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

APR 4 1995

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP# 0F03860. Glyphosate-trimesium (formerly known as Sulfosate) in or on in/on Soybean RACs. Amendments of 10/3/94 & 3/20/95. MRID#s 433970-01 to -03, 435895-00 & 434198-01. Barcodes D208740, D208742, 213615 & 213612. CBTS#s 14617, 14618, 15346 & 15347.

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THRU: R.B. Perfetti, Ph.D., Acting Section Head
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TO: Robert Taylor, Product Manager
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And

Jane Smith, Acting Section Head
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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):

Soybean Seed	1 ppm	Soybean Hay	1 ppm
Soybean Forage	0.1 ppm	Soybean Aspirated Grain Fractions	1 ppm
Soybean Hulls	1 ppm	Poultry Liver	0.1 ppm
Liver & Kidney*	0.1 ppm	Eggs	0.01 ppm
Milk	0.01 ppm	Poultry Fat	0.03 ppm
Fat*	0.03 ppm	Poultry Meat	0.03 ppm
Meat*	0.03 ppm	Poultry Meat By-Products[2]	0.03 ppm
Meat By-Products*,[1]	0.03 ppm		

*of cattle, goats, horses, hogs and sheep
[1]except liver and kidney, [2]except liver

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.

Due to Tox concerns, HED has determined that the tolerance expression for glyphosate-trimesium must include the TMS cation (Memo, G. Kramer et. al. 2/9/95). Tolerances for glyphosate-trimesium should be expressed as "residues of glyphosate-trimesium (Sulfonium, trimethyl- salt with N-(phosphonomethyl)glycine (1:1)) in or on..." In situations where the levels of both ions are expected to be below the levels of quantitation (0.05 ppm), tolerances should be established as:

RAC -- 0.05 ppm

In cases where quantifiable residues are expected, tolerances should be established as:

RAC (of which no more than x ppm is trimethylsulfonium) - y ppm

where x is the maximum expected residue of TMS and y is the maximum expected total of TMS and PMG.

The current amendment addresses deficiencies identified in CBTS' previous review (Memo S. Koepke 5/14/91).

RECOMMENDATIONS

CBTS recommends against the proposed tolerances for residues of glyphosate-trimesium in soybean and animal RACs for the reasons detailed in conclusions 2, 3, 4, 5c, 6b, 6c, 7a and 7b. However, a DRES run can be initiated at this time.

CONCLUSIONS

1a. **The registrant** has submitted a soybean metabolism study in which glyphosate-trimesium, radiochemically labelled in the methyl carbon (PMG-^{14}C), was applied to pots (greenhouse) in a single preemergence broadcast application at a rate of 7.5 lbs. ai/A (1.9X). Plants were grown to maturity and harvested for seed and hay. Immature plants were also harvested for forage (31 day PHI). The maximum residues were observed in forage (1.76 ppm).

1b. PMG accounted for only 0.6-4.1% of the TRR. The metabolite AMPA was observed in all RACs (1.6-5.7% of the TRR). The HED

Metabolism Committee has determined that this metabolite is not of regulatory concern (Memo, G. Otakie 12/7/93). Extensive incorporation into natural products was observed, accounting for 81-96% of the TRR. Studies with TMS-labelled glyphosate-trimesium have shown that at least 78% of the TRR is the un-metabolized parent cation (Memo S. Koepke 5/14/91). CBTS thus concludes that the residues of regulatory concern for glyphosate-trimesium in soybeans are the parent ions only.

2. 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.

3. 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.

4. 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.

5a. The registrant has submitted the results of seven soybean 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 43-99 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 8-12 days after the second application in three trials and prior to the spot application in four trials. Hay was harvested 7-8 weeks after the spot treatment. A wiper application was made in all trials 5-6 days prior to harvest of mature seed. Analysis of the treated samples showed no quantifiable residues; i.e. <0.25 ppm in seed, forage and hay for both TMS and PMG.

