perfetti, Ph.D., Acting Section Head
Chemistry Branch I, Tolerance Support
Health Effects Division (7509C) *[Signature: R.B. Perfetti]*

TO: Robert Taylor, Product Manager
Terri Stowe, Team 25 Reviewer
Registration Division (7505C)

And

Jane Smith, Acting Section Head
Registration Section, RCAB
Health Effects Division (7509C)

Zeneca has submitted an application to establish the following tolerances for N-(phosphonomethyl)glycine resulting from the application of the trimethylsulfonium salt (i.e., glyphosate-trimesium):

Corn Grain	--	0.05 ppm	Corn Fodder	--	0.1 ppm
Corn Forage	--	0.1 ppm			
Liver & Kidney*	--	0.1 ppm	Poultry Liver	--	0.1 ppm
Milk	--	0.01 ppm	Eggs	--	0.01 ppm
Fat*	--	0.03 ppm	Poultry Fat	--	0.03 ppm
Meat*	--	0.03 ppm	Poultry Meat	--	0.03 ppm
Meat By-Products* ¹		0.03 ppm	Poultry Meat By-Products ²	--	0.03 ppm

*of cattle, goats, horses, hogs and sheep

¹except liver and kidney

²except liver



Recycled/Recyclable
Printed with Soy/Canola ink on paper that
contains at least 50% recycled fiber

Glyphosate-trimesium (the trimethylsulfonium salt of glyphosate, formerly known as **sulfosate**) is a 1:1 molar salt of N-(phosphonomethyl)glycine anion (PMG) and the trimethylsulfonium cation (TMS) and is formulated as Touchdown Herbicide.

The current amendment addresses deficiencies identified in CBTS' previous review (Memo F. Griffith 9/30/92).

RECOMMENDATIONS

CBTS recommends against the proposed tolerances for residues of glyphosate-trimesium in corn and animal RACs for the reasons detailed in conclusions 1, 7, 8, 9, 10c, 11a and 11b. However, a DRES run can be initiated at this time using the following tolerances:

Corn Grain	--	0.05 ppm	Corn Fodder	--	0.1 ppm
Corn Forage	--	0.1 ppm			
Meat By-Products*		1.0 ppm	Milk	--	0.20 ppm
Fat*	--	0.10 ppm	Meat*	--	0.20 ppm
Poultry Liver	--	0.05 ppm	Eggs	--	0.02 ppm
Poultry Fat	--	0.05 ppm	Poultry Meat	--	0.05 ppm
Poultry Meat By-Products ¹	- 0.10 ppm				

¹except liver

*of cattle, goats, horses, hogs and sheep

CONCLUSIONS

1. The directions for use are adequate with the following exception: Instructions are provided for 'corn,' but the type of corn is not specified. As residue data was not provided for K+CWHR, the label should prohibit use on sweet corn.

2a. The registrant has submitted the results of a ruminant metabolism study in which lactating goats were treated orally with [Phosphonomethylene-¹⁴C]glyphosate-trimesium at a rate of 64 ppm of PMG (93 ppm of glyphosate-trimesium). The TRR was 0.02 ppm in milk and fat, 0.03 ppm in muscle, 5.6 ppm in kidney and 0.2 ppm in liver.

2b. Overall, in the milk samples, 91% of the TRR was identified; in the fat samples, 96% of the TRR was identified; in the liver samples, 81% of the TRR was identified; and in the kidney and muscle samples, 94% of the TRR was identified. The extent of PMG metabolism was limited as the parent accounted for 22% of the TRR

in milk, 91% in fat, 59% in liver, 86% in kidney and 87% in muscle. Incorporation into natural products (i.e., lactose and triglycerides) was observed only in milk. The metabolite AMPA (aminomethyl phosphonic acid) was also a major component of the residue in liver (21% of the TRR).

3a. The registrant has submitted the results of a ruminant metabolism study in which lactating goats were treated orally with [TMS-¹⁴C]glyphosate-trimesium at a rate of 9 ppm of TMS (25 ppm of glyphosate-trimesium). The TRR was 0.42 ppm in milk and fat, 0.54 ppm in muscle and 1.4 ppm in kidney and liver.

3b. Overall, in the milk samples, 44% of the TRR was identified; in the fat samples, 24% of the TRR was identified; in the liver samples, 45% of the TRR was identified; in the kidney, 59% of the TRR was identified; and muscle samples, 62% of the TRR was identified. The extent of TMS metabolism was fairly extensive as the parent accounted for 0% of the TRR in milk, 17% in fat, 19% in liver, 42% in kidney and 39% in muscle. Incorporation into natural products (i.e., choline, methionine and lactose) was observed in all tissues, especially milk.

4a. The registrant has submitted the results of a poultry metabolism study in which laying hens were treated orally with [Phosphonomethylene-¹⁴C]glyphosate-trimesium at a rate of 62 ppm of PMG (91 ppm of glyphosate-trimesium). The TRR was 0.24 ppm in egg yolks, 0.02 in egg whites and fat, 0.03-0.04 ppm in muscle, 2.2 ppm in kidney and 0.44 ppm in liver.

4b. Overall, in the egg yolk samples, 87% of the TRR was identified; in the egg white samples, 22% of the TRR was identified; in the fat samples, 88% of the TRR was identified; in the liver samples, 84% of the TRR was identified; and in the muscle samples, 44-65% of the TRR was identified. The extent of PMG metabolism was limited as the parent accounted for 60% of the TRR in egg yolk, 22% in egg white, 41% in fat, 61% in liver and 39-61% in muscle. Incorporation into natural products (i.e., lipids) was observed only in egg yolk and fat. The metabolite AMPA was also a major component of the residue in liver (22% of the TRR).

5a. The registrant has submitted the results of a poultry metabolism study in which laying hens were treated orally with [TMS-¹⁴C]glyphosate-trimesium at a rate of 7 ppm of TMS (20 ppm of glyphosate-trimesium). The TRR was 0.20 ppm in egg yolks, 0.05 in egg whites, 0.01 ppm in fat, 0.06-0.07 ppm in muscle, 0.11 ppm in kidney and 0.10 ppm in liver.

5b. Overall, in the egg yolk samples, 62% of the TRR was identified; in the egg white samples, 43% of the TRR was identified; in the liver samples, 34% of the TRR was identified; and in the muscle samples, 75% of the TRR was identified. The

extent of TMS metabolism was fairly extensive as the parent accounted for 0% of the TRR in egg white, 18% in egg yolk, 10% in liver and 56% in muscle. Incorporation into natural products (i.e., choline and fatty acids) was observed primarily in egg yolk and liver. The metabolite dimethyl sulfone was also a major component of the residue in liver (20% of the TRR), muscle (19% of the TRR) and egg white (43% of the TRR).

6. The results of the poultry and ruminant metabolism studies are quite similar. In the PMG studies, the parent compound was the primary component of the residue, except for milk in which extensive incorporation into natural products was observed. The metabolite AMPA was observed in all tissues, especially liver (21-22% of the TRR). The HED Metabolism Committee has determined that this metabolite is not of regulatory concern (Memo, G. Otakie 12/7/93). In the TMS studies, the parent compound was the major metabolite identified in muscle, egg yolk and goat liver and kidney. Extensive incorporation into natural products was observed in egg yolk and goat milk, liver and muscle. The metabolite dimethyl sulfone was the predominant residue identified in poultry liver and egg white. However, detectable levels of this metabolite would not be expected due to the exaggerated dose level and the low residues observed (maximum of 0.02 ppm dimethyl sulfone). CBTS thus concludes that the residues of regulatory concern for glyphosate-trimesium in meat, milk and eggs are the parent ions only.

