Flumetsulam ~~DE-498~~ 37

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

MAR 27 1992

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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: PP#1G04006 (CB #'s 8400 and 8646; Barcode #'s D167462 and D168563, respectively). DE-498 on Soybeans and Field Corn. (MRID #'s 419317-01, -02; 419317-12 through -21; 419521-01, -04, -05, -06; and 419938-02.

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Chemistry Branch I - Tolerance Support
Health Effects Division (H7509C)

THRU: Debra Edwards, Ph.D., Acting Chief Debra Edwards
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TO: Joanne Miller, PM #23
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and

Toxicology Branch II - Herbicide, Fungicide, and Antimicrobial Support
Health Effects Division (H7509C)

DowElanco proposes temporary tolerances of 0.05 ppm for residues of the herbicide N-(2,6-difluorophenyl)-5-methyl-1,2,4-triazolo-[1,5a]-pyrimidine-2-sulfonamide (DE-498, formerly XRD-498; flumetsulam) in/on field corn fodder, corn forage, corn grain, and soybeans.

No tolerances for DE-498 have been established. A crop destruct Experimental Use Permit (62719-EUP-13) for XRM-5019 (an end-use product containing DE-498) was issued by EPA on 3/8/91. A meeting was held on 2/23/90 to discuss residue data requirements for products containing XRD-498 (now called DE-498) in combination with trifluralin, metolachlor, and clopyralid.

The proposed experimental use permit for XRM-5019 (containing the active ingredient DE-498) would allow use on soybeans and corn during the 1992 and 1993 growing seasons (ie. 3/1/92 - 12/1/93).

A total of 66.1 lbs. XRM-5019 (49.6 lbs. ai) will be used on 730 acres of soybeans in 1992. A total of 93.55 lbs. XRM-5019 (70.2 lbs. ai) will be used on 1035 acres of soybeans in 1993. In both 1992 and 1993, applications to soybeans will be made in the following states: AL, AR, CO, DE, FL, GA, IL, IN, IA, KS, KY, LA, MD, MI, MN, MS, MO, NE, NJ, NY, NC, ND, OH, OK, PA, SC, SD, TN, TX, VA, and WI.

A total of 87.25 lbs. XRM-5019 (65.4 lbs. ai) will be used on 965 acres of field corn in 1992. A total of 105.25 lbs. XRM-5019 (78.9 lbs. ai) will be used on 1165 acres of field corn in 1993. In both 1992 and 1993, applications to field corn will be made in the following states: AL, AR, CA, CO, DE, FL, GA, IL, IN, IA, KS, KY, LA, MD, MI, MN, MS, MO, NE, NJ, NY, NC, ND, OH, OK, PA, SC, SD, TN, TX, VA, and WI.

Data reviewed in this review (including all MRID #'s listed above) were not generated by Craven Laboratories.

CONCLUSIONS

PRODUCT CHEMISTRY

§61-1

1. The following additional data are required under §61-1:

a) A typographical error is noted in #13b of the CSF. The petitioner should make the change as indicated in the Confidential Appendix.

b) The names of some of the impurities in the CSF are not satisfactory. The petitioner must identify these as indicated in the Confidential Appendix.

c) The chemical name from the Chemical Abstracts Index of Nomenclature was not given. This should be provided.

d) The petitioner states that "flumetsulam" is a proposed IUPAC name. CBTS believes that "flumetsulam" is a proposed ANSI name. The petitioner should clarify this point.

§61-2

2. The following additional data are required under §61-2:

a) For each beginning material, the petitioner should submit "a copy of all available technical specifications, data sheets, and

other documents by which the manufacturer, producer, or supplier of the beginning material describes its composition, properties, or toxicity".

b) The petitioner should state whether the process is a batch or continuous process.

c) The equipment is not adequately described. The petitioner should describe the equipment used to produce the product which may influence the product's composition.

d) The temperatures of the reactions are given. Any other physical conditions (eg. pressure, humidity) "which are controlled during each step of the process in order to influence the product's composition, and the parameters that are maintained" should be reported.

e) Parts of the descriptions of some reaction steps as described in the Confidential Appendix are missing from pages 111 and 112 of the report. These should be provided.

f) The durations of some of the reaction steps were not given. The duration of each step of the process should be provided.

g) "A description of any purification procedures, including procedures to recover or recycle starting materials, intermediates, or the final product" should be provided.

h) "A description of measures taken to assure the quality of the final product, including procedures involving the equipment used for blending product components and for filling and packaging," should be provided.

§61-3

3. The following additional information is required under §61-3:

An explanation for the formation of some of the impurities has not been given as discussed in the Confidential Appendix. The petitioner must explain the formation of those impurities in DE-498 Technical.

§62-1

4. The following additional information is required under §62-1:

a) The petitioner should identify some impurities as discussed in the Confidential Appendix.

b) For permanent tolerances, the batch analyses for the impurities should be reported as weight % (not area %). For the purposes of this EUP, CBTS will accept the use of "area %" as a

measure of the levels of the impurities discussed in the Confidential Appendix.

c) An impurity is not clearly identified in Table II, page 43, of MRID #419317-02. The batch analyses for the impurity should be reported as discussed in the Confidential Appendix.

d) The identities of some impurities in the batch analyses discussed in the Confidential Appendix and their weight percentages should be given if any impurity is present at a level equal to or greater than 0.1% by weight.

e) The petitioner should also report the relative standard deviation of the analyses.

§62-2

5. Certified limits have been submitted on a CSF. No additional information is required under §62-2.

§62-3

6. The following additional information is required under §62-3:

a) The petitioner should submit analytical methods for determining some impurities discussed in the Confidential Appendix.

b) The precision and accuracy of the methods for the impurities discussed in the Confidential Appendix should be reported.

§63-2 through 63-13

7. The following additional data are required under §63-2 to 63-13:

The references given in MRID#419521-01 give the name of the report or laboratory notebook reference but do not sufficiently identify the methods. Therefore, methods used to identify physical/chemical properties in §63-2 through 63-13 should be identified as described in §63-1(b) and (c).

Note: According to §63-1(b), methods used to determine physical/chemical properties should either be those referenced in §63-2 through 63-18 or other "scientifically-sound techniques, provided that data are presented to show that the techniques used produce results comparable to the referenced methodology".

§63-1(c) further states that "if methods used are listed in the references paragraphs of this section series, reference to the methods will suffice. If other methods are used, references may be used only

if the instructions are readily available in texts or periodicals; otherwise, copies of such methods must be submitted with this application".