5b. Between these trials and those submitted previously, the registrant has submitted a total of 20 residue trials. These trials were located in Regions 2 (3 trials), 4 (4 trials) and 5 (13 trials). CBTS concludes that the number of trials and the geographic representation are adequate to establish tolerances for glyphosate-trimesium on soybean RACs. The maximum residues observed were 0.78 ppm in forage, 1.19 ppm in hay and 0.73 ppm in seed for TMS; and 0.60 ppm in forage, 2.7 ppm in hay and 1.7 ppm in seed for PMG. The revised tolerances now proposed by the registrant for soybean RACs (1 ppm for seed, hay and forage) are lower than those proposed originally (1.0 ppm for forage, 2.0 for seed and 3.0 for hay). The registrant argues that the high

residues seen in the IN trial were a result of contamination and should thus be discarded. CBTS however is not willing to disregard this trial. Given the nature of the treatments (spot and wiper), contamination of forage and hay with treated weeds or inadvertent treatment of soybeans is a real possibility, especially given the short PHI for wiper treatments (7 days). Also, quantifiable residues were observed in a number of other trials (residues were non-quantifiable in all RACs in only two of 13 trials in MRID# 414621-03).

5c. The residue data support the following tolerances for residues of glyphosate-trimesium: soybean forage (of which no more than 1.0 ppm is trimethylsulfonium) - 2.0 ppm; soybean hay (of which no more than 2.0 ppm is trimethylsulfonium) - 5.0 ppm; and soybean seed (of which no more than 1.0 ppm is trimethylsulfonium) - 3.0 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.

6a. The registrant has submitted a new soybean processing study. Concentration of residues is seen in hulls and aspirated grain fractions.

6b. The appropriate concentration factors for hulls are 2.5 (PMG) and 2.0 (TMS). CBTS has recommended that the RAC tolerance for glyphosate-trimesium be set at 3.0 (of which no more than 1.0 ppm is trimethylsulfonium); i.e., 2.0 ppm for PMG and 1.0 ppm for TMS. The appropriate FAT for hulls is thus 7.0 ppm (of which no more than 2.0 ppm is trimethylsulfonium); i.e., (2.0 ppm PMG x 2.5 = 5.0 ppm) + (1.0 ppm TMS x 2.0 = 2.0 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..." **A revised Section F is required.**

6c. The registrant has also proposed to set a tolerance of 1 ppm for soybean aspirated grain fractions, based on the observed residue values. However, the composition of the fractions of the aspirated grain fractions in these studies is not comparable to commercial aspirated grain fractions. The <425 μm fraction comprised only 2-6% of the total aspirated grain fraction samples. In commercial aspirated grain fractions, the <400 μm fraction comprises approximately 50% of the total (*Aspirated Grain Fractions*

(Grain Dust): A Tolerance Perspective, 6/7/94). However, since the registrant determined the residues in each fraction separately, the expected concentration in commercial aspirated grain fractions can be calculated. The appropriate concentration factor for PMG is 73.8; and for TMS, is 57.5. Tolerances for aspirated grain fractions are calculated from the seed tolerance and the concentration factor observed in the processing study. The appropriate tolerance for aspirated grain fractions is thus 210 ppm (of which no more than 60 ppm is trimethylsulfonium); i.e., (2.0 ppm PMG x 73.8 = 147 ppm, rounded to 150 ppm) + (1.0 ppm TMS x 57.5 = 57.5 ppm, rounded to 60 ppm). Also, the registrant is proposing to regulate the PMG ion only and to set tolerances on "soybean aspirated grain fractions." However, HED has determined that the TMS cation is of regulatory concern and tolerances are set on "aspirated grain fractions" so that this tolerance should be expressed as "residues of glyphosate-trimesium (Sulfonium, trimethyl- salt with N-(phosphonomethyl)glycine (1:1)) in or on aspirated grain fractions." **A revised Section F is required.**

7a. The maximum ruminant dietary burden for glyphosate-trimesium, 54.4 ppm, results from a dairy cattle diet comprised of soybean RACs. CBTS has reviewed a cow feeding study (MRID# 414621-06) in which one of the dosing levels was 50 ppm, very close to 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

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.**

7b. 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			

[1]except liver

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.**

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

DETAILED CONSIDERATIONS

Deficiency - Conclusion 2a (from Memo S. Koepke 5/14/91)

2a) The proposed labels recommends the use of ammonium sulfate as an adjuvant. This recommendation must either be deleted from the labels and a revised Section B be submitted or residue data must be generated supporting the use of this adjuvant with sulfosate.

Petitioner's Response: The petitioner has removed the direction pertaining to ammonium sulfate.

CBTS' Conclusion: The label has been revised as requested. This deficiency is now resolved.

