



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

SEP 30 1992

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT:

PP# 9F3796 SULFOSATE (TOUCHDOWN®) IN OR ON CORN GRAIN,
FORAGE, AND FODDER.
Evaluation of the October 23, 1991, Amendment.
(MRID # 420681-01, -02, and 03) [CBTS# 9050, 9051,
and 9052] (HED Project #2-0706) (DP Barcode D-
171514, D171509, and D171511)

FROM:

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THRU:

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and

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Introduction

ICI Americas, Inc. Agricultural Products has submitted this amendment consisting of a cover letter, a new Section B, (revised labels for Touchdown®), and a supplementary Section D (addition plant and livestock metabolism data) in response to deficiencies outlined in our review of December 21, 1990, by S. Koepke. The deficiencies identified in that review are repeated below in the body of this review in the order they appeared in the December 21, 1990, review, followed by the petitioner's response, then CBTS comments. Our conclusions and recommendation follow.

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EXECUTIVE SUMMARY OF CHEMISTRY DEFICIENCIES

- Revise label,
- Additional identification of residues in poultry and ruminant metabolism studies,
- Methods,
 - Revise plant and tissue residue analytical methods,
 - Acquire independent laboratory validation data,
 - Complete petition method validation in EPA labs,
- Tolerances,
 - Revise tolerance expression,
 - Propose tolerances for meat, milk, poultry, and eggs,
- Additional geographically representative field trial data,

CONCLUSIONS

1. CBTS Conclusion on Directions for Use

- a. The petitioner has omitted any reference to the use of ammonium sulfosate as an adjuvant. The maximum amount of sulfosate that can be applied to corn is 4 lbs per acre per year as a broadcast spray, spot application, or any combination of broadcast plus spot application. Wiper applications to corn are prohibited. A 90 day PHI has been proposed. These deficiencies are all resolved.
- b. The petitioner needs to correct the table on the spot application recommendation for the Touchdown® Concentrate label to have a 1.0% solution, not a 0.1% solution, as 1 gallon of Touchdown® Concentrate in 100 gallons of water is a 1% solution, not a 0.1% solution.
- c. The label is still unclear as to the number of applications allowed per year. This part of the deficiency is not resolved and continues outstanding.

2. CBTS Conclusion on Nature of the Residue - Plants

- a. The petitioner has clarified that the 56.6% pure active ingredient number is pure material diluted with water. This part of the deficiency is resolved.
- b. The petitioner has provided the number of control, [¹⁴C-TMS], and [¹⁴C-CMPA] treated plants harvested at each sampling date after treatment. The weight of each sample was provided. These data show an adequate

number of plants were harvested and adequate weight of plant material was gathered for analyses. These parts of the deficiency are resolved.

- c. The flow diagrams show that the toluene and NH_4HCO_3 extracts were combined with the DMSO to get the maximum possible recovery of starch in each metabolism study. These points have been clarified and these parts of the deficiency have been resolved.
- d. In both metabolism studies the petitioner presented calculations to show that 81-84% of the radioactivity associated with the grain can be accounted for as being incorporated into the glucose of starch. The petitioner's explanation is satisfactory as to why no data are available for the final amount of glucosazone isolated as the reaction is neither quantitative nor consistent in recovery. These parts of the deficiency are resolved.
- e. The petitioner has adequately described the starch extraction schemes providing data on sample weights and solvents. These parts of the deficiency are resolved.
- f. In the [^{14}C -TMS] metabolism study CB concludes the characterization of residues in the 154 DAT mature corn leaves can be translated to the residues in the 48 and 33 DAT corn forage. CB concludes the petitioner has adequately characterized (but not fully identified) the residues in this part of the study. The petitioner has provided sufficient additional details of the study and explanations. This part of the deficiency is resolved.
- g. The petitioner provided details in a sample calculation of ppm [^{14}C -TMS] in 48 DAT corn forage leaf tissue in Appendix A to show how TMS residues were calculated. This part of the deficiency is resolved.
- h. In both plant metabolism studies the petitioner has now presented sufficient information to show that characterization of residue after hydrolyses was attempted and that no further information can be gained with additional work. These parts of the deficiency are resolved.
- i. The petitioner has presented adequate additional information on characterizations of residues from [^{14}C -CMPA] in corn leaves and grain to show that 69% to 86% of the residues have been reincorporated into natural constituents such as glucose/starch, cellulose, lignins, proteins, etc. This part of the deficiency is resolved.
- j. The nature of the sulfosate residue in corn is adequately understood. The residue of concern is sulfosate, per se.

3. CBTS Conclusion on Nature of the Residue - Livestock

- a. CBTS reiterates that the nature of the sulfosate residue in ruminants and poultry is not adequately understood. Deficiencies 9, 11, 13, and 15 are not resolved and continue outstanding.
- b. 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. CBTS suggests the petitioner provide the same or higher degree of characterization and identification of residues in poultry as have been provided for sulfosate residues in plants.
- c. 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 additional analytical work to strive to characterize and identify at least 90% of the ¹⁴C-sulfosate equivalent residues. With ¹⁴C-sulfosate equivalent residues ranging up to 9.7 ppm CBTS suggests that the petitioner provide a higher degree of characterization and identification of residues in goats than have been provided for sulfosate residues in plants.