§63-8

8. The following additional information is required under §63-8:

a) Solubility should be reported in g/100 ml solvent, or if sparingly soluble in other terms such as ppm (mg/kg).

b) Complete copies of all methods (ie. Standard Operating Procedure (SOP) 7i.02, Protocol #90108, and SOP 7h.01) should be submitted.

§63-13

9. The following additional information is required under §63-13:

a) Additional data should be provided on the stability at normal temperatures. Storage stability to metal ions and other metals (besides stainless steel and brass) should be determined.

b) Complete copies of all methods (SOP 7k.00 and Protocol 89081) should be submitted.

c) The time of exposure to sunlight before photodegradation determination was not stated in MRID #419521-01. The time of testing should be stated.

RESIDUE CHEMISTRY

Manufacture

10. The manufacturing process is not adequately described. Refer to the discussion in §61-2 above.

Formulation

11. CBTS defers to Registration Division concerning whether the inerts in XRM-5019 are cleared. Refer to the Confidential Statement of Formula for XRM-5019 (Attachment 7).

Proposed Use

12a) The petitioner should submit a revised Section B/label with the following additional information: the maximum number of applications, the maximum pounds ai/A/yr for postemergence uses, the maximum pounds ai/A/yr for all uses combined (preplant incorporated, preemergence, and postemergence), the minimum interval between applications, the minimum interval between the last application and harvest (preharvest interval), and the

application rate also expressed in terms of pounds of active ingredient per acre (lbs ai/A).

12b) The petitioner should also submit a revised Section F replacing the term "corn" with "corn (except pop and sweet)" since the proposed use is on field corn only.

Nature of the Residue

Soybeans:

13a) The nature of the residue in soybeans is adequately defined for the proposed EUP only. DE-498 can be considered to be the residue of concern.

13b) For a future permanent tolerance, additional metabolism data will be required. In the submitted studies on soybeans, residues were not adequately characterized in any plant part. Residue components accounting for ≥10% of the residue after exhaustive extraction should be identified, preferably by two techniques (eg. TLC, HPLC, MS). Such components may include components A2 and B1 which were present in the 12-day and 28-day forage samples from ^{14}C-phenyl-labelled DE-498 treated soybeans. Analysis should also include determination of the presence of 2,6-difluroaniline (possibly present as a product of hydrolysis of the sulfonamide linkage of ^{14}C-phenyl-labelled DE-498) and 5-methyl-(1,2,4)triazolo-(1,5a)pyrimidine-2-sulfonic acid [possibly present as a product of the hydrolysis of the sulfonamide linkage of (5-^{14}C) pyridine-labelled DE-498] at all sampling times by use of authentic standards.

Extractability of the residue into solvents used in the proposed analytical enforcement method should be determined. Most of the radioactivity should be extracted, or exhaustive attempts using acid, base, and/or enzymes should be made to do so. The petitioner should use the radiolabelled samples to determine what percentage of the total recovered radioactivity is determined by the proposed enforcement methodology.

The identity of the residues in all plant parts of the raw agricultural commodity which could be used for food or feed (seed, forage, and hay) should be determined. Samples should be either analyzed or frozen immediately after harvest. (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981 and to the "Standard Evaluation Procedure, Qualitative Nature of the Residue: Plant Metabolism", NTIS #PB87-208641.)

The additional work needed for the soybeans treated with phenyl labelled DE-498 may be done using reserve forage samples (12 and 28 day samples) provided they have been kept frozen. For the

pyridine labelled DE-498, CBTS recommends a new study be conducted at the maximum rate that does not result in significant phytotoxicity. The green plant should be analyzed at intervals similar to those in the previous phenyl labelled study.

Corn:

14a) The nature of the residue in corn is adequately defined for the proposed EUP only. DE-498 can be considered to be the residue of concern.

14b) For a future permanent tolerance, additional metabolism data will be required. In the submitted studies on corn, residues were not adequately characterized in any plant part. Residue components accounting for $\geq$10% of the residue after exhaustive extraction should be identified, preferably by two techniques (eg. TLC, HPLC, MS). Analysis should also include determination of the presence of 2,6-difluroaniline (possibly present as a product of hydrolysis of the sulfonamide linkage of ^{14}C-phenyl-labelled DE-498) and 5-methyl-(1,2,4)triazolo-(1,5a)pyrimidine-2-sulfonic acid [possibly present as a product of the hydrolysis of the sulfonamide linkage of (5-^{14}C) pyridine-labelled DE-498] at all sampling times by use of authentic standards.

Extractability of the residue into solvents used in the proposed analytical enforcement method should be determined. Most of the radioactivity should be extracted, or exhaustive attempts using acid, base, and/or enzymes should be made to do so. The petitioner should use the radiolabelled samples to determine what percentage of the total recovered radioactivity is determined by the proposed enforcement methodology.

The identity of the residues in all plant parts of the raw agricultural commodity which could be used for food or feed (grain, forage, silage, and fodder) should be determined. Concerning the (5-^{14}C)pyridine-labelled DE-498 corn study, CBTS further recommends that a new study be conducted using a higher rate (ie. the maximum rate not resulting in significant phytotoxicity) and examining plant parts at intervals similar to those used in the ^{14}C-phenyl-labelled DE-498 study. Samples should be either analyzed or frozen immediately after harvest. The additional work (eg. looking for the presence of 2,6-difluoroaniline) needed for corn treated with phenyl labelled DE-498 may be done using reserve samples provided they have been kept frozen. (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981 and to the "Standard Evaluation Procedure, Qualitative Nature of the Residue: Plant Metabolism", NTIS #PB87-208641.)

Animals:

15. The nature of the residue in animals is adequately defined for

this proposed use provided that no detectable or very low residues are found in feed items. The residue of concern in ruminants is DE-498 per se. The residues of concern in poultry are DE-498 per se and the 5-hydroxy metabolite. Provided that no detectable or very low residues are found in feed items, tolerances will not be required on animal commodities.

For uses which may result in detectable residues in feed items, additional animal metabolism data on ruminants and poultry may be required.