7. The PMV of TMS Method RR 93-105B has been initiated (Memos, G. Kramer 2/17/95 & 3/9/95). CBTS will be unable to recommend in favor of the requested tolerances until a successful PMV of the proposed analytical enforcement method for the TMS moiety in crops has been completed by the EPA laboratory.

8. The PMV of glyphosate Method RR 93-104B has been initiated (Memo, G. Kramer 3/10/95). CBTS will be unable to recommend in favor of the requested tolerances until a successful PMV of the proposed analytical enforcement method for the PMG moiety in meat, milk and eggs has been completed by the EPA laboratory.

9. The PMV of TMS Method RR 93-100B has been initiated (Memo, G. Kramer 3/10/95). CBTS will be unable to recommend in favor of the requested tolerances until a successful PMV of the proposed analytical enforcement method for the TMS moiety in meat, milk and eggs has been completed by the EPA laboratory.

10a. The registrant has submitted the results of 13 corn field trials. The first Touchdown application was a preemergence broadcast application at a rate of 8.0 lbs. ai/A (2X). A second (spot) treatment was made to a 10% area of each plot 30-57 days after the initial treatment. The application rate was 2-20 lbs. ai/A on a treated area basis. Forage samples were harvested from each treated plot 2-8 weeks after the second application. Fodder

and grain samples were obtained at maturity. Analysis of the treated samples showed no quantifiable residues; i.e. <0.1 ppm in forage and fodder and <0.05 ppm in grain for both TMS and PMG.

10b. Between these trials and those submitted previously, the registrant has submitted a total of 25 residue trials. These trials were located in Regions 1 (2 trials), 2 (2 trials), 5 (18 trials), 7 (1 trial), 8 (1 trial) and 10 (1 trial). CBTS concludes that the number of trials and the geographic representation are adequate to establish tolerances for glyphosate-trimesium on corn RACs. The maximum residues observed were <0.1 ppm in forage, 0.13 ppm in fodder and 0.06 ppm in grain for TMS; and <0.1 ppm in forage, <0.1 ppm in fodder and 0.07 ppm in grain for PMG.

10c. These data support the following tolerances for residues of glyphosate-trimesium: corn forage - 0.10 ppm; corn fodder (of which no more than 0.20 ppm is trimethylsulfonium) - 0.30 ppm; and corn grain (of which no more than 0.10 ppm is trimethylsulfonium) - 0.20 ppm. Also, The registrant is proposing to regulate the PMG ion only. However, HED has determined that the TMS cation is also of regulatory concern and that tolerances for glyphosate-trimesium should be expressed as "residues of glyphosate-trimesium (Sulfonium, trimethyl- salt with N-(phosphonomethyl)glycine (1:1)) in or on..." (Memo, G. Kramer et. al. 2/9/95). **A revised Section F is required.** The registrant should also document that "glyphosate-trimesium" is an ANSI acceptable name. If "glyphosate-trimesium" is not an ANSI acceptable name, then the tolerance expression should include only the chemical name.

11a. The maximum ruminant dietary burden for glyphosate-trimesium, 54.4 ppm, results from a dairy cattle diet comprised of soybean RACs (from PP# 3860). CBTS has reviewed a cow feeding study (MRID# 414621-06) in which one of the dosing levels was 50 ppm, very close the estimated ruminant dietary burden (Memo, S. Koepke 5/14/91). Based on these results, the appropriate tolerance levels are:

Meat By-Products*	1.0 ppm		Milk	--	0.20 ppm
Fat*	--	0.10 ppm		Meat*	-- 0.20 ppm

*of cattle, goats, horses, hogs and sheep

The meat and milk tolerances proposed by the registrant are based on the results of the animal metabolism studies. However, CBTS is not willing to establish tolerances based solely on the results of the metabolism studies while ignoring this feeding study, as requested by the registrant. The feeding study is more likely to reflect the real-world situation since cows were used instead of goats and the duration was 28 days instead of 7 days. Also, The registrant is proposing to regulate the PMG ion only. However, HED has determined that the TMS cation is also of regulatory concern and that tolerances for glyphosate-trimesium should be expressed as

"residues of glyphosate-trimesium (Sulfonium, trimethyl- salt with N-(phosphonomethyl)glycine (1:1)) in or on..." (Memo, G. Kramer et. al. 2/9/95). **A revised Section F is required.**

11b. The maximum poultry dietary burden for glyphosate-trimesium, 2.7 ppm, results from a dairy cattle diet comprised of soybean and corn RACs. CBTS has reviewed a poultry feeding study (MRID# 414621-05) in which one of the dosing levels was 5 ppm, similar to the estimated poultry dietary burden (Memo, S. Koepke 5/14/91). Based on these results, the appropriate tolerance levels are:

Poultry Liver	--	0.05 ppm	Eggs	--	0.02 ppm
Poultry Fat	--	0.05 ppm	Poultry Meat	--	0.05 ppm
Poultry Meat By-Products ¹ - 0.10 ppm					

¹except liver

The poultry and egg tolerances proposed by the registrant are based on the results of the animal metabolism studies. However, CBTS is not willing to establish tolerances based solely on the results of the metabolism studies while ignoring this feeding study, as requested by the registrant. The feeding study is more likely to reflect the real-world situation since the duration was 28 days instead of 10 days. Also, The registrant is proposing to regulate the PMG ion only. However, HED has determined that the TMS cation is also of regulatory concern and that tolerances for glyphosate-trimesium should be expressed as "residues of glyphosate-trimesium (Sulfonium, trimethyl- salt with N-(phosphonomethyl)glycine (1:1)) in or on..." (Memo, G. Kramer et. al. 2/9/95). **A revised Section F is required.**

12. There is no Codex proposal, nor Canadian or Mexican limits for residues of glyphosate-trimesium in corn and animal RACs. Therefore, a compatibility issue is not relevant to the proposed tolerance. A copy of the IRLS is attached to this memorandum.

DETAILED CONSIDERATIONS

Deficiency - Conclusion 1b (from Memo F. Griffith 9/30/92)

1b) The petitioner needs to correct the table on the spot application recommendation for the Touchdown Concentrate label.

Petitioner's Response: The petitioner has withdrawn this formulation.

CBTS' Conclusion: This deficiency is now resolved.

Deficiency - Conclusion 1c (from Memo F. Griffith 9/30/92)

1c) The label is unclear as to the number of applications allowed per year.

Petitioner's Response: Any number of applications (broadcast and/or spot treatments) as long as the total does not exceed 4 lbs. ai/A.

CBTS' Conclusion: Generally, labels must specify a maximum number of applications. However, as all applications would be performed early in the growing season (90 day PHI), CBTS concludes that the directions for use are acceptable as is. This deficiency is now resolved.

Other Considerations

Instructions are provided for 'corn,' but the type of corn is not specified. As residue data was not provided for K+CWHR, the label should prohibit use on sweet corn.

Deficiency - Conclusion 3b & 3c (from Memo F. Griffith 9/30/92)

3b) In the sulfosate poultry metabolism study, the petitioner needs to do additional analytical work to characterize and identify the residues, striving to reach at least 90% characterization and identification.

3c) In the sulfosate ruminant metabolism study, we feel there is sufficient residue present in a number of the caprine tissues and fluids that warrant extensive analytical work to strive to characterize and identify at least 90% of the ¹⁴C- sulfosate equivalent residues.