Deficiency - Conclusion 2b (from Memo S. Koepke 5/14/91)

2b) The proposed labels are unclear as to the number and type of applications allowed. The labels state that only one application is allowed. Does this mean one pre-emergent or one spot application or one of each is allowed as long as one does not exceed the 4 lbs a.i./A/yr? A revised Section B is required.

Petitioner's Response: Any number of applications (broadcast, wiper 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 residue trials included all three applications and most of the a.i. would be applied early in the growing season, CBTS concludes that the directions for use are acceptable as is. This deficiency is now resolved.

Deficiency - Conclusion 3a (from Memo S. Koepke 5/14/91)

3a) Contingent upon the successful review of the required raw data, CBTS finds the submitted metabolism studies for the cationic moiety of sulfosate on soybeans to be adequate for the purposes of this petition only. The hydroponic study seems to indicate that virtually no metabolism takes place within the plant and is considered adequate for this purpose. The preemergent study leaves 21% of low level residues uncharacterized. Should a different use pattern be proposed that may result in higher levels of residues, further characterization of the nature of the residue in the uncharacterized fractions would be required. Additional raw data detailing the quantitation of the radioactivity (such as sample weights, raw counts in each sample, etc.) are required for all cation metabolism studies.

Petitioner's Response: The requested data has been submitted (MRID# 433970-02).

CBTS' Conclusion: The requested information has been provided. This deficiency is now resolved.

Deficiency - Conclusion 3b (from Memo S. Koepke 5/14/91)

3b) CBTS finds the submitted metabolism studies for the anionic moiety of sulfosate on soybeans to be inadequate. The hydroponic study seems to indicate that virtually no metabolism takes place within the plant, but no quantitation data were submitted. In the preemergent study, it is required that the metabolism study be repeated separating the plants sufficiently that control and sample background levels generated from $^{14}CO_2$ from soil will be kept at a minimum. CBTS requires that the nature of at least 90% of the residue in the plant be determined.

Petitioner's Response: Submission of:

[^{14}C-Anion]ICIA0224 - Nature of the Residue: Soybeans. MRID# 433970-03

In Life Phase: Glyphosate-trimesium, radiochemically labelled in the methyl carbon (PMG-^{14}C), was diluted to a specific activity of 11.4 mci/mmol and applied to pots (greenhouse) in a single preemergence broadcast application at a rate of 7.5 lbs. ai/A (1.9X). Plants were grown to maturity and harvested for seed and hay. Immature plants were also harvested for forage (31 day PHI).

TRR: The tissues were ground to a powder and the TRR was determined by combustion (Table 1). The maximum residues were observed in forage (1.76 ppm).

Extraction and Fractionation: Tissues (except seed) were extracted 2-3 times with water, followed by methanol. Seeds were extracted with hexane and fats were partitioned into the organic phase. The pulp was extracted with aqueous buffer. The results of this procedure are shown in Table 2. Bound residues accounted for 46-60% of the TRR.

Table 1- TRR in soybean RACs from plants treated with PMG-labelled glyphosate-trimesium.

RAC	PHI (Days)	TRR (ppm)
Forage	31	1.76
Straw	97	0.859
Hulls	97	0.487
Seed, Yellow	97	1.31
Seed, Green	97	0.772
Hay	97	0.854

Table 2- Extractability of TRR in soybean RACs from plants treated with PMG-labelled glyphosate-trimesium.

	Total Extractable		Bound	
RAC	ppm	% TRR	ppm	% TRR
Forage	0.792	45.0	1.051	59.7
Straw	0.321	37.4	0.497	57.9
Hull	0.233	47.9	0.222	45.7
Seed	0.696	53.1	0.613	46.8

Bound Residues: The bound residue (except from seed) was treated sequentially with the following procedures: 1) Refluxing in 1 N HCl for 2 hours to release carbohydrates. 2) Refluxing with 20% NaOH for 24 hours to separate the protein and lignin from crude cellulose. 3) Precipitation of lignin from the alkaline hydrolysate. Seed bound residues were analyzed by separation of protein from other macromolecules.

Metabolite Identification: Extractable residues were cleaned-up by cation exchange, Chelex and anion exchange chromatography. Metabolites and sugars were resolved on HPLC and compared with reference standards.

Nature of the Residue in Forage: The extractable residues consisted of PMG, the metabolite AMPA and natural products (mono- and disaccharides and amino acids); accounting for 3.3%, 5.7% and 36% of the TRR, respectively (Table 3). The bound residues consisted of carbohydrates, protein, lignin and crude cellulose; accounting for 25%, 17%, 1.4% and 16% of the TRR, respectively (Table 4).