Analytical Methods

Plants:

16. The analytical methodology for soybeans and field corn is not adequate as submitted. The following additional information is needed:

a) The source/supplier of methylene chloride should be included in the method.

b) The complete method for field corn including the minor modifications to the method which are made for analysis of field corn grain, forage, and fodder and validation data (ie. recoveries, limit of quantitation of the method, and chromatograms) should be submitted.

c) An independent laboratory validation of the method for field corn may be required depending upon how the method differs from the soybean procedure.

d) Method No. ACR 91.6 uses an internal standard. Generally, an enforcement method cannot use an internal standard. However, the deuterated standard is expected to behave the same chemically as the DE-498. This internal standard is acceptable in the enforcement method provided that the deuterated internal standard is made available along with the DE-498 analytical standard to RTP and enforcement labs.

e) Enforcement methods should require a maximum of 24 hours for completion, whereas this method took the validating lab 30 person-hours and 4 calendar days. Efforts should be made to shorten the method for enforcement purposes.

f) A confirmatory method should be provided for enforcement purposes.

g) An interference study should be conducted to determine if other pesticides registered on corn and soybeans would interfere with the method. This specificity study is needed for enforcement purposes.

h) Analytical reference standards for DE-498 including the deuterated analog and other residues of concern, if any, should be sent to the Pesticide and Industrial Chemicals Repository (MD8), U.S. Environmental Protection Agency, Research Triangle Park, North Carolina 27711. Two grams each of the purified analytical standards should be provided for the pesticide and principal degradation products or metabolites. The Material Safety Data Sheets should be included as required by OSHA in 29 CFR 1910.1200. A letter of transmittal accompanying the standards should include the following: the purity of the standards; analytical methods used to assay the standards; a statement of principal impurities; purification procedures; storage requirements; and special precautions for safe handling.

i) When the necessary information is provided, CBTS will request an EPA lab to perform a method validation for Method No. ACR 91.6 on corn and soybeans.

Multiresidue Methods:

17a) The petitioner has submitted some data for Multiresidue Protocols B and C on soybeans (fatty food) and wheat grain (non-fatty food) (MRID #419938-02). CBTS will forward the submitted data on Protocols B and C to FDA for review to determine sufficiency.

17b) The petitioner should explain why testing through Multiresidue Protocols D and E was not submitted. Testing through Protocol A is not required because DE-498 does not contain the N-methylcarbamate structure.

Animals:

18. No analytical methods have been submitted for animal commodities. Analytical methods for animal commodities will not be required provided that no detectable or very low residues are found in feed items and no detectable residues are expected to occur in animal commodities as a result of the proposed use.

Storage Stability

Soybeans:

19. DE-498 in soybeans in frozen storage is fairly stable for at least 411 days, with a possible loss of $\leq$11% DE-498.

Corn:

20. CBTS cannot determine storage stability of DE-498 on corn based on a table alone. The interim and then the complete storage stability study on corn should be submitted for evaluation instead of just a table. Storage stability data for a period equal to or

exceeding the actual storage time of the residue samples will be needed to support the residue data on corn discussed below. (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981; a Position Document: "Effects of Storage (Storage Stability) on Validity of Pesticide Residue Data", NTIS #PB88-112362; and "Storage Stability Study", Addendum on Data Reporting.)

Residue Data

Field Corn:

21. The residue data on field corn are not adequate for reasons a-e and g below: (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981; "Magnitude of the Residue: Crop Field Trials", Standard Evaluation Procedure, NTIS #PB86-129426; and "Magnitude of the Residue: Crop Field Trials", Addendum #2 on Data Reporting, NTIS # PB86-248192.)

a) Adequate geographic representation is not provided for field corn. Additional residue data should be obtained from TX, CA, MD, and WA.

b) The following information is needed to evaluate the adequacy of the residue data: the maximum number of applications, the maximum pounds ai/A/yr for postemergence uses, the maximum pounds ai/A/yr for all uses combined (preplant incorporated, preemergence, and postemergence), the minimum interval between applications, and the minimum interval between the last application and harvest (preharvest interval).

c) The label indicates that field corn can be treated up to the height of 12 inches. The height of the corn at treatment in all field trials should be indicated. Since the highest residues would be expected to result from postemergence treatment of corn which was 12 inches high, that use pattern must be adequately represented.

d) The label indicates that postemergence applications can be made with a crop oil concentrate at 1% v/v (1 gal/100 gal) or a non-ionic surfactant at 0.25% v/v (1 qt/100 gal) in the spray. No residue data were submitted reflecting use of the crop oil concentrate. (All sprays included a non-ionic surfactant.) Therefore, references on the label to the crop oil concentrate should be deleted or additional residue data should be submitted reflecting use of the crop oil concentrate.

e) The petitioner has indicated that samples were stored frozen. Storage temperature should be specified.

f) Residue data on silage are not needed since residue data on forage and fodder will be available.

g) Adequate storage stability data on corn have not been provided.

Processing Study on Field Corn:

22a. For the temporary tolerance, no processing study is needed since no detectable residues were found at the 3X application rate.

22b. For the permanent tolerance, a processing study is needed and food additive tolerances may be needed for processed fractions of corn grain. The theoretical concentration factor from corn grain to corn oil is 28X. However, the petitioner should apply the maximum practical exaggerated foliar application rate, which would be considered to be 5X or less if phytotoxicity occurs at 5X. Even if no detectable residues were found in corn grain after postemergence treatment at 5X, the corn grain should be processed. If no detectable residues are found in the processed products, then no food additive tolerance would be required. Processed commodities from field corn are starch, crude oil and refined oil from wet milling; and grits, flour, meal, crude oil and refined oil from dry milling. Grain dust residue data are not required for this use on corn since applications are preplant incorporated, preemergence, and early postemergence. "The grain dust data are needed only in those cases in which detectable, primarily surface residues are found on the grain." ("Overview of Residue Chemistry Guidelines", R.D. Schmitt, 10/10/89). (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981; "Magnitude of the Residue: Processed Food/Feed Studies", Standard Evaluation Procedure, NTIS #PB88-243209; and "Magnitude of the Residue: Processed Food/Feed Study", Addendum on Data Reporting, NTIS #PB88-117270.)