4. CBTS Conclusion on Residue Analytical Methods

- a. There have not been successful PMVs for the 4 residue analytical methods. The petitioner needs to revise all 4 analytical methods to incorporate ACB comments and requested clarifications noted in their pre-trial review.
- b. The petitioner needs to gather ILV (independent laboratory validation) data on all 4 revised residue analytical methods.
- c. PMVs are necessary for all 4 residue analytical methods before CBTS will recommend for sulfosate tolerances on corn products; and secondary sulfosate tolerances in tissues, milk, and eggs. However, the PMVs will not be reinitiated until the petitioner has presented adequate revised methods with supporting ILV data.

5. CBTS Conclusion on Magnitude of the Residue - Crop Field Trials

- a. After careful reconsideration CBTS concludes an additional year of crop field trial residue data from the states where field trials have been conducted are not necessary, per se.

- b. Additional magnitude of the residue data are necessary. The petitioner has not presented sulfosate in/on corn from all areas of the country and has not included residue data from all major corn producing states; e.g., Michigan, Indiana, and Ohio. CBTS reiterates that magnitude of the residue data are required from NY and PA. Deficiency 5a is not resolved and continues outstanding.

6. CBTS Conclusion on Magnitude of the Residue - Meat, Milk, Poultry, and Eggs

- a. CBTS reiterates that the petitioner has conducted an adequate bovine sulfosate feeding study if the goat metabolism study reveals that CMPA, AMPA, and TMS are the only significant residues. From a probable bovine diet that contains both corn and soybean feed items with sulfosate residues (about 3 - 5 ppm) CBTS concludes that no measurable residues of the parent sulfosate were detected. However, from feeding exaggerated levels of sulfosate residues were detected in milk and tissues. Thus, we would categorize the use as 40 CFR §180.6(a)2 in that it is not possible to establish with certainty that finite residues will be incurred, but there is reasonable expectation of finite residues. CBTS reiterates that the petitioner needs to submit a revised Section F proposing secondary sulfosate tolerances in milk at 0.04 ppm, at 0.1 ppm in meat, fat, and meat by-products (except liver) of cattle, goats, hogs, horses, and sheep, and in liver at 0.4 ppm of cattle, goats, hogs, horses, and sheep. These residues would be expressed as parent sulfosate calculated as either the magnitude of the CMP residue or the magnitude of the TMS residue, whichever is greater. Deficiencies 14 and 16 are tentatively resolved.
- b. CBTS reiterates that the petitioner has conducted an adequate poultry sulfosate feeding study if the poultry metabolism study reveals that CMPA, AMPA, and TMS are the only significant residues. From a probable poultry diet that contains both corn and soybean feed items with sulfosate residues (about 3 - 5 ppm) CBTS concludes that no measurable residues of the parent sulfosate were detected. However, from feeding exaggerated levels of sulfosate residues were detected in eggs and tissues. Thus, we would categorize the use as 40 CFR §180.6(a)2 in that it is not possible to establish with certainty that finite residues will be incurred, but there is reasonable expectation of finite residues. CBTS reiterates that the petitioner needs to submit a revised Section F proposing secondary sulfosate tolerances in eggs at 0.03 ppm, at 0.1 ppm in meat, fat, and meat by-products of poultry. These residues would be expressed as parent sulfosate calculated as either the

magnitude of the CMP residue or the magnitude of the TMS residue, whichever is greater. Deficiencies 10 and 12 are tentatively resolved.

- c. CBTS concludes that the sulfosate metabolite AMPA need not be regulated and should be dropped from the proposed tolerance expression. CBTS concludes that the petitioner needs to submit a revised sulfosate expression deleting the reference to AMPA and regulate sulfosate in terms of the parent herbicide, per se. in plants. The livestock tolerance expression can be determined when the requested metabolism studies are completed and reviewed.

RECOMMENDATION

CBTS can not recommend for the requested sulfosate tolerances in corn grain at 0.1 ppm, corn forage and corn fodder at 0.2 ppm for the reasons cited in the EXECUTIVE SUMMARY and further explained in Conclusions 1, 3, 4, 5, and 6 above.

For further consideration of this petition the petitioner should be advise to resolve the deficiencies noted above.

DETAILED CONSIDERATIONS

DIRECTIONS FOR USE

Deficiencies

- 2a. The proposed labels recommend 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.
- 2b. The proposed labels are unclear as to the number and type of application 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./Acre/yr? A revised Section B is required.
- 5b. Revised labels (Section B) requiring a PHI of 90 days for grain and fodder are required. This will preclude late spot treatments that may raise residue levels. The primary source of residue appears to be the spot treatments.

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Petitioner's Response

The petitioner has submitted revised labels for Touchdown® Concentrate and Touchdown 4-LC for use as a non-selective herbicide to control weeds in corn.

CBTS COMMENTS

The revised Touchdown labels omit any reference to use of ammonium sulfate as an adjuvant. Deficiency 2a is resolved.

In the section "General Use Precautions" the label now reads "Do not exceed a total 4 lbs per acre per year." This can be a total of 1 gallon Touchdown 4-LC or 5.8 pints of Touchdown Concentrate. CB agrees the total of 4 lbs sulfosate can be applied as a broadcast, or spot spray application, or a combination of the two applications as long as the total amount applied does not exceed 4 lbs per acre per year. This part of the deficiency is resolved.

In our previous review CBTS requested a revised label explicitly stating that wiper applications are not allowed. The directions for use have a wiper application section for use in non-crop areas. Beside the title "Wiper Application" in parenthesis is the phrase "except in corn". CB concludes this is an adequate direction in that wiper application is not allowed in corn. This part of the deficiency is resolved.