Petitioner's Response: Submission of four new metabolism studies- a goat study with TMS-labelled glyphosate-trimesium, a goat study with PMG-labelled glyphosate-trimesium, a hen study with TMS-labelled glyphosate-trimesium and a hen study with PMG-labelled glyphosate-trimesium.

Nature of Residue in Animals: Ruminants

PMG Label. Submitted with this petition:

The Nature of the Residues of Orally Administered [Phosphonomethylene-¹⁴C]Glyphosate-Trimesium in Goat tissues and Milk. MRID# 432736-01

In-Life Phase: [Phosphonomethylene-¹⁴C]glyphosate-trimesium (50 Ci/mmol) was mixed with cellulose in a dosing capsule and administered orally to a lactating mixed-breed goat (weight of 54.3 kg) with the aid of a balling gun. The goat was dosed at a rate of

64 ppm of PMG (93 ppm of glyphosate-trimesium, 1.7X). Doses were administered twice daily for seven consecutive days. The animals were sacrificed approximately 12-15 hours after administration of the final dose. This portion of the study was conducted at Battelle laboratories, OH.

Quantitation of Total Radioactivity: Milk was collected twice daily and pooled. Tissues were obtained after sacrifice. All results are expressed as PMG equivalents. The distribution of the radioactivity is shown in Table 1. Of the administered radioactivity, 81% was recovered in feces. Another 9% was recovered in the urine and less than 0.2% was recovered in the milk, blood and tissues. The total recovery was 100%. The TRR in tissues and milk is shown in Table 2. The greatest tissue residues were 5.58 ppm in kidney and 0.23 ppm in liver.

Table 1- Recovery of radioactivity from goats following seven consecutive twice daily doses of PMG-labelled glyphosate-trimesium.

Fraction	% of Total Radioactivity Administered
Urine	9.0
Feces	81.0
Milk	0.03
Tissues	0.12
Blood	0.03
GI Tract & Contents	9.3
Cage Rinse	1.4
Total	101

Table 2- TRR in goat milk and tissues following seven consecutive twice daily doses of PMG-labelled glyphosate-trimesium.

Fraction	TRR	
	ppm	% of Total Dose
Fat	0.018	0.00
Kidney	5.58	0.09
Muscle	0.026	0.01
Liver	0.234	0.02
Heart	0.042	0.00
Milk*	0.022	0.01

*Day 7 Sample

Extraction and Fractionation: Tissues (except fat) were extracted

in aqueous 0.1 N HCl and the debris removed by centrifugation. Fat was extracted with water and chloroform. The debris was reextracted using acetonitrile. The extract was partitioned with organic solvents (dichloromethane for kidney and liver, diethyl ether for muscle), dividing the residues into three fractions-organic-soluble, aqueous-soluble and bound (Table 3). Bound residues were removed from milk by precipitation with acetic acid. The pellet was washed with chloroform and water. The majority of the residue in all samples was aqueous-soluble. The levels of bound and organic-soluble residues never exceeded 10% of the TRR and 0.05 ppm.

Table 3- Fractionation of TRR of goats treated with PMG-labelled glyphosate-trimesium.

Sample	Aqueous Soluble		Organic Soluble		Bound	
	ppm	% TRR	ppm	% TRR	ppm	% TRR
Kidney	5.56	99.6	0.01	0.2	<0.01	0.1
Liver	0.21	91.7	0.01	5.7	<0.01	2.7
Muscle	0.02	95.6	<0.01	3.2	<0.01	1.2
Fat	0.03	99.0	<0.01	0.0	<0.01	1.0
Milk ¹	0.01	58.7	<0.01	20.4	<0.01	21.1

¹Day 7 sample

Metabolite Identification: Aqueous-soluble residues were analyzed by HPLC and TLC and the retention times compared with those of possible metabolites (PMG and AMPA). The identity of PMG was further confirmed by GC-MS of peaks isolated from the liver sample. Lactose was identified in the aqueous-soluble residues by HPLC and TLC. Triglycerides were identified in the milk organic-soluble fraction by TLC. All quantitative data was calculated from the values from the HPLC chromatograms.

Nature of the Residue in Kidney: The identification of aqueous-soluble residues in kidney samples is shown in Table 4. PMG was the predominant component of the residue, accounting for 86.3% of the TRR. The metabolite AMPA was also identified, accounting for 7.5% of the TRR.

Table 4- Identification of PMG-labelled metabolites in tissues and milk of goats.

I.D.	Kidney		Liver		Muscle		Fat		Milk ¹	
	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR
PMG	4.82	86.3	0.14	59.4	0.02	87.1	0.03	91.3	<0.01	22.3
AMPA	0.42	7.5	0.05	21.4	<0.01	6.3	<0.01	4.7	<0.01	2.4
Lactose	-		-		-		-		<0.01	25.2
Triglycerides	-		-		-		-		<0.01	20.4
PES Protein	-		-		-		-		<0.01	21.1
Total	5.23	93.8	0.19	80.8	0.02	93.5	0.03	96.0	0.02	91.4

¹Day 7 sample

PES = PostExtraction Solids

Nature of the Residue in Liver: The identification of aqueous-soluble residues in liver samples is shown in Table 4. PMG was the predominant component of the residue, accounting for 59.4% of the TRR. The metabolite AMPA was also identified, accounting for 21.4% of the TRR.

Nature of the Residue in Muscle: The identification of aqueous-soluble residues in muscle samples is shown in Table 4. PMG was the predominant component of the residue, accounting for 87.1% of the TRR. The metabolite AMPA was also identified, accounting for 6.3% of the TRR.

Nature of the Residue in Fat: The identification of aqueous-soluble residues in fat samples is shown in Table 4. PMG was the predominant component of the residue, accounting for 91.3% of the TRR. The metabolite AMPA was also identified, accounting for 4.7% of the TRR.

Nature of the Residue in Milk: The identification of soluble residues in Day 7 milk samples is shown in Table 4. Lactose was the predominant component of the residue, accounting for 25.2% of the TRR. PMG and triglycerides (22.3 and 20.4% of the TRR, respectively) were also identified. The tentative identification of the bound residues as protein is based on the composition of milk and the observed incorporation into lactose and triglycerides.

Bound Residues: As the levels of bound residues never exceeded 10% of the TRR and 0.05 ppm, further analysis was not attempted.

Storage Stability: As the initial HPLC analysis was completed within 4 months of sacrifice, storage stability is not an issue for this study.

TMS Label. Submitted with this petition:

Glyphosate-trimesium: Metabolism in Lactating Goats Following Dosing at 25 mg/kg in the Diet. MRID# 432891-02

In-Life Phase: [TMS-¹⁴C]glyphosate-trimesium (1.98 GBq/mmol) was mixed with gelatin in a dosing capsule and administered orally to a lactating Saanen goat (weight of 45 kg) with the aid of a balling gun. The goat was dosed at a rate of 25 ppm of glyphosate-trimesium (0.5X, 8.9 ppm of TMS). Doses were administered once daily for seven consecutive days. The animals were sacrificed approximately 16 hours after administration of the final dose.

Quantitation of Total Radioactivity: Milk was collected twice daily and pooled. Tissues were obtained after sacrifice. All results are expressed as glyphosate-trimesium equivalents. The distribution of the radioactivity is shown in Table 5. Of the administered radioactivity, 34% was recovered in urine. Another 9% was recovered in the feces and less than 3% was recovered in the milk, blood and tissues. The total recovery was 47%. The unrecovered radioactivity was believed to have been metabolized to methane. This contention was supported by a study in which TMS-labelled glyphosate-trimesium was incubated with rumen fluid and labelled methane was evolved. The TRR in tissues and milk is shown in Table 6. The greatest tissue residues were 1.40 ppm in liver and 1.35 ppm in kidney.