Soybeans:

23. Residue data on soybeans are not adequate for reasons b-g and i below: (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981; "Magnitude of the Residue: Crop Field Trials", Standard Evaluation Procedure, NTIS #PB86-129426; and "Magnitude of the Residue: Crop Field Trials", Addendum #2 on Data Reporting, NTIS # PB86-248192.)

a) Adequate geographic representation is provided.

b) The following information is needed to evaluate the adequacy of the residue data: the maximum number of applications, the maximum pounds ai/A/yr for postemergence uses, the maximum pounds ai/A/yr for all uses combined (preplant incorporated, preemergence, postemergence), the minimum interval between applications, and the minimum interval between the last application and harvest (preharvest interval).

c) Adequate bridging data for comparison of residues resulting from the proposed formulation XRM-5019 (a water dispersible granular formulation) and the experimental formulation XRM-4950R (an aqueous suspension concentrate) are not available. Although not required, CBTS recommends that a protocol for bridging data should be submitted before additional work is done.

d) The complete second method (ie. other than method ACR 91.6) which was used to analyze residues in soybeans (in MRID #419521-06) should be submitted.

e) The label indicates that soybeans can be treated up to the fifth trifoliate leaf stage of growth. The growth stage of the soybeans at treatment in all field trials should be indicated. Since the highest residues would be expected to result from postemergence treatment of soybeans which were at the fifth trifoliate leaf stage of growth, that use pattern must be adequately represented.

f) The label indicates that postemergence applications must be made with a non-ionic surfactant at 0.25% v/v (1 qt/100 gal) or a crop oil concentrate at 1% v/v (1 gal/100 gals) in the spray. No residue data were submitted reflecting use of the crop oil concentrate or nonionic surfactant in the DE-498 spray solution. Therefore, references on the label to the crop oil concentrate and non-ionic surfactant should be deleted or additional residue data should be submitted reflecting use of the crop oil concentrate and the nonionic surfactant.

g) The petitioner has indicated that samples were stored frozen. Storage temperature should be specified.

h) Label restrictions against feeding soybean hay and forage are acceptable since these are considered to be under grower control and not routinely fed to livestock.

i) Available storage stability data (up to 411 days) do not support residue data on soybean samples stored longer (ie. up to 32 1/2 months).

Processing Study on Soybeans:

24. A processing study and food additive tolerances are not needed for soybeans since no residues were found in soybeans after postemergence treatment at 6X, the theoretical concentration factor for soybean oil.

25. Grain dust residue data are not required for this use on soybeans since detectable, primarily surface residues are not expected.

Meat, Milk, Poultry, and Eggs

26. CBTS must reserve its conclusion regarding the need for animal feeding studies until questions regarding the proposed use, plant metabolism, plant analytical methods, and residue data are resolved. If no detectable residues are found in feed items, no animal feeding studies and no tolerances for animal commodities will be required.

Other Considerations

27. An International Residue Limits (IRL) Status Sheet is attached. There are no Codex, Canadian, or Mexican tolerances for DE-498 (flumetsulam) on corn or soybeans. Therefore, no compatibility questions exist with respect to Codex.

RECOMMENDATIONS

CBTS recommends against the proposed temporary tolerance for use of DE-498 on corn and soybeans for the reasons given in Conclusions 1a, 1c, 1d, 2a-h, 3, 4c, 4e, 10, 11, 12a-b, 16a-f, 16h, 16i, 20, 21b, 21c, 21e, 21g, 23b, 23d, 23e, 23g, 23i, and 26.

For a future permanent tolerance, deficiencies listed in Conclusions 1b, 4a, 4b, 4d, 6a, 6b, 7, 8a-b, 9a-c, 13b, 14b, 16g, 17b, 21a, 21d, 22b, 23c, and 23f above must also be addressed.

CBTS recommends that a copy of this entire review be sent to the petitioner.

Notes to the PM:

The following reports should be sent to Registration Division (Bipin Gandhi) for review since they involve Product Chemistry of formulations: MRID#'s 419317-22, 419317-23,and 419317-24 concerning the formulation XRM-5019; and MRID #'s 420033-01, 419938-03, and 419938-04 concerning the formulation XRM-5313. CBTS's Product Chemistry review is for the technical only. As required by the Registration Standard Policy group, the product chemistry data for end-use products are not included in this review.

CBTS no longer addresses the physical/chemical properties of manufacturing-use products. These will be considered later by the Registration Division as manufacturers respond to the "Data Call-in" program. This means that §63-14, 63-17, and 63-20 of MRID #419521-01 should be sent to Registration Division (Bipin Gandhi)

for review. CBTS will, however, still consider physical/chemical properties of technical grades of the active ingredient.

CBTS is not commenting concerning the directions on the label for rotational crops. That part of the label should be reviewed by the Environmental Fate and Effects Division.

DETAILED CONSIDERATIONS

PRODUCT CHEMISTRY

Refer to the Confidential Appendix, Attachment 5.

RESIDUE CHEMISTRY

Manufacture

The manufacturing process is not adequately described. Refer to the discussion in §61-2 of the Product Chemistry section, Confidential Appendix A (Attachment 5).

Formulation

XRM-5019 is a water dispersible granular formulation containing 74.9% N-(2,6-difluorophenyl)-5-methyl-1,2,4-triazolo-[1,5a]-pyrimidine-2-sulfonamide and 25.1% inerts. XRM-5019 contains 0.749 lbs ai/lb product. (Refer to Attachment 7 for the Confidential Statement of Formula for XRM-5019.) CBTS defers to Registration Division concerning whether the inerts in XRM-5019 are cleared.

Proposed Use

Soybeans and Field Corn

Application Methods:

Apply in a spray volume of 10-40 gals./A. For minimum or no-till soybeans or field corn, apply in a spray volume of at least 20 gals/A.

Dry bulk fertilizer may be impregnated or coated with XRM-5019. For best results when applied impregnated on dry bulk fertilizers, XRM-5019 should be incorporated twice with the second incorporation 3-5 days after the first. Apply a minimum of 200 lbs/A of dry fertilizer impregnated with XRM-5019 at the recommended rate. Do not impregnate coated ammonium nitrate and/or limestone when used alone.

Preplant Incorporated, Preemergence, No-till or Reduced Tillage:

Apply to soybeans and field corn at the rate of 0.04-0.09 lb XRM-5019/A (0.03-0.07 lb ai/A) when applied preplant incorporated or preemergence. Do not apply more than 0.09 lb XRM-5019 per acre during a single crop year.

For preplant incorporated applications to soybeans and field corn, apply and incorporate into the top 2-3 inches of seedbed 0 to 30 days before planting.

For preemergence (surface applications) to soybeans and field corn, apply 0-30 days before planting (either before, during, or after planting but before crop emergence). Rain or irrigation are needed; otherwise, shallow cultivate in 7-10 days.

For no-till or reduced tillage, apply before, during or after planting but prior to crop emergence. XRM-5019 can be tank mixed with Gramoxone Super or Roundup to control existing vegetation in addition to a product for preemergence grass control.

Preplant incorporated or preemergence applications can be tank mixed. Tank mixes for soybeans could include Treflan, Sonalan, Dual, alachlor, or Prowl, or another herbicide registered for use on soybeans. Tank mixes for field corn could include alachlor, atrazine, Bladex, Dual, Eradicane, Sutan+, or another herbicide registered for field corn.