The petitioner has proposed a 90 day PHI for corn grain and corn fodder. Deficiency 5b is resolved.

In corn the types of applications are broadcast, ground equipment (application by aircraft is prohibited) and spot treatment. This part of the deficiency is resolved.

The label is still unclear as to number of applications allowed. This part of the deficiency is not resolved and continues outstanding.

On the proposed Touchdown® Concentrate label CB points out a typographical error rather than a major deficiency. Page 10 of the booklet has a label of increasing solution strengths with the amount of concentrate added to X gallons. We feel the "0.1%" solution strength should be 1.0% as the amount of Touchdown added is 1 gallon per 100 gallons of solution. This is a 1% solution, not a 0.1% solution. The petitioner needs to amend/revise this label accordingly prior to final registration.

NATURE OF THE RESIDUE - PLANTSDeficiency

- 3a. The corn plant metabolism study submitted for the cation is inadequate to determine the nature of the

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residue. Additional detail is needed in order to properly evaluate the study. The reviewer should have enough detail to duplicate the calculations used to determine the concentrations of the residues.

- 3b. The corn plant metabolism study submitted for the anion is inadequate to determine the nature of the residue. Additional detail is needed in order to properly evaluate the study. The reviewer should have enough detail to duplicate the calculations used to determine the concentrations of the residues.

Petitioner's Response (MRID# 420681-01 and - 02)

The petitioner provided additional sulfosate (cation and anion) plant metabolism data in two studies, one titled "Supplemental Information/Metabolism of [14 C-anion] ICI A0224 in Corn" by D.R. Tambling, dated July 5, 1991 and coded RR-89-010B, and the other titled "Supplemental Information/Metabolism of [14 C-cation] ICI A0224 in Corn" by D.R. Tambling, dated July 5, 1991 and coded RR 89-011B.

CBTS Comments

For both studies the radiolabeled compounds (14 C-anion and 14 C-cation) were diluted with unlabeled material. The petitioner points out the non-radioactive standard is 56.6% ICI A0224 (sulfosate) and 43.4% water. This part of the deficiency is resolved. The petitioner has clarified that the 56.6% pure active ingredient number is pure material diluted with water.

Corn seeds were treated with [14 C-TMS] sulfosate at a rate of 4.36 lbs/acre. In a separate sulfosate metabolism study corn seeds were treated with [14 C-CMPA] sulfosate at a rate of 4.57 lbs per acre. Samples were harvested at 33, 48, and 154 days after treatment. At 33 days after treatment [DAT] 10 control plants were harvested (16.2 grams of stems and 17.1 gram of leaves) and 15 [14 C-TMS] treated plants were harvested (90.4 grams of stems and 89.3 grams of leaves). Also, at 33 DAT 20 [14 C-CMPA] treated plants were harvested (56.2 grams stems and 57.2 grams of leaves). At 48 days DAT 7 control plants were harvested, 10 [14 C-TMS] sulfosate treated plants, and 11 [14 C-CMPA] sulfosate treated corn plants plus 5 mature corn plants were harvested. At 154 DAT when the corn was mature 5 control corn plus 5 mature [14 C-CMPA] treated corn plants from each tub were harvested. At 159 DAT when the corn was mature 5 plants of control corn plus 5 mature [14 C-TMS] treated corn plants from each tub were harvested. For the mature plants the petitioner divided the plants into stems, leaves and tassels, husk and silks, kernels, and cobs and shanks. The weight for each sample were provided. The amount of plant material harvested is reasonable for a plant metabolism study. This part of the deficiency is resolved. The petitioner has provided data to show an adequate number of plants were

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harvested and adequate weight of plant material was gathered for analyses.

The petitioner presented flow diagrams for the isolation of starch from [^{14}C -TMS] and [^{14}C -CMPA] sulfosate treated corn kernels. The starch is extracted 3 X with 87% aqueous DMSO and the layers separated by centrifugation. The pulp was extracted 2 X with toluene and 2 X with NH_4HCO_3 . The flow diagrams shows these extracts were combined with the DMSO to get the maximum possible recovery of starch. These points have been clarified and these parts of the deficiency have been resolved.

In both metabolism studies the petitioner used the entire glucose hydrolysate which is equivalent to 10 grams starch in the derivatization with phenylhydrazine. The final amount of the glucosazone was not determined as the reaction is neither quantitative, nor consistent in recovery. Calculation of the % ^{14}C in starch was based on the specific activity of the purified product. The specific activity (dpm/mole) of glucose liberated from starch is equal to the specific activity of the purified glucosazone. The petitioner presented calculations to show that 81-84% of the radioactivity associated with the grain can be accounted for as being incorporated into the glucose of starch. The petitioner explanation is satisfactory as to why no data are available for the final amount of glucosazone isolate. These parts of the deficiency are resolved.