Table 5- Recovery of radioactivity from goats following seven consecutive daily doses of TMS-labelled glyphosate-trimesium.

Fraction	% of Total Radioactivity Administered
Urine	33.70
Feces	9.29
Milk	1.13
Tissues	1.10
GI Tract & Contents	1.39
Cage Rinse	0.47
Total	47.09

Table 6- TRR in goat milk and tissues following seven consecutive daily doses of TMS-labelled glyphosate-trimesium.

Fraction	TRR	
	ppm	% of Total Dose
Liver	1.397	0.38
Kidney	1.353	0.06
Muscle (Forequarter)	0.527	0.23
Muscle (Hindquarter)	0.544	0.38
Peritoneal Fat	0.079	0.02
Subcutaneous Fat	0.152	0.01
Perirenal Fat	0.217	0.01
Milk*	0.422	1.13

*Day 7 Sample

Extraction and Fractionation: Tissues (except fat) were extracted in aqueous 0.1 N HCl and the debris removed by centrifugation. The liver debris was reextracted using 2% SDS (sodium dodecyl sulfate). The majority of the residue in all samples was extractable (Table 7). The bound residues were extracted with organic solvents and 6 N HCl until all radioactivity was solubilized.

Table 7- Initial Fractionation of TRR of goats treated with TMS-labelled glyphosate-trimesium.

Sample	Acid Extractable		2% SDS Extractable		Bound	
	ppm	% TRR	ppm	% TRR	ppm	% TRR
Feces	9.09	55.9	-		6.52	40.1
Liver	0.56	45.6	0.56	46.2	0.12	9.7
Kidney	0.94	77.5	-		0.27	22.5
Muscle	0.37	81.2	-		0.09	18.8

- = Not Extracted

Metabolite Identification: Residues were analyzed by HPLC or TLC and the retention times compared with those of possible metabolites (figure 1, copied from p. 165 of MRID# 432891-02). The identity of metabolites was further confirmed by a second TLC or HPLC system.

Nature of the Residue in Feces and Urine: TMS was the predominant component of the residue, accounting for 94.0% of the TRR in urine and 31.0% in feces.

Nature of the Residue in Kidney: The identification of residues in kidney samples is shown in Table 8. TMS was the predominant component of the residue, accounting for 42.4% of the TRR. The natural products choline, creatine, and methionine were also identified; accounting for 7.6%, 4.3% and 4.9% of the TRR, respectively. A total of 59.2% of the TRR was identified. The remainder of the TRR consisted of uncharacterized extracts (maximum of 5.9% of the TRR), unknowns (maximum of 2.2% of the TRR) and areas of the TLC plates which contain no discrete components (total of 15.3% of the TRR).

Nature of the Residue in Liver: The identification of residues in liver samples is shown in Table 8. TMS was the predominant component of the residue, accounting for 19.4% of the TRR. The natural products choline, creatine, creatinine, and methionine were also identified; accounting for 18.8%, 3.3%, 1.7% and 2.1% of the TRR, respectively. A total of 45.3% of the TRR was identified. The remainder of the TRR consisted of uncharacterized extracts (maximum of 6.3% of the TRR), an unknown (2.2% of the TRR) and areas of the TLC plates which contain no discrete components (total of 15.9% of the TRR).

Table 8- Identification of TMS-labelled metabolites in tissues and milk of goats.

I.D.	Liver		Kidney		Muscle		Fat		Milk ¹	
	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR
TMS	0.24	19.4	0.14	42.4	0.18	39.4	0.04	17.3	-	
DMS	-		-		0.01	1.6	<0.01	1.5	0.01	1.7
Choline	0.23	18.8	0.09	7.6	-		<0.01	1.8	-	
Creatine	0.04	3.3	0.05	4.3	0.06	12.5	0.01	3.0	0.01	3.5
Creatinine	0.02	1.7	-		0.02	4.2	-		-	
Lactose	-		-		-		-		0.04	8.4
Ol/Pa Acid	-		-		-		-		0.05	12.4
Capric acid	-		-		-		-		0.01	3.5
Lauric Acid	-		-		-		-		0.01	1.8
Methionine	0.03	2.1	0.06	4.9	0.02	4.5	-		0.05	12.6
Total	0.55	45.3	0.72	59.2	0.28	62.2	0.05	23.6	0.19	43.9

¹Day 7 sample

DMS = DiMethyl Sulfone

Ol/Pa Acid = Oleic/Palmitic Acids

Nature of the Residue in Muscle: The identification of residues in muscle samples is shown in Table 8. TMS was the predominant component of the residue, accounting for 39.4% of the TRR. The metabolite dimethyl sulfone and the natural products , creatine,

creatinine, and methionine were also identified; accounting for 1.6%, 12.5%, 4.2% and 4.5% of the TRR, respectively. A total of 62.2% of the TRR was identified. The remainder of the TRR consisted of uncharacterized extracts (maximum of 7.0% of the TRR), an unknown (1.9% of the TRR) and areas of the TLC plates which contain no discrete components (total of 10.2% of the TRR).

Nature of the Residue in Fat: Samples were initially extracted with hexane, releasing 31.8% of the TRR. The debris was further extracted with acetonitrile, 1 N HCl and dichloromethane; releasing 22.4%, 11.0%, and 20.3% of the TRR, respectively. The remaining bound residues, 14.5% of the TRR, were not further analyzed. The identification of the released residues in perirenal fat samples is shown in Table 8. TMS was the predominant component of the residue, accounting for 17.3% of the TRR. The metabolite dimethyl sulfone and th natural products choline and creatine were also identified; accounting for 1.5%, 1.8% and 3.0% of the TRR, respectively. A total of 23.6% of the TRR was identified. The remainder of the TRR consisted of unidentified long-chain fatty acids (42.3% of the TRR), uncharacterized extracts (maximum of 4.1% of the TRR) and areas of the TLC plates which contain no discrete components (total of 3.0% of the TRR).

Nature of the Residue in Milk: Samples were initially separated into butterfat (43.3% of the TRR) and skim milk (56.7% of the TRR). Protein was precipitated from the skim milk (29.9% of the TRR) and hydrolyzed with 6 N HCl. Butterfat was partitioned with organic solvents. The identification of the residues in milk samples is shown in Table 8. Methionine was the predominant component of the residue, accounting for 12.6% of the TRR. The metabolite dimethyl sulfone and the natural products creatine, lactose, oleic/palmitic acids, capric acid and lauric acid were also identified; accounting for 1.7%, 3.5%, 8.4%, 12.4%, 3.5% and 1.8% of the TRR, respectively. A total of 43.9% of the TRR was identified. The remainder of the TRR consisted of unknowns (maximum of 4.4% of the TRR), uncharacterized extracts (maximum of 5.2% of the TRR) and areas of the TLC plates which contain no discrete components (total of 15.5% of the TRR).

Storage Stability: Samples were chromatographed within 6 months of sacrifice and the analysis repeated at the end of the study. No evidence of degradation was observed. Storage stability is thus not an issue for this study.

Nature of Residue in Animals: Poultry

PMG Label. Submitted with this petition:

[¹⁴C-PMG)Glyphosate-trimesium: Nature of the Residue in Tissues and Eggs of Laying Hens. MRID# 432736-02

In-Life Phase: [Phosphonomethylene-¹⁴C]glyphosate-trimesium (50 Ci/mmol) was mixed with cellulose in a dosing capsule and administered orally to three laying leghorn hens (average weight of 1.63 kg). The hens were dosed at a rate of 62.4 ppm of PMG (91 ppm of glyphosate-trimesium, 33.7X). Doses were administered once daily for 10 consecutive days. The animals were sacrificed approximately 12-15 hours after administration of the final dose. This portion of the study was conducted at Battelle laboratories, OH.