Postemergence:

Apply postemergence to field corn at the rate of 0.02-0.08 lb XRM-5019/A (0.015-0.06 lb ai/A). For postemergence application to field corn, apply to field corn up to 12 inches tall. Do not apply to corn grown for seed. Apply XRM-5019 alone or in tank mixes with other herbicides registered for postemergence application in field corn.

Apply postemergence to soybeans at the rate of 0.01-0.02 lb XRM-5019/A (0.0075-0.015 lb ai/A). For postemergence application to soybeans, applications can be made to soybeans from the first to the fifth trifoliate leaf stage of growth. XRM-5019 can be tank mixed with other herbicides registered for postemergence application to soybeans such as 2,4-DB, Basagran, Blazer, Storm, Galaxy, Cobra, Tackle, and Reflex. For best grass control performance, application of products for postemergence grass control (such as Assure, Fusilade 2000, or Poast) should be delayed for 3 days after applying XRM-5019 to soybeans.

For postemergence application to soybeans and field corn, do not apply if rainfall is expected with 6 hours of application.

All postemergent applications of XRM-5019 to field corn and soybeans must include a non-ionic surfactant at 0.25% v/v (1 qt/100 gal) or a crop oil concentrate at 1% v/v (1 gal/100 gal). Use a surfactant with at least 80% ai. Use a petroleum based crop oil concentrate with at least 15% emulsifiers/surfactant.

General Restrictions:

"Do not aerially apply XRM-5019."

"Do not graze or feed treated soybean forage, hay, or straw to livestock."

"Do not apply where the soil pH is greater than 7.8 as this may result in decreased crop tolerance."

"Do not apply to areas where (both apply) the soil pH is less than 5.9 and organic matter is greater than 5%."

"Do not apply when air temperature is near freezing or when freezing conditions are expected for several days following application."

"Chemigation: Do not apply this product through any type of irrigation system."

"Do not rotate to any crop other than corn or soybeans for 4 months after application of XRM-5019."

"The following rotational crops may be planted at the indicated interval following application of rates up to 0.09 lb/acre of XRM-5019:

crop -[1/]	interval (months)
alfalfa	4
dry beans	4
peas	4
peanuts	4
wheat	4
rice	6
grain sorghum	18
sunflower	18
cotton	20
sugarbeets	22
rapeseed (canola)	22

-[1/]Note: Rotation to all other crops requires a successful field bioassay."

Conclusion

The petitioner should submit a revised Section B/label with the following additional information: the maximum number of applications, the maximum pounds ai/A/yr for postemergence uses, the maximum pounds ai/A/yr for all uses combined (preplant incorporated, preemergence and postemergence), the minimum interval

between applications, the minimum interval between the last application and harvest (preharvest interval), and the application rate also expressed in terms of pounds of active ingredient per acre (lbs ai/A).

The petitioner should also submit a revised Section F replacing the term "corn" with "corn (except pop and sweet)" since the proposed use is on field corn only.

Note to PM: CBTS is not commenting concerning the directions on the label for rotational crops. That part of the label should be reviewed by the Environmental Fate and Effects Division.

Nature of the Residue

Plants

Soybeans

Soybeans were treated with a formulation of (5-^{14}C)pyridine-labelled DE-498 (MRID #419317-12). The radioactive compound was formulated as an aqueous suspension concentrate containing 11.3% XRD-498 by weight. (Before formulation, the radioactive chemical was mixed with nonradioactive chemical to obtain a test substance with a specific activity of 2.90 mCi/mmol (19,800 dpm/ug) with a purity of >98%.) The formulation was applied at the second and third trifoliate stage (27 days after planting) at the rate of 56 g ai/ha (0.05 lb ai/A). [This is 3.3X the proposed maximum postemergence rate of 17 g ai/ha (0.015 lb ai/A)]. Forage was sampled at the late bloom stage [43 days after application (DAA)]. At harvest (111 days after application), beans and field trash (vines, leaves, and pods) were sampled. These at-harvest samples were dried in a greenhouse for approximately one week before being frozen. Samples were analyzed by liquid scintillation counting (LSC). Late bloom forage was combusted 41 days after sampling. Beans and trash were combusted 15 days after sampling. Characterization of harvest trash was completed 494 days after sampling. Some field trash samples were submitted to acid or base hydrolysis before analysis by high performance liquid chromatography (HPLC). Radioactivity (expressed as XRD-498 equivalents) were as follows:

substrate	ppm
forage (43 day)	0.031
mature beans at harvest	0.015
field trash at harvest	0.120

Extractability of ^{14}C from soybean plant tissues with acetonitrile/water (1:1) was determined as reported below:

forage (43 DAA)	% Soluble	% Insoluble
leaves	60.5	41.6
vines	53.7	45.7
harvest samples	**% Soluble**	**% Insoluble**
beans	49.7	43.6
trash	62.9	35.0

Residues in forage (43 DAA) and beans at harvest were too low to characterize.

Attempts were made to identify residues in harvest trash. Sixty-four percent of the radioactivity (0.077 ppm) was extracted with acetonitrile/water (1:1). Sixty-three percent (0.076 ppm) remained after concentration and water/methylene chloride partitioning. PoraPak (a styrene-divinylbenzene copolymer) fractionation yielded the following fractions:

18% (0.022 ppm)- very polar compounds which eluted with water
40% (0.048 ppm)- eluted with (1:1) methanol/water
4% (less than the minimum quantifiable amount)-eluted with methanol

By HPLC analysis of the methanol/water (1:1) fraction, a minimum of 10 radioactive components were found. The three major peaks each comprised $\leq$0.01 ppm. Acid hydrolysis (1N HCl) and base hydrolysis (0.5 M NaOH) of the methanol/water fraction did not release additional compounds. None of the residues chromatographed with the parent, the 5-hydroxymethyl metabolite, or the 7-hydroxy metabolite. [The 5-hydroxymethyl metabolite is N-(2,6-difluorophenyl)-5-hydroxymethyl-1,2,4-triazolo(1,5a)pyrimidine-2-sulfonamide. The 7-hydroxy metabolite is N-(2,6-difluorophenyl)-7-hydroxy-5-methyl-1,2,4-triazolo(1,5a)pyrimidine-2-sulfonamide.]