The petitioner presented flow diagrams in sufficient detail for the extraction of [^{14}C -TMS] and [^{14}C -CMPA] sulfosate from various leaf tissues. Both 33 DAT leaves had 10 grams extracted 4 X 20 ml CH_3OH . The 48 DAT leaves had 89.34 grams of [^{14}C -TMS] corn and 69.8 grams of [^{14}C -CMPA] corn extracted 4 X 150 ml Na_2CO_3 . The mature leaves at 159 and 154 DAT were extracted using 3 different schemes. One extraction had 16.98 grams [^{14}C -TMS] corn leaves and 14.9 grams of [^{14}C -CMPA] corn leaves extracted 3 X 100 ml 1.0 M EDTA. The other two schemes used 40.2 grams of [^{14}C -TMS] and [^{14}C -CMPA] corn leaves extracted 4 X 400 ml H_2O , then the water is extracted with EtOAc . The third extraction has 20 grams of [^{14}C -TMS] and 21 grams of [^{14}C -CMPA] mature corn leaves extracted 4 X 200 ml H_2O , then the water extracts are mixed in 80% EtOH to precipitate out the ^{14}C -material. The petitioner has now adequately described the starch extraction schemes providing sample weights and solvents. These parts of the deficiency are resolved.

For the [^{14}C -TMS] metabolism study the petitioner has presented additional data in tabular form showing what percentage of the residue is extractable and what percentage is bound. Some characterization of residues is reported. Mature corn leaves at 154 DAT were analyzed. The petitioner presented a detailed flow diagram showing that 60 grams of mature leaf pulp were hydrolyzed to release the bound residue. The petitioner characterized the 0.06 ppm bound ^{14}C -TMS sulfosate equivalents as 0.023 ppm soluble carbohydrate, 0.015 ppm as crude cellulose, 0.008 ppm as lignin, and 0.013 ppm as protein. The extractable residues in the 154

DAT corn leaves were 0.034 ppm of which 0.005 ppm was ^{14}C -TMS and the remainder was uncharacterized. It is reasonable to expect this characterized residue in 154 DAT leaves to be similar to the uncharacterized residues in 33 and 48 DAT leaves; ie, soluble carbohydrates, crude cellulose, lignin, and protein.

In corn kernels at 154 DAT 80-81% (0.019 ppm) of the 0.024 ppm residue was extractable starch with only 0.003 ppm bound uncharacterized residue. In corn forage (leaves) at 33 DAT 0.13 ppm out of the 0.39 ppm was extractable and half of that 0.07 ppm was ^{14}C -TMS. The remainder extractable residue of 0.06 ppm was not characterized. At 48 DAT corn forage leaves have 0.034 ppm extractable residues of which 0.01 ppm was ^{14}C -TMS and 0.015 ppm was uncharacterized. None of the bound residues (0.21 ppm) in the 33 DAT corn forage and 0.06 ppm in the 48 DAT corn leaves were characterized. CB concludes the characterization of the 154 DAT mature corn leaves can be translated to the 48 and 33 DAT corn forage. CB concludes the petitioner has adequately characterized (but not fully identified) the residue in this part of the study. Additional analytical work to further characterize and identify residues is not expected to yield significant improvement in our understanding of the nature of the residue. The petitioner has provided sufficient additional details of the study and explanations. This part of the deficiency is resolved.

From the cation metabolism study [^{14}C -TMS] sulfosate is the primary residue identified in corn foliage and corn kernels. The cation part is further broken at the C-S bond and the CH_3 fragments go into the carbon pool, then they are reincorporated into natural constituents such as starch, cellulose, protein, lignin, etc. For this sulfosate plant metabolism study no further data are required.

The petitioner provided details in a sample calculation of ppm [^{14}C -TMS] in 48 DAT corn forage leaf tissue in Appendix A. This is adequate to show how TMS residue equivalents were calculated. This part of the deficiency is resolved.

The petitioner has presented a detailed flow chart showing acid hydrolysis. 25 ml of HCl hydrolysate from the 154 DAT mature corn leaf was filtered through #1 Whatman filter paper, then partitioned with 5 ml EtOAc. The aqueous fraction which contained 87% of the radiolabeled residue was separated through C-18 Sep Paks, and eluted off the sep pak with water/ CH_3OH . 52% of the ^{14}C - residue eluted in the loading fraction. The petitioner has now presented sufficient information to show that characterization of residue after hydrolyses was attempted and that no further information can be gained with additional work. This part of the deficiency is resolved.

Mature corn leaves in the anion sulfosate metabolism study have 0.67 ppm ^{14}C residues of which 0.42 ppm was extractable and 0.25 ppm (37%) was bound. The primary residues identified in the soluble fraction were 0.0009 ppm CMPA and 0.0004 ppm identified as AMPA (aminomethyl-phosphonate). This indicates extensive

degradation of CMPA into fragments. Since AMPA is formed this indicates a break of the C-N bond to form AMPA and the carboxy fragment. AMPA can be further broken in a phosphate fragment, CH_2 fragment, and amino fragment. Since these fragments are all basic building components it is natural that they would be reincorporated into various natural constituents. In the amendment additional details such as a 25 gram initial sample size, and further characterization of the bound residue showed that 0.092 ppm was soluble carbohydrates, 0.027 ppm was crude cellulose, 0.042 ppm was lignin, and 0.025 ppm was protein. At least 1/3 (0.14 ppm) to 1/2 (0.21 ppm) in the water soluble fraction is associated with the color of the corn leaves. These radioresidues are now incorporated into natural products. Further characterization of these residues are not expected to yield additional information. The petitioner has adequately characterized and identified the [^{14}C -CMPA] sulfosate residues in corn foliage. This part of the deficiency is resolved.

The anion sulfosate metabolism study shows that in corn grain 84% of the 0.39 ppm ^{14}C residue was incorporated into starch. This also indicates there is extensive metabolism of the CMPA (carboxymethyl-aminomethyl phosphate) molecule. CH_2 fragments are liberated as the C-N and C-P bonds are broken. CH_2 goes into the carbon pool and are incorporated into glucose-starch. No CMPA or AMPA residues were detected in corn grain.