Table 3- Identification of extractable residues in soybean RACs from plants treated with PMG-labelled glyphosate-trimesium.

RAC	PMG		AMPA		Natural Products	
	ppm	% TRR	ppm	% TRR	ppm	% TRR
Forage	0.058	3.30	0.100	5.70	0.634	36.0
Straw	0.005	0.57	0.023	2.70	0.293	34.1
Hull	0.020	4.10	0.007	1.50	0.206	42.3
Seed	0.034	2.60	0.021	1.60	0.641	48.9

Table 4- Identification of bound residues in soybean RACs from plants treated with PMG-labelled glyphosate-trimesium.

RAC	Carbohydrate		Protein		Lignin		Cellulose		Natural Prod.	
	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR
Forage	0.445	25.3	0.303	17.2	0.025	1.43	0.278	15.8	NA	
Straw	0.148	17.2	0.137	16.0	0.025	2.93	0.187	21.8	NA	
Hull	0.082	16.9	0.071	14.5	ND		0.037	7.6	NA	
Seed	ND		0.314	24.0	ND		ND		0.299	22.8

ND = Not Determined
NA = Not Applicable

Nature of the Residue in Straw: The extractable residues consisted of PMG, the metabolite AMPA and natural products (mono- and disaccharides and amino acids); accounting for 0.6%, 2.7% and 34% of the TRR, respectively (Table 3). The bound residues consisted of carbohydrates, protein, lignin and crude cellulose; accounting for 17%, 16%, 2.9% and 22% of the TRR, respectively (Table 4).

Nature of the Residue in Hulls: The extractable residues consisted of PMG, the metabolite AMPA and natural products (mono- and disaccharides and amino acids); accounting for 4.1%, 1.5% and 42% of the TRR, respectively (Table 3). The bound residues consisted of carbohydrates, protein and crude cellulose; accounting for 17%, 14% and 7.6% of the TRR, respectively (Table 4).

Nature of the Residue in Yellow (Mature) Seed: The extractable residues consisted of PMG, the metabolite AMPA and natural products (monosaccharides and small proteins); accounting for 2.6%, 1.6% and 49% of the TRR, respectively (Table 3). The bound residues consisted of protein and uncharacterized natural products;

accounting for 24% and 23% of the TRR, respectively (Table 4).

Storage Stability: Samples were extracted and hydrolyzed 6 months of harvest 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 Soybeans: PMG accounted for only 0.6-4.1% of the TRR. The metabolite AMPA was observed in all RACs (1.6-5.7% of the TRR). The HED Metabolism Committee has determined that this metabolite is not of regulatory concern (Memo, G. Otakie 12/7/93). Extensive incorporation into natural products was observed, accounting for 81-96% of the TRR. Studies with TMS-labelled glyphosate-trimesium have shown that at least 78% of the TRR is the un-metabolized parent cation (Memo S. Koepke 5/14/91). CBTS thus concludes that the residues of regulatory concern for glyphosate-trimesium in soybeans are the parent ions only.

Deficiency - Conclusion 4 (from Memo S. Koepke 5/14/91)

4) CBTS concluded that sufficient detail was provided to submit the methods for method trials. ACL has requests for clarifications on each of these methods. A copy of their preliminary findings is attached. A copy should be forwarded to the registrant. Contingent upon these clarifications and the successful completion of these method trials, CBTS would consider the methods to be adequate for both the anionic (carboxymethylamino methyl phosphonate [CMP] and its metabolite, aminomethylphosphonic acid [AMPA]) and cationic (trimethylsulfonium ion [TMS]) moieties of sulfosate. The milk, egg and edible tissue method for the cationic moiety of sulfosate requires further development prior to the initiation of its method trial. There are interferences in milk and cow liver that need to addressed. Both methods for milk, eggs and edible tissues were received after August 1, 1989 and must be subjected to an independent method validation trial prior to an Agency method trial (PR Notice 88-5, 7/15/88).