In another study, soybeans were treated with a formulation of ^{14}C-phenyl-labelled DE-498 (MRID #419317-13). The radioactive compound was formulated as a water dispersible granule containing 75% DE-498 with 0.25% X-77. [Before formulation, the radioactive compound was mixed with nonradioactive compound to form a test substance with a specific activity of 39,900 dpm/ug (5.90 uCi/umol) and a radiochemical purity of 99.0%.] The formulation was applied to emerged soybeans in the V5 to V6 growth stage (42 days after planting) at the rate of 85.5 g ai/ha (0.076 lb ai/A). [This is 5X the maximum proposed postemergence rate of 17 g ai/ha (0.015 lb ai/A)]. Stunting and necrosis were observed in treated plants.) Forage was sampled at 0, 12, and 28 days after application, the latter being late bloom stage. Trash (desiccated vines and pods) and beans were harvested at maturity (120 days after application). Samples were stored frozen between sampling and analysis.

Radioactivity was initially determined within 8 days of harvest by combustion/liquid scintillation counting (^{14}C expressed as DE-498 equivalents). Additional ^{14}C determinations were made over the period of the study. See attachment 1 for average radioactivity levels found.

Extraction of ^{14}C activity from soybean trash with various organic solvents was reported as follows:

Solvent	%
60% hexane:40% ethyl acetate	1.0
60% chloroform:40% methanol	8.7
50% acetone:50% water	17.1
50% acetonitrile:50% water	19.8

Residues were extracted with aqueous acetonitrile. In some cases, HCl and H_2SO_4 were used to solubilize residues. Nonsoluble residues remaining after H_2SO_4 extraction were considered to be lignin precipitates. Radioactive fractions were reported as follows:

Sample	Total PPM	Organic Extract		1N HCl Extract		H_2SO_4 Soluble		Pellet or Ppt		Recovery
		ppm	%	ppm	%	ppm	%	ppm	%	%
0-day forage	10.8	10.5	98					1.1	11	108
st. dev.	1.7	1.3	7					0.1	1	8
12-day forage										
initial	2.65	2.17	85					1.10	42	124
st. dev.	0.29	0.42	15					0.25	8	22
prep*	2.65	1.64	62	0.31	12			0.70	26	100
st. dev.	0.29	0.15	4	0.05	1			0.12	2	5
reanal**	2.65	1.37	52	0.26	10	0.19	7	0.31	12	80
st. dev.	0.29	0.33	12	0.09	3	0.05	1	0.06	2	17
28-day forage										
initial	1.74	0.73	42	0.21	12			0.40	23	77
st. dev.	0.33	0.11	2	0.04	1			0.09	3	4
reanal**	1.74	1.15	66	0.20	12	0.18	10	0.34	19	107
st. dev.	0.33	0.25	5	0.04	1	0.03	0	0.07	2	4

Sample	Total PPM	Organic Extract		1N HCl Extract		H_2SO_4 Soluble		Pellet or Ppt		Recovery
		ppm	%	ppm	%	ppm	%	ppm	%	%
120-day trash										
initial	0.453	0.074	16	0.049	11			0.284	63	90
st. dev.	0.049	0.007	1	0.009	1			0.053	5	5
reanal**	0.453	0.110	24	0.035	8	0.069	15	0.223	49	96
st. dev.	0.049	0.005	2	0.005	1	0.013	2	0.026	2	2
120-day bean	0.021	0.013	60					0.008	39	99
st. dev.	0.000	0.001	5					0.000	1	4

*prep- refers to analysis with large sample sizes to compensate for possible uneven distribution of ^{14}C

**reanal- refers to reanalysis at the end of the study since the initial analysis extended over 3-5 months

The distribution of the ^{14}C residues in the organic extract as determined by high performance liquid chromatography (HPLC) was reported. (See attachment 1.)

Distribution of ^{14}C activity in the acid extract from soybean tissues as determined by HPLC was also reported. (See attachment 2.)

A tentative metabolic pathway for soybeans was submitted. (See attachment 3.) The major metabolites in forage were A_2 and B_1. The major metabolite in beans, C, was present at a low level.

Characterization of A_1, A_2, B_1, and D was attempted following reverse phase HPLC in two different mobile phases, ultraviolet spectrometry (UV), and/or mass spectrometry. B_1 eluted at a similar retention time as aminotriazole, but cochromatography indicated that the compounds are different. The UV spectrum for acetylated B_1 suggests a possible ring opening or saturation of the pyrimidine ring. A structure for Metabolite C was not proposed, but Metabolite C does not correspond to any reference standards. The mass spectrums for acetylated B_1 and acetylated D were similar. Acid hydrolysis of A_2 followed by HPLC yielded B and/or D, which indicates that the A_2 is a conjugate of B and/or D. Acid hydrolysis of A_1 yielded metabolite H, which indicates that A_1 is a conjugate of H. Metabolite H has a similar retention time by HPLC as 7-hydroxy DE-498.

Conclusion

The nature of the residue in soybeans is adequately defined for the proposed EUP only. DE-498 can be considered to be the residue of concern.

For a future permanent tolerance, additional metabolism data will be required. In the submitted studies on soybeans, residues were not adequately characterized in any plant part. Residue components accounting for ≥10% of the residue after exhaustive extraction should be identified, preferably by two techniques (eg. TLC, HPLC, MS). Such components may include components A2 and B1 which were present in the 12-day and 28-day forage samples from ^{14}C-phenyl-labelled DE-498 treated soybeans. Analysis should also include determination of the presence of 2,6-difluroaniline (possibly present as a product of hydrolysis of the sulfonamide linkage of ^{14}C-phenyl-labelled DE-498) and 5-methyl-(1,2,4)triazolo-(1,5a)pyrimidine-2-sulfonic acid [possibly present as a product of the hydrolysis of the sulfonamide linkage of (5-^{14}C) pyridine-labelled DE-498] at all sampling times by use of authentic standards.

Extractability of the residue into solvents used in the proposed analytical enforcement method should be determined. Most of the radioactivity should be extracted, or exhaustive attempts using acid, base, and/or enzymes should be made to do so. The petitioner should use the radiolabelled samples to determine what percentage of the total recovered radioactivity is determined by the proposed enforcement methodology.

The identity of the residues in all plant parts of the raw agricultural commodity which could be used for food or feed (seed, forage, and hay) should be determined. Samples should be either analyzed or frozen immediately after harvest. (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981 and to the "Standard Evaluation Procedure, Qualitative Nature of the Residue: Plant Metabolism", NTIS #PB87-208641.)

The additional work needed for the soybeans treated with phenyl labelled DE-498 may be done using reserve forage samples (12 and 28 day samples) provided they have been kept frozen. For the pyridine labelled DE-498, CBTS recommends a new study be conducted at the maximum rate that does not result in significant phytotoxicity. The green plant should be analyzed at intervals similar to those in the previous phenyl labelled study.