The nature of the sulfosate residue in corn is adequately understood. The residue of concern is sulfosate, per se.

NATURE OF THE RESIDUE - LIVESTOCK

Deficiencies

9. The submitted laying hen metabolism anion study is inadequate. None of the residues present in tissues have any kind of identification attempt. No attempts were made to determine the nature of the residue in eggs. Further characterization of the nature of the residues in the tissues of laying hens and eggs is required. Although CBTS recognizes the difficulty in determining the nature of residues from a compound that is so poorly absorbed, it is still necessary to determine not the nature of the residue in unabsorbed material (such as feces and urine) but of that present in various edible tissues. CBTS normally requires the identification of 90+% of the absorbed residues.
11. The submitted laying hen metabolism cation study is inadequate. None of the residues present in tissues have any kind of identification attempt. No attempts were made to determine the nature of the residue in eggs. Further characterization of the nature of the residues in the tissues of laying hens and eggs is required. Although CBTS recognizes the difficulty in

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determining the nature of residues from a compound that is so poorly absorbed, it is still necessary to determine not the nature of the residue in unabsorbed material (such as feces and urine) but of that present in various edible tissues. CBTS normally requires the identification of 90+% of the absorbed residues.

13. The goat anion metabolism study is inadequate. Although CBTS recognizes the difficulty in determining the nature of residues from a compound that is so poorly absorbed, it is still necessary to determine the nature of the residue in unabsorbed material (such as urine, feces, and gut contents) but of that present in various edible tissues. CBTS normally requires the identification of 90+% of the absorbed residues. In this case, only the residues present in kidney have any kind of identification attempt. This is approximately 30% of the residue absorbed into the 10X goat. No attempts were made to determine the nature of the residue in milk.
15. The goat cation metabolism study is inadequate. Although CBTS recognizes the difficulty in determining the nature of residues from a compound that is so poorly absorbed, it is still necessary to determine the nature of the residue in unabsorbed material (such as urine and feces) but of that present in various edible tissues. CBTS normally requires the identification of 90+% of the absorbed residues. In this case, only the residues present in liver have any kind of identification attempt. This is approximately 9% of the residue present in the goat. No attempts were made to determine the nature of the residue in milk.

Petitioner's Response (MRID No.420681-03)

The petitioner provided additional sulfosate (cation and anion) livestock metabolism data in a study titled "Addendum to MRID 412099-01, 412099-12, 412099-13, and 412099-14 - Nature of Residues of Orally Administered [Trimethylsulfonium and Phosphonomethyl -¹⁴C] ICI A0224 in Tissues, Milk, and Eggs." by J.B. Tarr, dated July, 1989.

CBTS Comments

The petitioner's response is a narrative concluding that CMPA, AMPA, and TMS are the only significant residues. No new analytical data that would address our concerns were presented. The petitioner continues to expand on the nature of the sulfosate residues in poultry and goat excreta. CBTS reiterates that the nature of the sulfosate residues in excreta is not germane to our understanding the nature of the sulfosate residues in liver, kidney, fat, and muscle in these animals. The petitioner is reminded that the sulfosate residues in feces have passed through the body and has not crossed various membranes and been adsorbed

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into the body such as would be the case for sulfosate residues in liver, fat, or muscle. The purpose of the nature of the sulfosate residue study is to determine the distribution of residues, and then to characterize and identify at least 90+% of the residues. The petitioner has only presented sufficient analytical data to determine distribution of residues among the various tissues. CBTS reiterates that the nature of the sulfosate residue in ruminants and poultry is not adequately understood. Deficiencies 9, 11, 13, and 15 are not resolved and continue outstanding.

In the poultry metabolism study where the White Leghorn hens received a high dose of 10.9 mg or 90.8 ppm of ^{14}C -CMPA the ^{14}C -sulfosate equivalent residues in heart were 0.09 ppm, 1.81 ppm in kidney, 0.34 ppm in liver, and 0.05 ppm in thigh muscle. ^{14}C -CMPA equivalent residues in egg whites were 0.057 to 0.06 ppm and in egg yolk were 0.117 ppm. In a separate poultry metabolism study where White Leghorn hens received a high dose of 10.6 mg or 87.9 ppm of ^{14}C -TMS the ^{14}C -sulfosate equivalent residues in breast muscle were 0.23 ppm, 0.17 ppm in heart, 1.00 ppm in kidney, 0.04 ppm in liver, and 0.22 ppm in thigh muscle. ^{14}C -TMS equivalent residues in egg yolk ranged from 0.002 ppm to 0.15 ppm. CBTS recognizes that characterization of residues at these levels may present an analytical challenge. However, the petitioner needs to do additional analytical work to characterize and identify these residues striving to reach at least 90+% characterization and identification. CBTS suggests the petitioner provide the same or higher degree of characterization and identification of residues in poultry as have been provided for sulfosate residues in plants.