Quantitation of Total Radioactivity: Eggs were collected daily. Tissues were obtained after sacrifice. All results are expressed as PMG equivalents. The distribution of the radioactivity is shown in Table 9. Of the administered radioactivity, 99% was recovered in excreta. Another 4% was recovered in the GI tract and less than 0.2% was recovered in the eggs, blood and tissues. The total recovery was 100%. The TRR in tissues and eggs is shown in Table 10. The greatest tissue residues were 2.17 ppm in kidney and 0.44 ppm in liver.

Table 9- Recovery of radioactivity from hens following 10 consecutive daily doses of PMG-labelled glyphosate-trimesium.

Fraction	% of Total Radioactivity Administered
Excreta	99.3
Egg Yolks	0.03
Egg Whites	0.01
Tissues	0.09
Blood	0.02
GI Tract & Contents	3.9
Cage Rinse	0.6
Total	104

Table 10- TRR in hen eggs and tissues following 10 consecutive twice doses of PMG-labelled glyphosate-trimesium.

Fraction	TRR	
	ppm	% of Total Dose
Liver	0.440	0.03
Kidney	2.17	0.04
Breast Muscle	0.029	0.01
Thigh Muscle	0.040	0.01
Blood	0.139	0.02
Fat	0.022	0.01
Egg Yolk*	0.238	0.01
Egg White*	0.017	<0.01

*Day 10 Sample

Extraction and Fractionation: Tissues and eggs were extracted with aqueous 0.1 N HCl/chloroform and the debris removed by centrifugation, dividing the residues into three fractions- organic-soluble, aqueous-soluble and bound (Table 11). The bound residues of the egg and muscle samples were solubilized by hydrolyzing the debris in 6 N HCl. The level of bound residues after this treatment was 2.2% of the TRR in egg yolk, 0% of the TRR in egg white, 1.5% of the TRR in thigh muscle, and 2.8% of the TRR in breast muscle.

Table 11- Initial Fractionation of TRR of hens treated with PMG-labelled glyphosate-trimesium.

Sample	Aqueous-Soluble		Organic-Soluble		Bound	
	ppm	% TRR	ppm	% TRR	ppm	% TRR
Egg Yolk	0.16	65.5	0.06	24.7	0.02	9.8
Egg Whites	0.01	44.9	<0.01	1.0	0.01	54.0
Thigh Muscle	0.03	68.1	<0.01	2.2	0.01	29.7
Breast Muscle	0.02	66.8	<0.01	0.6	0.01	32.5
Liver	0.40	90.7	0.01	3.0	0.03	6.3
Fat	0.01	47.5	0.01	44.1	<0.01	8.5

Metabolite Identification: Soluble residues were analyzed by HPLC and TLC and the retention times compared with those of possible metabolites.

Nature of the Residue in Egg Yolk: The identification of residues in egg yolk samples is shown in Table 12. PMG was the predominant

component of the residue, accounting for 59.5% of the TRR. The metabolite AMPA was also identified, accounting for 2.3% of the TRR. Phospholipids and nonpolar lipids accounted for 7.4% and 17.3% of the TRR, respectively. A total of 86.5% of the TRR was identified. The remainder of the TRR consisted of unidentified polar extracts released from the bound residue by hydrolysis (6.7% of the TRR), a polar conjugate fraction (3.2% of the TRR) and Unknown 1 (1.4% of the TRR). Unknown 1 was a compound which eluted prior to PMG in the HPLC analysis of aqueous-soluble residues. Hydrolysis of the polar conjugate fraction from liver released both PMG and AMPA.

Nature of the Residue in Egg White: The identification of residues in egg white samples is shown in Table 12. PMG was the predominant component of the residue identified, accounting for 21.5% of the TRR. The metabolite AMPA was also identified, accounting for 0.8% of the TRR. A total of 22.3% of the TRR was identified. The remainder of the TRR consisted of unidentified polar extracts released from the bound residue by hydrolysis (37.8% of the TRR), a polar conjugate fraction (38.4% of the TRR) and Unknown 1 (0.5% of the TRR).

Nature of the Residue in Thigh Muscle: The identification of residues in thigh muscle samples is shown in Table 12. PMG was the predominant component of the residue identified, accounting for 61.0% of the TRR. The metabolite AMPA was also identified, accounting for 4.1% of the TRR. A total of 65.1% of the TRR was identified. The remainder of the TRR consisted of unidentified polar extracts released from the bound residue by hydrolysis (10.8% of the TRR), a polar conjugate fraction (16.6% of the TRR) and Unknown 1 (3.8% of the TRR).

Table 12- Identification of PMG-labelled metabolites in tissues and eggs of hens.

I.D.	Egg Yolk ¹		Egg White ¹		Thigh Muscle		Breast Muscle		Liver		Fat	
	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR
PMG	0.14	59.5	<0.01	21.5	0.02	61.0	0.01	39.0	0.27	61.0	0.01	40.7
AMPA	0.01	2.3	<0.01	0.8	<0.01	4.1	<0.01	5.0	0.10	22.5	<0.01	3.3
Unknown 1	<0.01	1.4	<0.01	0.5	<0.01	3.8	<0.01	1.2	0.02	5.1	<0.01	1.5
Phospholipids	0.02	7.4	-	-	-	-	-	-	-	-	-	-
Nonpolar Lipids	0.04	17.3	-	-	-	-	-	-	-	-	0.01	44.1
Polar Conjugate	0.01	3.2	0.01	38.4	0.01	16.6	0.01	21.5	<0.01	0.3	<0.01	2.0
Total Identified	0.21	86.5	<0.01	22.3	0.02	65.1	0.01	44.0	0.37	83.5	0.02	88.1

¹Day 10 sample

- = Not detected

Nature of the Residue in Breast Muscle: The identification of

residues in breast muscle samples is shown in Table 12. PMG was the predominant component of the residue identified, accounting for 39.0% of the TRR. The metabolite AMPA was also identified, accounting for 5.0% of the TRR. A total of 44.0% of the TRR was identified. The remainder of the TRR consisted of uncharacterized extracts released from the bound residue by hydrolysis (29.7% of the TRR), a polar conjugate fraction (21.5% of the TRR) and Unknown 1 (1.2% of the TRR).

Nature of the Residue in Liver: The identification of residues in liver samples is shown in Table 12. PMG was the predominant component of the residue identified, accounting for 61.0% of the TRR. The metabolite AMPA was also identified, accounting for 22.5% of the TRR. A total of 83.5% of the TRR was identified. The remainder of the TRR consisted of unidentified polar extracts released from the polar conjugate fraction by hydrolysis (1.8% of the TRR), the remainder of the polar conjugate fraction after hydrolysis (0.3% of the TRR) and Unknown 1 (5.1% of the TRR).

Nature of the Residue in Fat: The identification of residues in fat samples is shown in Table 12. PMG was the predominant component of the residue, accounting for 40.7% of the TRR. The metabolite AMPA was also identified, accounting for 3.3% of the TRR. Nonpolar lipids accounted for 44.1% of the TRR. A total of 88.1% of the TRR was identified. The remainder of the TRR consisted of a polar conjugate fraction (2.0% of the TRR) and Unknown 1 (1.5% of the TRR).