Corn

Field corn was treated with a formulation of (5-^{14}C)pyridine-labelled DE-498 (MRID #419317-14). The radioactive compound was

formulated as an aqueous suspension concentrate containing 11.3% XRD-498 by weight. [Before formulation, the radioactive chemical was mixed with nonradioactive chemical to obtain a test substance with a specific activity of 2.90 mCi/mmol (19,800 dpm/ug) with a purity >98%]. The formulation was sprayed on plants at the six leaf stage when plants were 8" high (27 days after planting) at the rate of 56 g ai/ha (0.05 lb ai/A). (This is 0.83X the proposed postemergence rate.) At the early dent stage (57 days after application), silage stage forage was sampled as the whole plant and as plant parts (leaves/husks, stalks, cobs, and grain). Desiccated plants were also sampled at harvest (111 days after application) as fodder components (leaves/husks, stalks, cobs, and grain). Silage stage forage which was sampled as the whole plant was frozen for a total of 2 months before determination of ^{14}C levels by combustion and liquid scintillation counting (LSC). (These whole plants were chopped and stored frozen for 30 days. Then they were thawed, lyophilized, and stored frozen for another month before ^{14}C determination.) Silage stage forage which was separated into plant parts (leaves and husks, stalks, cobs, and grain) was dried in a greenhouse for 2 weeks, ground, and stored frozen for 2 weeks before total ^{14}C was determined. Plant parts sampled 111 days after application were dried in a greenhouse 2-3 weeks, ground, and then frozen 1-2 weeks before total ^{14}C was determined. Extraction and analysis of silage stage forage and harvest samples were completed approximately 18 and 16 months after sampling. Total ^{14}C residues in silage stage forage expressed as XRD-498 equivalents are reported below:

Plant Part	ppm (field weight)
leaves and husks	0.221
stalks	0.007
cobs	ND
grain	ND
composite forage (whole plant)	0.047

Total ^{14}C residues in desiccated plants at harvest expressed as XRD-498 equivalents are reported below:

Plant Part	ppm
stalk	0.026
leaf and husk	0.222

Plant Part	ppm
composite fodder (calculated from stalk, leaf & husk)	0.115
cob	ND
grain	ND

Extractability of spiked ^{14}C from control corn tissue with acetonitrile/water (1:1) was reported as follows:

Matrix	% ^{14}C extracted
forage-leaf & husk (57 DAA)	99
forage-stalk (57 DAA)	92
fodder-leaf & husk (111 DAA)	97
fodder-stalk (111 DAA)	93

Extractability of ^{14}C activity from corn plant tissues using acetonitrile/water (1:1) was reported as follows:

Sample	Total ^{14}C (ppm)	Distribution of ^{14}C Soluble (ppm)	Insoluble (ppm)	Percent Extracted
forage-leaf & husk (57 days after application [DAA])	0.221	0.153	0.066	69
composite forage (57 DAA)	0.047	0.031	0.014	66
harvest stalk (111 DAA)	0.026	0.015	0.013	58
harvest leaf & husk (111 DAA)	0.222	0.151	0.070	68

Attempts were made to analyze the extract from silage stage forage by HPLC. The extract from silage stage forage (leaf & husk) did not elute with the 5-hydroxymethyl or 7-hydroxy metabolites. Acid and base hydrolysis of the extract changed the HPLC but none

of the components eluted with the 5-hydroxymethyl or 7-hydroxy metabolite. Polar and insoluble residues were too low to identify.

Attempts were also made to identify the soluble radioactivity (68.4% of the total) in the harvest fodder (leaf & husk) by partitioning with methylene chloride, and subjecting the aqueous fraction (65.6%) to Porapak Q fractionation. Most of the radioactivity was eluted in the aqueous fraction (54.2%) as compared to methanol/water (9%) and methanol (2%). HPLC was not possible due to viscosity and lack of enough ^{14}C.

In another study, field corn was treated with a formulation of ^{14}C-phenyl-labelled DE-498 (MRID #419317-15). The radioactive material was formulated as a water dispersible granule containing 75% DE-498 by weight. [Before formulation, the radioactive chemical was mixed with nonradioactive chemical to obtain a specific activity of 5.4 mCi/mmol (37,000 dpm/ug) with a purity >97%.] The formulation was sprayed on plants at the V_5 to V_6 stage (27 days after planting) at the rate of 197 g ai/ha (0.18 lb ai/A). (This is 3X the proposed postemergence rate.) Samples were taken at 0 days after application (DAA), 14 DAA (intermediate forage; V_{10} stage), 81 DAA (R_5; early dent stage; silage stage forage), and 131 DAA (maturity). Samples at maturity were separated into fodder (including leaf, husk, and stalk), cobs, and grain. After sampling, the samples were stored frozen. (Before being stored frozen, the samples were processed as follows: The 0 and 14 DAA samples were rinsed with methanol, frozen, and ground. The 81 DAA samples and the fodder from the 131 DAA samples were shredded, frozen, and chopped to a powder. The grain and cobs sampled 131 DAA were frozen and ground.) Total ^{14}C, reported below, was determined within ten days after sampling.

Plant Part	DAA	Total ^{14}C (ppm)	Distribution % Methanol[a]	CH_3CN/H_2O	Insoluble
green plant	0	21.8	98.3	1.6	<1
green plant	14	0.38	20	71	8.6
silage-stage forage	81	0.02	--	64	34
maturity	131				
-grain		<0.005	--	--	--
-cob		<0.005	--	--	--
-fodder		0.04	--	61	36

a/ rinse of foliage prior to processing

Extractability from corn plant tissues using acetonitrile/water (1:1) was reported as follows:

DAA	Orig. Conc. (ppm)	% Extracted
0	0.36	97.2
14	0.30	89.0
silage-stage	0.02	65.4
fodder	0.04	60.9

Residues were extracted with acetonitrile/water (1:1) after 8-63 days frozen storage. Characterization of extractable residues was attempted by reversed phase high performance liquid chromatography (HPLC). 0-day forage contained 97-98% DEA-498. No DEA-498 was found in later samplings. One minor component (6.8%) in the extract from 14-day silage-stage forage chromatographed over the retention time range of the 5-hydroxymethyl metabolite, but the identity of this minor component was not confirmed. Extracts of 81-day forage and 131-fodder samples contained 3 major components; however, the extracted polar residues did not chromatograph with DEA-498 or three reference compounds (ie. [N-(2,6-difluorophenyl)-5-hydroxymethyl-1,2,4-triazolo(1,5a)pyrimidine-2-sulfonamide, N-(2,6-difluorophenyl)-7-hydroxy-5-methyl-1,2,4-triazolopyrimidine-2-sulfonamide or N-(2,6-difluorophenyl)-5-amino-1,2,4-triazolo-3-sulfonamide].