In the caprine metabolism study where an Alpine goat received 100 ppm dose of ^{14}C -CMPA the ^{14}C -sulfosate equivalent residues were 9.74 ppm in kidney, 0.056 ppm in heart, and 0.26 ppm in liver. The ^{14}C -CMPA equivalent residues in goat milk ranged from 0.02 ppm (at 0.5 day) to 0.07 ppm (at 3.5 day). In a separate caprine metabolism study where a Nubian goat received a 100 ppm dose of ^{14}C -TMS the ^{14}C -sulfosate equivalents in caprine milk ranged from 0.21 ppm to 1.08 ppm with a majority of this residue being in the skim milk fraction. ^{14}C -TMS equivalent residues were 0.59 ppm in fat, 1.47 ppm in heart, 4.39 ppm in kidney, 2.28 ppm in liver, and 1.93 ppm in muscle. CBTS recognizes that it is an analytical challenge to characterize and identify these residues. However, we feel there is sufficient residue present in a number of these caprine tissues and fluids that warrant extensive additional analytical work to strive to characterize and identify at least 90% of the ^{14}C -sulfosate equivalent residues. With ^{14}C -sulfosate equivalent residues ranging up to 9.7 ppm CBTS suggests that the petitioner provide a higher degree of characterization and identification of residues in goats than have been provided for sulfosate residues in plants.

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RESIDUE ANALYTICAL METHOD**Deficiencies**

- 4a. Subject to successful completion of the Agency method validation trials, CBTS would consider the methods for the anionic and cationic moieties of sulfosate to be adequate for corn only.
- 4b. Because small residues may be carried into feed items, it is necessary to have available an enforcement method for residues in meat, milk, poultry, and eggs. The submitted methods were not validated with these commodities. Both petitioner and independent method validation are required for these commodities.

Petitioner's Response

The petitioner did not respond.

CBTS Comments

In a memorandum dated November 2, 1990 by S. Koepke to D. Marlow of ACB/BEAD CBTS requested PMVs (petition method validations) for 4 sulfosate residue analytical methods. The PMVs were for this petition and co-pending petition PP# OF3860, sulfosate on soybeans. Method WRC 85-33 was to be validated with trimethyl sulfonium chloride at 0.05 ppm and 0.1 ppm in corn grain and forage. Method WRC 85-34R was to be validated CMP (carboxymethyl aminomethyl phosphate) and AMPA (aminomethylphosphonic acid) in corn grain at 0.05 ppm and 0.1 ppm, and in corn forage at 0.1 ppm and 0.2 ppm. Method RRC-87-42 was to be validated with TMS at 0.02 ppm and 0.05 ppm in milk, and at 0.1 ppm and 0.2 ppm in bovine liver. Method RRC-87-41 was to be validated with CMP and AMPA at 0.02 ppm and 0.05 ppm in milk, and at 0.2 ppm and 0.5 ppm in bovine liver. As part of its pre-trial review ACB detected a number of minor problems that needed clarification. In the memoranda from E. Greer on January 13, 1991 and H. Hundley on January 30, 1991 ACB requested additional information on the methods. The PMVs would be terminated without this information. There have not been successful PMVs. The ACB findings were reviewed by S. Koepke in PP# OF3860 in his memorandum of April 24, 1991. The 4 residue analytical methods needed to be rewritten to incorporate ACB comments and requested clarifications. The ACB pre-trial review was attached to PP# OF3860 and all ACB comments are incorporated herein by reference.

CBTS reiterates that the revised methods will need ILV (independent laboratory validation) data. We suggest that the 4 methods be rewritten, then the ILV data acquired. The PMVs will not be reinitiated until the petitioner has revised his residue analytical methods and generated satisfactory ILV data. Since there has not been successful PMVs, deficiency 4a has not been resolved. CBTS reiterates that there have to be successful PMVs prior to our recommendation for sulfosate tolerances in corn

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products and secondary sulfosate tolerances in meat, milk, poultry, and eggs.

Deficiency 4b is moot. The petitioner has presented residue analytical methods for the anion and cation sulfosate in tissues, milk, and eggs as part of PP# 0F3860, thus validation data for sulfosate in tissues are not necessary for the plant residue methods.

MAGNITUDE OF THE RESIDUE - CROP FIELD TRIALS

Deficiency

- 5a. Twelve residue field trials from ten states were submitted all from one growing season. CBTS does not consider either geographical or total representation to be adequate. Additional field trials from the Northeast corn growing region (PA and NY) are required. Residue fields trials for each represented state from an additional growing season are also required.

Petitioner's Response

In his cover letter the petitioner presented a discussion why no additional crop field trials are necessary.

CBTS Comments

After careful reconsideration CBTS concludes an additional year of crop field trial residue data from the states where field trials have been conducted are not necessary, per se. The EPA response noted on page 46 of the "Pesticide Reregistration Rejection Rate Analysis Residue Chemistry" is adequate guidance to the petitioner. In this instance there are too few studies for a national tolerance on a major food/feed commodity. Additional sulfosate on corn crop field trials are necessary. In the October 10, 1989, "Overview of Residue Chemistry Guidelines" in Attachment 4 where guidance is offered on suggested states for crop field trials CBTS noted that residue data on corn were required from all areas of the country. The petitioner has not presented sulfosate in/on corn residue data from all areas of the country and has not included residue data from all major corn producing states. Additional sulfosate crop field trial residue data are necessary. Corn should be treated with Touchdown® at or above the proposed use rate and harvested at the proposed PHI.