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 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 PP# 3796:

> Touchdown: Determination of Residues of the Trimethylsulfonium Cation in Agricultural Crops by Gas Chromatography. MRID# 432736-04
>
> Touchdown: Independent Laboratory Conformation 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 PP# 3796:

> Touchdown: Determination of Residues of Glyphosate and Aminomethylphosphonic Acid in Animal Products by Gas Chromatography. MRID# 432736-06
>
> Touchdown: Independent Laboratory Conformation 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 PP# 3796:

> Touchdown: Determination of Residues of the Trimethylsulfonium Cation in Milk, Eggs and Animal Tissues by Gas Chromatography. MRID# 432736-08
>
> Touchdown: Independent Laboratory Conformation 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 8 (from Memo S. Koepke 5/14/91)

8) Since soybean is a major crop additional residue data are required. Fifteen values all from the same crop year for the magnitude of the residue in soybean are insufficient. At least ten additional geographically relevant field trials are required.

Petitioner's Response: Submission of :

> Touchdown: Magnitude-of-the-Residue of Glyphosate-trimesium on Soybeans. MRID# 434198-01

A total of seven field residue trials were conducted in 1989 in seven different states (MS, MO, 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 15-27 gal/A. A second (spot) treatment was made to a 10% area of each plot 43-99 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 8-12 days after the second application in three trials and prior to the spot application in four trials. Hay was harvested 7-8 weeks after the spot treatment. A wiper application was made in all trials 5-6 days prior to harvest of mature seed. The samples were stored for up to 3 years 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 soybean seed for up to 4 years of storage (Memo, S. Koepke 4/14/91). Sample analysis for TMS was performed using the proposed enforcement method. Sample analysis for PMG was performed using a HPLC method previously reviewed by CBTS (Memo, S. Koepke 4/14/91). The results were confirmed by the use of the proposed

enforcement method (GC/MSD) on selected samples. The methods were validated in soybean RACs at 0.25 ppm. The average recovery was 91 ± 17% for PMG and 86 ± 15 for TMS. Analysis of the treated samples showed no quantifiable residues; i.e. <0.25 ppm in seed, forage and hay for both TMS and PMG.

Conclusions: Between these trials and those submitted previously, the registrant has submitted a total of 20 residue trials. These trials were located in Regions 2 (3 trials), 4 (4 trials) and 5 (13 trials). CBTS concludes that the number of trials and the geographic representation are adequate to establish tolerances for glyphosate-trimesium on soybean RACs. The maximum residues observed were 0.78 ppm in forage, 1.19 ppm in hay and 0.73 ppm in seed for TMS; and 0.60 ppm in forage, 2.7 ppm in hay and 1.7 ppm in seed for PMG (Table 5, copied from Memo, S. Koepke 4/14/91). The revised tolerances now proposed by the registrant for soybean RACs (1 ppm for seed, hay and forage) are lower than those proposed originally (1.0 ppm for forage, 2.0 for seed and 3.0 for hay). The registrant argues that the high residues seen in the IN trial were a result of contamination and should thus be discarded. CBTS however is not willing to disregard this trial. Given the nature of the treatments (spot and wiper), contamination of forage and hay with treated weeds or inadvertent treatment of soybeans is a real possibility, especially given the short PHI for wiper treatments (7 days). Also, quantifiable residues were observed in a number of other trials (residues were non-quantifiable in all RACs in only two of 13 trials in MRID# 414621-03).

The residue data support the following tolerances for residues of glyphosate-trimesium: soybean forage (of which no more than 1.0 ppm is trimethylsulfonium) - 2.0 ppm; soybean hay (of which no more than 2.0 ppm is trimethylsulfonium) - 5.0 ppm; and soybean seed (of which no more than 1.0 ppm is trimethylsulfonium) - 3.0 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.

TABLE 5.

Residue Data in Soybeans (MRID# 414621-03)