Storage Stability: As the sample analysis was completed within 4-6 months of sacrifice (except for egg white, 6.5 months), storage stability is not an issue for this study.

TMS Label. Submitted with this petition:

Glyphosate-trimesium: Metabolism in Laying Hens Following Dosing at 20 mg/kg in the Diet. MRID# 432736-03

In-Life Phase: [TMS-¹⁴C]glyphosate-trimesium (1.98 GBq/mmol) was mixed with gelatin in a dosing capsule and administered orally to 10 laying Ross Hisex Brown hens (weights of 1.8-2.2 kg). The hens were dosed at a rate of 20.5 ppm of glyphosate-trimesium (7.6X, 7.3 ppm of TMS). Doses were administered once daily for 10 consecutive days. The animals were sacrificed approximately 16 hours after administration of the final dose.

Quantitation of Total Radioactivity: Eggs were collected daily. Tissues were obtained after sacrifice. All results are expressed as glyphosate-trimesium equivalents. The distribution of the radioactivity was not reported. Of the administered radioactivity, 88-92% was recovered in excreta. The TRR in tissues and eggs is

shown in Table 13. The greatest tissue residues were 0.20 ppm in egg yolk and 0.11 ppm in kidney.

Table 13- TRR in hen eggs and tissues following 10 consecutive daily doses of TMS-labelled glyphosate-trimesium.

Fraction	TRR
Skin & Fat	0.027
Egg Yolks	0.204
Egg Whites	0.048
Leg Muscle	0.059
Breast Muscle	0.073
Liver	0.095
Kidney	0.112
Peritoneal Fat	0.014

Extraction and Fractionation: Tissues (except fat) and eggs were sequentially extracted with aqueous 1 M trichloroacetic acid, hexane and 2% SDS (Table 14). The peritoneal fat samples were initially extracted with hexane and then partitioned with 1 M trichloroacetic acid.

Table 14- Initial Fractionation of TRR of hens treated with TMS-labelled glyphosate-trimesium.

Sample	Acid-Extract		Hexane-Extract		SDS-Extract		Bound	
	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR
Liver	0.04	54.9	0.01	15.5	0.01	7.2	0.02	17.8
Muscle	0.06	84.8	<0.01	1.8	-		0.01	13.2
Egg Whites	0.03	60.3	0.01	1.3	<0.01	9.7	0.01	23.4
Egg Yolk	0.06	33.2	0.11	57.8	0.02	8.6	0.01	6.1
Fat	0.01	46.9	0.01	50.7	-		<0.01	4.9

- = Not extracted

Metabolite Identification: Soluble residues were analyzed by HPLC and TLC and the retention times compared with those of possible metabolites (PMG, AMPA). The identity of PMG was further confirmed by GC-MS. Nonpolar lipids were identified using two different TLC systems while polar lipids were characterized with a single TLC system.

Nature of the Residue in Egg Yolk: The identification of soluble

residues in egg yolk samples is shown in Table 15. TMS was a predominant component of the residue, accounting for 17.9% of the TRR. Dimethyl sulfone and the natural products choline, fatty acids and cholesterol were also identified; accounting for 4.9%, 18.9%, 17.3% and 3.0% of the TRR, respectively. A total of 62.0% of the TRR was identified. The remainder of the TRR consisted of uncharacterized extracts (maximum of 8.6% of the TRR), unknowns (maximum of 0.9% of the TRR) and areas of the TLC plates which contain no discrete components (total of 2.3% of the TRR).

Nature of the Residue in Egg White: The identification of soluble residues in egg white samples is shown in Table 15. Dimethyl sulfone was the only component of the residue identified, accounting for 43.3% of the TRR. The remainder of the TRR consisted of uncharacterized extracts and eluates (maximum of 9.7% of the TRR), unknowns (maximum of 3.3% of the TRR) and areas of the TLC plates which contain no discrete components (total of 3.8% of the TRR).

Nature of the Residue in Excreta: The identification of soluble residues in excreta samples is shown in Table 15. TMS was the only component of the residue identified, accounting for 86.8% of the TRR. The remainder of the TRR consisted of bound residues (3.7% of the TRR), uncharacterized extracts (maximum of 1.6% of the TRR) and areas of the TLC plates which contain no discrete components (total of 1.3% of the TRR).

Table 15- Identification of TMS-labelled metabolites in tissues and eggs of hens.

I.D.	Liver		Muscle		Egg Yolk		Egg White		Excreta
	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	
TMS	0.01	9.5	0.04	55.7	0.04	17.9	-		86.8
DMS	0.01	19.6	0.01	18.8	0.01	4.9	0.02	43.3	-
PC	<0.01	4.5	-		-		-		-
Choline	-		-		0.04	18.9	-		-
Fatty Acids	-		-		0.03	17.3	-		-
Cholesterol	-		-		0.01	3.0	-		
Total Identified	0.02	33.6	0.05	74.5	0.13	62.0	0.02	43.3	86.8

PC = Phosphatidylcholine

DMS = DiMethyl Sulfone

- = Not detected

Nature of the Residue in Muscle: The identification of soluble residues in combined breast and leg muscle samples is shown in

Table 15. TMS was the predominant component of the residue, accounting for 55.7% of the TRR. Dimethyl sulfone was also identified; accounting for 18.8% of the TRR. A total of 74.5% of the TRR was identified. The remainder of the TRR consisted of uncharacterized extracts (maximum of 3.4% of the TRR), unknowns (maximum of 3.2% of the TRR) and areas of the TLC plates which contain no discrete components (total of 5.0% of the TRR).

Nature of the Residue in Liver: The identification of soluble residues in liver samples is shown in Table 15. Dimethyl sulfone was the predominant component of the residue, accounting for 19.6% of the TRR. TMS and the natural product phosphatidylcholine were also identified; accounting for 9.5% and 4.5% of the TRR, respectively. A total of 33.6% of the TRR was identified. The remainder of the TRR consisted of uncharacterized extracts and eluates (maximum of 11.2% of the TRR), unknowns (maximum of 3.3% of the TRR) and areas of the TLC plates which contain no discrete components (total of 6.1% of the TRR).

Nature of the Residue in Fat: Metabolite identification was not performed on fat samples as no fraction of the residue contained >0.01 ppm (Table 14).

Bound Residues: As the levels of bound residues never exceeded 0.02 ppm (Table 14), further analysis was not attempted.

Storage Stability: Liver and excreta samples were extracted and chromatographed within 6 months of sacrifice and the analysis repeated at the end of the study. No evidence of degradation was observed. Storage stability is thus not an issue for this study.

Conclusions on the Nature of the Residue in Animals: The results of the poultry and ruminant metabolism studies are quite similar. In the PMG studies, the parent compound was the primary component of the residue, except for milk in which extensive incorporation into natural products was observed. The metabolite AMPA was observed in all tissues, especially liver (21-22% of the TRR). The HED Metabolism Committee has determined that this metabolite is not of regulatory concern (Memo, G. Otakie 12/7/93). In the TMS studies, the parent compound was the major metabolite identified in muscle, egg yolk and goat liver and kidney. Extensive incorporation into natural products was observed in egg yolk and goat milk, liver and muscle. The metabolite dimethyl sulfone was the predominant residue identified in poultry liver and egg white. However, detectable levels of this metabolite would not be expected due to the exaggerated dose level and the low residues observed (maximum of 0.02 ppm dimethyl sulfone). CBTS thus concludes that the residues of regulatory concern for glyphosate-trimesium in meat, milk and eggs are the parent ions only.