The petitioner's discussion on why the crop field trial data are sufficient has been given careful consideration. However, CBTS feels that the present residue data are too limited geographically. CBTS reiterates that magnitude of the residue data are required from NY and PA. For NY the petitioner should consider having 2 separate field trials, one in up state close to the Great Lakes and one down state maybe on Long Island or in the Hudson River valley. This site would be sufficient for New

England geographical representation. The petitioner needs to have a field trial or two in the Southeastern area of the USA in the states of Florida, Georgia, Alabama. Georgia is the largest state east of the Mississippi River in land area. Another area from which sulfosate in corn field trial residue data should be presented is the Texas, Oklahoma, Louisiana region. Sulfosate on corn field trial data should be presented from the Pacific Northwest from either Washington, Oregon, or Idaho. The petitioner should consider having a field trial in the major corn producing states of Michigan, Ohio, and Indiana. No sulfosate on corn residue data have been presented from these states.

For the major corn producing states where sulfosate crop field trial residue data have already been presented the petitioner is encouraged to recheck climate conditions to be certain the residue data are not skewed. If there is any question on the reliability of the residue data, then the petitioner is encouraged to gather new magnitude of the residue data for the states in question. With these nine additional field trial there should be adequate geographical representation. While this is a second year of crop field trial data, generation is not due to the need for data from a second year, per se. Data from a second year bring the sulfosate in corn field trial data in line with Codex requirements for magnitude of the residue data. In all field trials the petitioner is reminded to monitor the weather conditions carefully to be certain that conditions do not skew the data.

NOTE: In response to a verbal inquiry from ICI this information on the need for additional crop field trial residue data has been conveyed to ICI in a telcon on September 8 between D. Griffith, EPA and Becky Rhodes, ICI.

MAGNITUDE OF THE RESIDUE-MEAT, MILK, POULTRY, AND EGGS

Deficiency

10. Feeding studies are required to be carried out for 30 days on poultry and eggs using unlabeled material and the required analytical method for the anion in order to determine if residues may build up over time. It is CBTS policy that feeding studies should continue for at least four weeks.
12. Feeding studies are required to be carried out for 30 days on poultry and eggs using unlabeled material and the required analytical method for the cation in order to determine if residues may build up over time. It is CBTS policy that feeding studies be continued for at least four weeks.
14. Dairy cattle feeding studies are required to be carried out for 30 days on meat and milk using unlabeled material and the required analytical method for the anion in order to determine if residues may build up over time. It is CBTS

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policy that feeding studies should be continued for at least four weeks.

16. Dairy cattle feeding studies are required to be carried out for 30 days on meat and milk using unlabeled material and the required analytical method for the cation in order to determine if residues may build up over time. It is CBTS policy that feeding studies should be continued for at least four weeks.

Petitioner's Response

In the cover letter the petitioner points out that sulfosate bovine feeding studies and sulfosate poultry feeding studies were submitted as part of PP# 0F3860. These studies were adequately reviewed by S. Koepke in his memorandum of April 24, 1991, and found to be acceptable. The Agency suggested appropriate secondary sulfosate tolerances for meat, milk, poultry, and eggs.

CBTS Comments

Ruminants

The petitioner presented the results of bovine sulfosate feeding studies where 6 groups of 3 each lactating cows were dosed with sulfosate for 28 days at levels of 0 (control), 0.5 ppm, 5 ppm, 50 ppm, 300 ppm, and 1000 ppm. Milk samples were collected throughout the study for analysis. Two cows in each group were sacrificed at 28 days and the remaining cow in each group was sacrificed at 35 days to determine the decline of sulfosate residues in milk and tissues. At sacrifice, samples of liver, kidney, fat, and muscle were recovered for residue analysis. There are adequate storage stability data to support these feeding studies.

The 5 ppm feeding dose most closely approximates the expected sulfosate feeding level for both corn and soybeans in potential bovine diets.

The maximum TMS and CMP sulfosate residues in milk from the 5 ppm feeding were below the residue analytical methods' limits of detection. TMS was detected in milk at 0.18 ppm from 50 ppm sulfosate dose and up to 4.0 ppm from the 1000 ppm dose. No AMPA residues were detected in milk, even from the 1000 ppm sulfosate dose. CMP residues in milk were 0.02 ppm at the 300 ppm dose and 0.04 ppm at the 1000 ppm sulfosate dose.

Kidneys showed residue levels at 0.03 ppm TMS from the 5 ppm sulfosate dose. TMS was detected in muscle at 0.04 - 0.05 ppm. No TMS was detected in liver or fat to the method's limit of detection. Likewise, no CMP or AMPA residues were detected in kidney, liver, fat and muscle at the methods' limit of detection at this 5 ppm sulfosate dose.

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Maximum TMS residues in kidneys were 0.18 ppm at the 50 ppm sulfosate dose, increasing to 1.9 ppm at the 300 ppm dose, and to 4.5 ppm from the 1000 ppm sulfosate dose. Maximum CMP residues in kidneys were 0.44 ppm at the 50 ppm dose increasing to 7.6 ppm at 1000 ppm sulfosate dose. Maximum AMPA residues in kidneys ranged from 0.08 ppm at 50 ppm dose to 1.7 ppm from the 1000 ppm sulfosate dose.

Maximum TMS residues in liver were 0.32 ppm at the 50 ppm dose, increasing to 0.69 ppm for the 300 ppm dose, and to 2.0 ppm at the 1000 ppm sulfosate dose. No AMPA residues were detected in liver; even at the 1000 ppm sulfosate dose. CMP residues were detected in liver at a maximum of 0.51 ppm from the 1000 ppm sulfosate dose.