Location	PHI* (days)	Rate (lb ai/A)	Sample Type	TMS (ppm)	PMG (ppm)	AMPA (ppm)
Mississippi	65	10.0	Forage	0.10	<0.10	<0.10
	51		Hay	<0.10	<0.10	<0.10
	7		Seed	0.14	<0.10	<0.10
Alabama	79	10.0	Forage	<0.10	<0.10	<0.10
	61		Hay	<0.10	<0.10	<0.10
	61		Seed	<0.05	<0.20	<0.20
Iowa	63	10.0	Forage	<0.10	<0.10	<0.10
	55		Hay	<0.10	<0.10	<0.10
	6		Seed	0.10	0.35	0.17
Illinois	78	10.0	Forage	0.73	**0.60**	<0.10
	56		Hay	<0.10	<0.10	<0.10
	7		Seed	0.05	<0.10	<0.10
Arkansas	0	10.0	Forage	<0.10	<0.10	<0.10
	56		Hay	0.25	0.10	<0.10
	6		Seed	0.07	<0.10	<0.10
Minnesota	0	10.0	Forage	<0.10	<0.10	<0.10
	55		Hay	0.61	<0.10	<0.10
	6		Seed	**0.73**	<0.20	0.10
Missouri	16	10.0	Forage	**0.78**	0.38	<0.10
	16		Hay	0.88	<0.10	<0.10
	7		Seed	0.11	<0.10	<0.10
Tennessee	0	10.0	Forage	<0.10	<0.20	<0.10
	67		Hay	0.10	<0.20	<0.10
	14		Seed	0.19	<0.20	<0.20
Nebraska	26	10.0	Forage	<0.10	<0.10	<0.10
	34		Hay	<0.10	<0.10	<0.10
	11		Seed	<0.05	<0.10	<0.10
Virginia	6	10.0	Forage	<0.10	<0.10	<0.10
	69		Hay	<0.10	<0.10	<0.10
	5		Seed	0.05	<0.20	<0.20
Indiana	89	10.0	Forage	<0.10	<0.10	<0.10
	142		Hay	**1.19**	**2.7**	0.38
	15		Seed	0.22	**1.7**	<0.20
Illinois	7	10.0	Seed	<0.05	0.11	<0.10
	7	26.0	Seed	0.16	0.29	<0.10
Iowa	11	10.0	Seed	0.09	<0.20	<0.10
	11	26.0	Seed	0.40	1.04	0.50

* Time from last application: For forage, time from pre-emergent application; For hay, time from spot treatment; for seed, time from wiper application.

Deficiency - Conclusion 9 (from Memo S. Koepke 5/14/91)

9) CBTS does not consider the processing study to be adequate since the processor's sample did not contain any measurable residue. It is required that the processing study be repeated using a seed sample that has measurable residues at or near the proposed tolerance level in order to determine if the residues concentrated in any processed fraction.

Petitioner's Response: Submission of :

> Touchdown: Processing Study for Residues of Glyphosate-Trimesium on Soybeans and Magnitude of the Residue in Soybean Aspirated Grain Fractions. MRID# 433970-04

Samples of soybean were obtained from one field trial conducted in IL in 1993. Two treated plots were established. The first plot received a preemergence broadcast application at a rate of 24.0 lbs. ai/A (6X), a spot treatment (1.8 lbs. ai/A) to a 10% area of the plot 10 weeks prior to harvest and a wiper application 7 days prior to harvest of mature seed. Plot two received a single broadcast application at a rate of 1.0 lbs. ai/A 7 days prior to harvest. Seed from each plot was harvested and shipped TX A & M for processing. The seed samples were stored for up to 223 days and processed fractions for 34 days 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 soybean seed for up to 4 years of storage (Memo, S. Koepke 4/14/91). Sample analysis for TMS and PMG was performed using the proposed enforcement methods. The methods were validated in soybean processed fractions over a range of 0.05-5.0 ppm. The average recovery was 106 ± 12.9% for PMG and 84.1 ± 13.4 for TMS. The results of the analysis of the treated samples are shown in Tables 6 (seed from first plot) and 7 (seed from second plot). Concentration of residues is seen in hulls and aspirated grain fractions. The total residue level in aspirated grain fractions was calculated from the concentration of PMG and TMS in each size fraction and the percent of the total which the fraction represented.

Table 6- Residues in soybean processed fractions using seed which received a preemergence broadcast application at a rate of 24.0 lbs. ai/A (6X), a spot treatment (1.8 lbs. ai/A) to a 10 % area of the plot 10 weeks prior to harvest and a wiper application 7 days prior to harvest of mature seed.

Fraction	Residue (ppm)		Concentration Factor	
	PMG	TMS	PMG	TMS
Seed	(0.029)	0.07	-	-
Meal	<0.05	0.09	-	1.3
Hulls	0.09	0.08	3.1	1.1
Soapstock	<0.05	<0.05	-	-
Crude Oil	<0.05	<0.05	-	-
Refined Oil	<0.05	<0.05	-	-
2030-2540 µm AGF	0.81	0.56	27.9	8.0
1180-2030 µm AGF	0.39	0.30	13.4	4.3
850-1180 µm AGF	0.34	0.47	11.7	6.7
425-850 µm AGF	1.17	0.42	40.3	6.0
<425 µm AGF	2.15	0.80	74.1	11.4
Calculated AGF	0.69	0.44	23.8	6.3

AGF = Aspirated Grain Fractions

Table 7- Residues in soybean processed fractions using seed which received a single broadcast application at a rate of 1.0 lbs. ai/A 7 days prior to harvest.