Deficiency - Conclusion 4 (from Memo F. Griffith 9/30/92)

4) The petitioner was required to revise the four required enforcement methods- PMG in crops, PMG in animals, TMS in crops and TMS in animals- and submit ILVs of each method.

Petitioner's Response: Submission of four revised enforcement methods: PMG in crops, PMG in animals, TMS in crops and TMS in animals; and an ILV of each method.

CBTS' Conclusions: PMG in Crops

Submitted with PP#s PP#3F04238 & 4F04343:

Touchdown: Determination of Glyphosate and Aminomethylphosphonic Acid in Corn Grain, Corn Forage and Corn Fodder by Gas Chromatography and Mass-Selective Detection. RR 92-042B. MRID# 428487-02.

Confirmation of the Tolerance Enforcement Method RR 92-042B Entitled "Touchdown: Determination of Glyphosate and Aminomethylphosphonic Acid in Corn Grain, Corn Forage and Corn Fodder by Gas Chromatography and Mass-Selective Detection" MRID# 431658-02

There is currently an enforcement method for PMG in PAM II, so that this will not be considered to be a deficiency for this petition. As this method is considerably faster than the enforcement method, CBTS initiated a PMV in order to assess acceptability for inclusion in PAM II (Memo, G. Kramer 7/14/94). Once the requested revisions to the method write-up are made, Method RR 92-042B will be suitable for enforcement of glyphosate tolerances in crops (Memo, G. Kramer 3/21/95).

TMS in Crops

Submitted with this petition:

Touchdown: Determination of Residues of the Trimethylsulfonium Cation in Agricultural Crops by Gas Chromatography. MRID# 432736-04

Touchdown: Independent Laboratory Confirmation of the Method RR 93-105B for Residues of the Trimethylsulfonium Cation in Agricultural Crops. Morse Laboratories, Sacramento, CA MRID# 432736-05

The PMV of TMS Method RR 93-105B has been initiated (Memos, G. Kramer 2/17/95 & 3/9/95). CBTS will be unable to recommend in favor of the requested tolerances until a successful PMV of the proposed analytical enforcement method for the TMS moiety in crops

has been completed by the EPA laboratory.

PMG in Meat, Milk and Eggs

Submitted with this petition:

Touchdown: Determination of Residues of Glyphosate and Aminomethylphosphonic Acid in Animal Products by Gas Chromatography. MRID# 432736-06

Touchdown: Independent Laboratory Confirmation of the Method RR 93-104B for Residues of Glyphosate and (Aminomethyl) phosphonic Acid in Milk, Eggs and Animal Tissues. Morse Laboratories, Sacramento, CA MRID# 432736-07

The PMV of glyphosate Method RR 93-104B has been initiated (Memo, G. Kramer 3/10/95). CBTS will be unable to recommend in favor of the requested tolerances until a successful PMV of the proposed analytical enforcement method for the PMG moiety in meat, milk and eggs has been completed by the EPA laboratory.

TMS in Meat, Milk and Eggs

Submitted with this petition:

Touchdown: Determination of Residues of the Trimethylsulfonium Cation in Milk, Eggs and Animal Tissues by Gas Chromatography. MRID# 432736-08

Touchdown: Independent Laboratory Confirmation of the Method RR 93-100B for Residues of the Trimethylsulfonium Cation in Milk, Eggs and Animal Tissues. Morse Laboratories, Sacramento, CA MRID# 432736-09

The PMV of TMS Method RR 93-100B has been initiated (Memo, G. Kramer 3/10/95). CBTS will be unable to recommend in favor of the requested tolerances until a successful PMV of the proposed analytical enforcement method for the TMS moiety in meat, milk and eggs has been completed by the EPA laboratory.

Deficiency - Conclusion 5b (from Memo F. Griffith 9/30/92)

5b) Additional magnitude of the residue data are necessary. The petitioner has not submitted residue data from all of the major corn-producing states; e.g. MI, IN and OH. Data are also required for NY and PA.

Petitioner's Response: Submission of two volumes of field residue data.

Submitted with this petition:

Touchdown: Magnitude-of-the-Residue of Glyphosate-trimesium on Corn from Trials Conducted in the USA During 1989. MRID# 432736-10

A total of eight field residue trials were conducted in 1989 in eight different states (SD, NE, MN, IA, WI, IL, KY and OH). The first Touchdown application was a preemergence broadcast application at a rate of 8.0 lbs. ai/A (2X). The spray volume was 19-26 gal/A. A second (spot) treatment was made to a 10% area of each plot 30-57 days after the initial treatment. The application rate was 20 lbs. ai/A on a treated area basis. Forage samples were harvested from each treated plot 4-8 weeks after the second application. Fodder and grain samples were obtained at maturity. The samples were stored for up to 43 months prior to analysis. CBTS has previously reviewed a storage stability for residues of TMS and PMG in crops and concluded that these residues are stable in corn RACs for up to 4 years of storage (Memo, S. Koepke 12/21/90). Sample analysis for PMG and TMS was performed using the proposed enforcement methods. The methods were validated in corn RACs over a range of 0.05-0.5 ppm. The average recovery was $94.1 \pm 12.5\%$ for PMG and 86.8 ± 4.4 for TMS. Analysis of the treated samples showed no quantifiable residues; i.e. <0.1 ppm in forage and fodder and <0.05 ppm in grain for both TMS and PMG.

Submitted with this petition:

Touchdown: Magnitude-of-the-Residue of Glyphosate-trimesium on Corn from Trials Conducted in the USA During 1993. MRID# 432736-11

A total of five field residue trials were conducted in 1993 in five different states (GA, MI, NY, PA and TX). The first Touchdown application was a preemergence broadcast application at a rate of 8.0 lbs. ai/A (2X). The spray volume was 10-20 gal/A. A second (spot) treatment was made to a 10% area of each plot 6 weeks after the initial treatment. The application rate was 2-6 lbs. ai/A on a treated area basis. Two forage samples were harvested from each treated plot, 14 days and 7-8 weeks after the second application. Fodder and grain samples were obtained at maturity. The samples were stored for up to 6 months prior to analysis. Sample analysis for PMG and TMS was performed using the proposed enforcement methods. The methods were validated in corn RACs over a range of 0.05-0.5 ppm. The average recovery was $98 \pm 13.9\%$ for PMG and 91 ± 14.1 for TMS. Analysis of the treated samples showed no quantifiable residues; i.e. <0.1 ppm in forage and fodder and <0.05 ppm in grain for both TMS and PMG.

Conclusions: Between these trials and those submitted previously,

the registrant has submitted a total of 25 residue trials. These trials were located in Regions 1 (2 trials), 2 (2 trials), 5 (18 trials), 7 (1 trial), 8 (1 trial) and 10 (1 trial). CBTS concludes that the number of trials and the geographic representation are adequate to establish tolerances for glyphosate-trimesium on corn RACs. The maximum residues observed were <0.1 ppm in forage, 0.13 ppm in fodder and 0.06 ppm in grain for TMS; and <0.1 ppm in forage, <0.1 ppm in fodder and 0.07 ppm in grain for PMG. These data support the following tolerances for residues of glyphosate-trimesium: corn forage - 0.10 ppm; corn fodder (of which no more than 0.20 ppm is trimethylsulfonium) - 0.30 ppm; and corn grain (of which no more than 0.10 ppm is trimethylsulfonium) - 0.20 ppm. Also, The registrant is proposing to regulate the PMG ion only. However, HED has determined that the TMS cation is also of regulatory concern and that tolerances for glyphosate-trimesium should be expressed as "residues of glyphosate-trimesium (Sulfonium, trimethyl- salt with N-(phosphonomethyl)glycine (1:1)) in or on..." (Memo, G. Kramer et. al. 2/9/95). **A revised Section F is required.** The registrant should also document that "glyphosate-trimesium" is an ANSI acceptable name. If "glyphosate-trimesium" is not an ANSI acceptable name, then the tolerance expression should include only the chemical name.