In fat, from the 50 ppm sulfosate dose the TMS residues were 0.01 ppm, increasing to 0.1 ppm from the 50 ppm dose, and remaining nearly constant at 0.08 ppm for the 1000 ppm sulfosate dose. No AMPA residues were detected in fat, even from the 1000 ppm sulfosate dose. CMP residues were 0.06 ppm at the 50 ppm and 300 ppm sulfosate dose. Maximum CMP residues in fat from the 1000 ppm dose increased slightly to 0.1 ppm.

In muscle no AMPA residues were detected to the method's limit of detection. CMP residue were detected only from the 1000 ppm sulfosate dose at a maximum of 0.08 ppm. Maximum TMS residues in muscle from the 50 ppm sulfosate dose were 0.11 ppm, increasing to 0.63 ppm from the 300 ppm sulfosate dose, and to 1.6 ppm from the 1000 ppm sulfosate dose.

CBTS reiterates that the petitioner has conducted an adequate bovine sulfosate feeding study if the goat sulfosate metabolism study reveals only CMPA, AMPA, and TMS as the only significant residues. From a probable bovine diet that contains both corn and soybean feed items with sulfosate residues (about 3 - 5 ppm) CBTS concludes that no measurable residues of the parent sulfosate were detected. However, from feeding exaggerated levels of sulfosate residues were detected in milk and tissues. Thus, we would categorize the use as 40 CFR §180.6(a)2 in that it is not possible to establish with certainty that finite residues will be incurred, but there is a reasonable expectation of finite residues. CBTS reiterates that the petitioner needs to submit a revised Section F proposing secondary sulfosate tolerances in milk at 0.04 ppm, at 0.1 ppm in meat, fat, and meat by-products (except liver) of cattle, goats, hogs, horses, and sheep, and in liver at 0.4 ppm of cattle, goats, hogs, horses, and sheep. These residues would be expressed as parent sulfosate calculated as either the magnitude of the CMP residue or the magnitude of the TMS residue, whichever is greater. Deficiencies 14 and 16 are tentatively resolved.

Poultry

The petitioner presented the results of poultry sulfosate feeding studies where 4 groups of 10 each laying hens were dosed

with sulfosate for 28 days at levels of 0 (control), 0.5 ppm, 5 ppm, and 50 ppm. Egg samples were collected throughout the study for analysis. Seven hens in each group were sacrificed at 28 days and the remaining hens in each group was sacrificed at 35 days to determine the decline of sulfosate residues in eggs and tissues. At sacrifice samples of liver, kidney, fat, and muscle were recovered for residue analysis. There are adequate storage stability data to support these feeding studies.

The 5 ppm feeding dose most closely approximates the expected sulfosate feeding level for both corn and soybeans in potential poultry diets.

No residues of AMPA, CMP, and TMS were detected in eggs, fat, liver, kidney, and muscle from the 5 ppm sulfosate dose. 0.072 ppm CMP was detected in poultry liver from the 5 ppm sulfosate dose.

In eggs no TMS and no AMPA residues were detected from the 50 ppm sulfosate dose. CMP residues in eggs from 50 ppm sulfosate dose ranged from 0.010 ppm at day 7 to 0.014/0.015 ppm at 28 days.

In poultry muscle and fat no TMS, AMPA, and CMP residues were detected even with the 50 ppm sulfosate dose. No AMPA and TMS residues were detected in poultry kidney from the 50 ppm dose. CMP residues were detected in kidney at 0.31 ppm at 28 days declining to 0.11 ppm at 35 days (7 days withdrawal). TMS was also detected in poultry kidney at 0.18 ppm. TMS was the only residue detected in poultry liver at 0.13 ppm from the 50 ppm sulfosate dose.

CBTS reiterates that the petitioner has conducted an adequate poultry sulfosate feeding study if the sulfosate poultry metabolism study reveals that the only significant residues are CMPA, AMPA, and TMS. From a probable poultry diet that contains both corn and soybean feed items with sulfosate residues (about 3 - 5 ppm) CBTS concludes that no measurable residues of the parent sulfosate were detected; however, from feeding exaggerated levels of sulfosate residues were detected in eggs and tissues. Thus, we would categorize the use as 40 CFR §180.6(a)2 in that it is not possible to establish with certainty that finite residues will be incurred, but there is reasonable expectation of finite residues. CBTS reiterates that the petitioner needs to submit a revised Section F proposing secondary sulfosate tolerances in eggs at 0.03 ppm, at 0.1 ppm in meat, fat, and meat by-products of poultry. These residues would be expressed as parent sulfosate calculated as either the magnitude of the CMP residue or the magnitude of the TMS residue, whichever is greater. Deficiencies 10 and 12 are tentatively resolved.

The need to regulate the metabolite AMPA as part of the glyphosate tolerance has come before the HED Metabolism Committee. The Committee concluded that aminomethylphosphonic acid (AMPA) need not be regulated and should be dropped from the

glyphosate tolerance regulation. This would harmonize the glyphosate expressions for the USA tolerances and the Codex MRL's. By inference CBTS will extend the conclusion to the sulfosate tolerance expression. CBTS concludes that the sulfosate metabolite AMPA need not be regulated and should be dropped from the proposed tolerance expression. CBTS concludes that the petitioner needs to submit a revised sulfosate expression deleting the reference to AMPA and regulate sulfosate in terms of the parent herbicide, per se, in plants. The livestock tolerance expression can be determined when the requested metabolism studies are completed and revised.

cc: R.F., Circ, PP#9F3796, Reviewer(FDG), Sulfosate Subject File.

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