Fraction	Residue (ppm)		Concentration Factor	
	PMG	TMS	PMG	TMS
Seed	0.12	0.06	-	-
Meal	<0.05	<0.05	-	-
Hulls	0.30	0.12	2.5	2.0
Soapstock	<0.05	<0.05	-	-
Crude Oil	<0.05	<0.05	-	-
Refined Oil	<0.05	<0.05	-	-
425-2540 µm AGF	3.8	1.8	31.7	30.0
<425 µm AGF	13.9	5.1	116	85.0
Calculated AGF	4.0	1.9	33.3	31.7

AGF = Aspirated Grain Fractions

Conclusions: In the processing study submitted by the registrant, two different sets of soybean seeds were utilized. The registrant's proposed tolerances for hulls and aspirated grain fractions are based on the first set in which soybeans were treated by the methods specified on the label (preemergence, spot and wiper). The results of this study are, however, questionable as the PMG residues in the RAC were below the LOQ and the results for PMG and TMS concentration in fractions derived from surface residues differ significantly (Table 6). CBTS concludes that the

results from the second set are more reliable as quantifiable residues of both ions were observed in the RAC. Also, residues resulting from a broadcast application should approximate those resulting from inadvertent treatment of seed during a wiper application. Using the results of this study (Table 7), the appropriate concentration factors for hulls are 2.5 (PMG) and 2.0 (TMS). CBTS has recommended that the RAC tolerance for glyphosate-trimesium be set at 3.0 (of which no more than 1.0 ppm is trimethylsulfonium); i.e., 2.0 ppm for PMG and 1.0 ppm for TMS. The appropriate FAT for hulls is thus 7.0 ppm (of which no more than 2.0 ppm is trimethylsulfonium); i.e., (2.0 ppm PMG x 2.5 = 5.0 ppm) + (1.0 ppm TMS x 2.0 = 2.0 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..." **A revised Section F is required.**

The registrant has also proposed to set a tolerance of 1 ppm for soybean aspirated grain fractions, based on the actual residue values resulting from processing of the first set of seeds (Table 6). However, the composition of the fractions of the aspirated grain fractions in these studies is not comparable to commercial aspirated grain fractions. The <425 µm fraction comprised only 2-6% of the total aspirated grain fraction samples. In commercial aspirated grain fractions, the <400 µm fraction comprises approximately 50% of the total (*Aspirated grain fractions (Grain Dust): A Tolerance Perspective, 6/7/94*). However, as the registrant determined the residues in each fraction separately, the expected concentration in commercial aspirated grain fractions can be calculated. Assuming that 50% of the aspirated grain fractions is <425 µm and 50% is 425-2540 µm, the concentration factor for PMG is 0.5 x 116 + 0.5 x 31.7 = 73.8, the concentration factor for TMS is 0.5 x 85 + 0.5 x 30 = 57.5. Tolerances for aspirated grain fractions are calculated from the seed tolerance and the concentration factor observed in the processing study. The appropriate tolerance for aspirated grain fractions is thus 210 ppm (of which no more than 60 ppm is trimethylsulfonium); i.e., (2.0 ppm PMG x 73.8 = 147 ppm, rounded to 150 ppm) + (1.0 ppm TMS x 57.5 = 57.5 ppm, rounded to 60 ppm). Also, the registrant is proposing to regulate the PMG ion only and to set tolerances on "soybean aspirated grain fractions." However, HED has determined that the TMS cation is also of regulatory concern and tolerances are set on "aspirated grain fractions" so that this tolerance for glyphosate-trimesium should be expressed as "residues of glyphosate-trimesium (Sulfonium, trimethyl- salt with N-(phosphonomethyl)glycine (1:1)) in or on aspirated grain fractions" **A revised Section F is required.**

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Deficiency - Conclusion 10 (from Memo S. Koepke 5/14/91)

10) 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
[1]except liver and kidney

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

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 to 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

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 11 (from Memo S. Koepke 5/14/91)

11) 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 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

[1]except liver

CBTS' Conclusions: The maximum poultry dietary burden for glyphosate-trimesium results from a dairy cattle 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			

[1]except liver

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.**

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