Deficiency - Conclusion 6a (from Memo F. Griffith 9/30/92)

6a) The petitioner needs to submit a revised Section F proposing sulfosate tolerances in milk at 0.04 ppm, at 0.1 ppm in meat, fat and meat by-products (except liver) of cattle, goats, horses, hogs and sheep and in liver at 0.4 ppm of cattle, goats, horses, hogs and sheep.

Petitioner's Response: Based on the results of the metabolism study, the petitioner has proposed the following tolerances (for PMG only):

Liver & Kidney*	--	0.1 ppm	Milk	--	0.01 ppm
Fat*	--	0.03 ppm	Meat*	--	0.03 ppm
Meat By-Products* ¹		0.03 ppm			

*of cattle, goats, horses, hogs and sheep

¹except liver and kidney

CBTS' Conclusions: The maximum ruminant dietary burden for glyphosate-trimesium results from a dairy cattle diet comprised of soybean RACs (from PP# 3860):

Feed Item	% Diet	Recommended Tolerance	% DM	ppm in Diet
Aspirated Grain Fractions	20	210 ppm	85	49.4
Forage	60	2.0 ppm	35	3.4
Hulls	20	7.0 ppm	90	1.6
Total	100			54.4

CBTS has reviewed a cow feeding study (MRID# 414621-06) in which one of the dosing levels was 50 ppm, very close the estimated ruminant dietary burden (Memo, S. Koepke 5/14/91). At this dosing level, the maximum residues observed were:

Tissue	TMS (ppm)	PMG (ppm)
Milk	0.18	<0.02
Kidney	0.18	0.44
Liver	0.32	<0.2
Fat	0.01	0.06
Muscle	0.11	<0.05

Based on these results, the appropriate tolerance levels are:

Meat By-Products*	1.0 ppm		Milk	--	0.20 ppm
Fat*	--	0.10 ppm		Meat*	-- 0.20 ppm

*of cattle, goats, horses, hogs and sheep

CBTS is not willing to establish tolerances based solely on the results of the metabolism studies while ignoring this feeding study, as requested by the registrant. The feeding study is more likely to reflect the real-world situation since cows were used instead of goats and the duration was 28 days instead of 7 days. Also, The registrant is proposing to regulate the PMG ion only. However, HED has determined that the TMS cation is also of regulatory concern and that tolerances for glyphosate-trimesium should be expressed as "residues of glyphosate-trimesium (Sulfonium, trimethyl- salt with N-(phosphonomethyl)glycine (1:1)) in or on..." (Memo, G. Kramer et. al. 2/9/95). **A revised Section F is required.**

Deficiency - Conclusion 6b (from Memo F. Griffith 9/30/92)

6b) The petitioner needs to submit a revised Section F proposing sulfosate tolerances in eggs at 0.03 ppm, at 0.1 ppm in meat, fat and meat by-products of poultry.

Petitioner's Response: Based on the results of the metabolism

27

study, the petitioner has proposed the following tolerances (for PMG only):

Poultry Liver	--	0.1 ppm		Eggs	--	0.01 ppm
Poultry Fat	--	0.03 ppm		Poultry Meat	--	0.03 ppm
Poultry Meat By-Products ¹ - 0.03 ppm						

¹except liver

CBTS' Conclusions: The maximum poultry dietary burden for glyphosate-trimesium results from a poultry diet comprised of soybean and corn RACs:

Feed Item	% Diet	Recommended Tolerance	ppm in Diet
Soybean Meal*	40	3.0 ppm	1.2
Soybean Hulls	20	7.0 ppm	1.4
Corn Grain	40	0.20 ppm	0.1
Total	100		2.7

*Covered by RAC tolerance

CBTS has reviewed a poultry feeding study (MRID# 414621-05) in which one of the dosing levels was 5 ppm, similar to the estimated poultry dietary burden (Memo, S. Koepke 5/14/91). At this dosing level, the maximum residues observed were:

Tissue	TMS (ppm)	PMG (ppm)
Eggs	<0.02	<0.02
Kidney	<0.02	0.07
Liver	<0.05	<0.05
Fat	<0.05	<0.05
Muscle	<0.05	<0.05

Based on these results, the appropriate tolerance levels are:

Poultry Liver	--	0.05 ppm		Eggs	--	0.02 ppm
Poultry Fat	--	0.05 ppm		Poultry Meat	--	0.05 ppm
Poultry Meat By-Products ¹ - 0.10 ppm						

¹except liver

CBTS is not willing to establish tolerances based solely on the results of the metabolism studies while ignoring this feeding study, as requested by the registrant. The feeding study is more likely to reflect the real-world situation since the duration was 28 days instead of 10 days. Also, The registrant is proposing to regulate the PMG ion only. However, HED has determined that the TMS cation is also of regulatory concern and that tolerances for

28

glyphosate-trimesium should be expressed as "residues of glyphosate-trimesium (Sulfonium, trimethyl- salt with N-(phosphonomethyl)glycine (1:1)) in or on..." (Memo, G. Kramer et. al. 2/9/95). **A revised Section F is required.**

cc: PP#9F3796, Kramer, circ., R.F.

RDI: R.B. Perfetti (3/31/95), M.T. Flood (4/3/95), E. Zager (4/3/95)

G.F. Kramer:804V:CM#2:(703)305-5079:7509C

Memo # 43298101 + 432736-01

Page 29 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.
- ☐ Internal deliberative information.
- ☐ Attorney-Client work product.
- ☐ Claimed Confidential by submitter upon submission to the Agency.

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.

30

L. Jones 2/14/95
Page 1 of 1

Attachment:

INTERNATIONAL RESIDUE LIMIT STATUSCHEMICAL Glyphosate-trimesium⁵

CODEX NO. _____

CODEX STATUS:

☒ No Codex Proposal
Step 6 or Above (there are
limits for glyphosate)

Residue (if Step 8): _____

PROPOSED U.S. TOLERANCES:

Petition No.: 9F03796CBTS Reviewer: G.F. KramerResidue: Parent ions

<u>Crop(s)</u>	<u>Limit</u> <u>(mg/KG)</u>	<u>Crop(s)</u>	<u>Limit</u> <u>(mg/KG)</u>
		Corn Grain	0.05
		Corn Fodder	0.1
		Corn Forage	0.1
		Liver & Kidney [*]	0.1
		Poultry Liver	0.1
		Milk	0.01
		Eggs	0.01
		Meat and Fat [*]	0.03
		Poultry Meat & Fat	0.03
		Meat By-Products ^{*1}	0.03
		Meat By-Products ² -	0.03

^{*}of cattle, goats, horses, hogs and sheep¹except liver and kidney²poultry, except liver

CANADIAN LIMITS:

☒ No Canadian Limits

Residue: _____

MEXICAN LIMITS:

☒ No Mexican Limits

Residue: _____

<u>Crop(s)</u>	<u>Limit</u> <u>(mg/KG)</u>	<u>Crop(s)</u>	<u>Limit</u> <u>(mg/KG)</u>
----------------	--------------------------------	----------------	--------------------------------

NOTES

⁵trimethylsulfonium carboxymethyl-aminomethyl phosphonate or Sulfonium, trimethyl- salt with N-(phosphonomethyl)glycine (1:1). This chemical is also known as "sulfosate."