Conclusion

The nature of the residue in corn is adequately defined for the proposed EUP only. DE-498 can be considered to be the residue of concern.

For a future permanent tolerance, additional metabolism data will be required. In the submitted studies on corn, residues were not adequately characterized in any plant part. Residue components accounting for $\geq$10% of the residue after exhaustive extraction should be identified, preferably by two techniques (eg. TLC, HPLC, MS). Analysis should also include determination of the presence of 2,6-difluroaniline (possibly present as a product of hydrolysis of the sulfonamide linkage of ^{14}C-phenyl-labelled DE-498) and 5-methyl-(1,2,4)triazolo-(1,5a)pyrimidine-2-sulfonic acid [possibly present as a product of the hydrolysis of the sulfonamide linkage of (5-^{14}C) pyridine-labelled DE-498] at all sampling times by use of authentic standards.

Extractability of the residue into solvents used in the proposed analytical enforcement method should be determined. Most of the radioactivity should be extracted, or exhaustive attempts

using acid, base, and/or enzymes should be made to do so. The petitioner should use the radiolabelled samples to determine what percentage of the total recovered radioactivity is determined by the proposed enforcement methodology.

The identity of the residues in all plant parts of the raw agricultural commodity which could be used for food or feed (grain, forage, silage, and fodder) should be determined. Concerning the (5-^{14}C)pyridine-labelled DE-498 corn study, CBTS further recommends that a new study be conducted using a higher rate (ie. the maximum rate not resulting in significant phytotoxicity) and examining plant parts at intervals similar to those used in the ^{14}C-phenyl-labelled DE-498 study. Samples should be either analyzed or frozen immediately after harvest. The additional work (e.g., looking for the presence of 2,6-difluoroaniline) needed for corn treated with phenyl labelled DE-498 may be done using reserve samples provided they have been kept frozen. (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981 and to the "Standard Evaluation Procedure, Qualitative Nature of the Residue: Plant Metabolism", NTIS #PB87-208641.)

Animal Metabolism

Goats

Two lactating goats were fed (5-^{14}C)pyridine-labelled DE-498 in capsules for five consecutive days (MRID #419317-16). One control goat was included in the study. The dosage was 21 mg/day (approximately 10 ppm in feed). The test substance had a radiochemical purity of 99.9%. The specific activity of the test substance was 3.50 mCi/mmol (23,900 dpm/ug.) Animals were sacrificed six hours after the last dose. Samples were stored frozen between sampling and analysis. Combustion analysis and liquid scintillation counting of tissue, urine, feces and milk was completed within one month of sampling. Initial chromatographic analysis of urine was conducted within 8 months. Kidney extraction analysis was conducted within 9 months. Milk extraction analysis was conducted within 20 months. Feces extraction analysis was conducted within approximately 24 months. Isolation and identification of ^{14}C in urine was conducted within 30.5 months. The distribution of the dose recovered in the excreta, milk, and tissues of the treated goats was reported below as a percent value:

matrix	% in Goat #2	% in Goat #3
kidney	0.03	0.07
liver	0.02	0.03
muscle	ND	<0.01
fat (omental)	<0.01	0.01
fat (renal)	0.01	<0.01

matrix	% in Goat #2	% in Goat #3
bile	<0.01	<0.01
gastrointestinal (GI) tract	15.24	13.72
milk	0.19	0.09
feces	19.54	11.09
urine	56.53	69.22
urine (bladder)	0.85	0.59
pan rinse	0.19	0.95
Total recovery	92.60	95.77

The distribution of the radioactivity in ppm (XRD-498 equivalents) was reported as below:

tissue	ppm in Goat #2	ppm in Goat #3
kidney	0.2	0.4
liver	0.02	0.03
muscle	ND	0.007
renal fat	0.02	0.01
omental fat	<0.007	0.025
GI tract	1.48	1.98
milk	ND-0.035	ND-0.027
urine	0.02-9.7	0.03-20
feces	ND-3.9	ND-5.2

Residues in kidney were characterized. An average of 94% of the radioactive residue was extracted from kidneys of goats #2 and #3 with acetone. 97% of the radioactivity was extracted from spiked kidney from the control goat (goat #1). The extract was analyzed by reversed phase liquid chromatography after extracting the residue from acetone with acetonitrile/water and concentrating the extract to aqueous solution. An average of 88% of the total radioactivity had a retention time similar to XRD-498.

Residues in milk were also characterized. Two extraction methods were used for goat milk, one method for goat #2 and a spiked control sample, and one method for goat #3 and a spiked control sample. The two methods are summarized below:

Milk from goat #2 was centrifuged and the whey was decanted. The curds/cream was washed with warm water. This step involved heating the warm water/curds/cream mixture at 40°C for 45 minutes. The wash water and whey was combined, acidified with glacial acetic acid, and passed through a SEP-Pak. The acetonitrile flush from the SEP-Pak was concentrated to an aqueous residue, centrifuged, and analyzed by reversed phase liquid chromatography.

Milk from goat #3 was centrifuged and the whey was decanted. The curds were washed with water two times. The wash water and whey was combined and acidified with glacial acetic acid. The

washed curds and cream were extracted with acetone. The whey and acetone extracts were combined, acidified with glacial acetic acid, and passed through a SEP-Pak. The concentrated aqueous residue was analyzed by reversed phase liquid chromatography.

The two methods yielded similar results for both the treated goats and control samples. 92% and 94% of the radioactive residue was present in the concentrated extract of milk from goats #2 and #3, respectively. Recoveries in the concentrated extracts from spiked controls analyzed in parallel with milk from goats #2 and #3 were 91% and 115%, respectively. An average of 92% of the radioactive residue in the milk chromatographed with XRD-498.

Feces were extracted with 50% aqueous acetone and analyzed by reversed phase liquid chromatography. One major component (92% of the total radioactivity) had a similar retention time as XRD-498.

Urine was centrifuged and analyzed by reversed phase liquid chromatography, ultraviolet spectroscopy, and mass spectroscopy. The only component comprising more than 2% of the total radioactivity was identified as XRD-498.

Residues in muscle (ND-0.007 ppm), fat (<0.007-0.025 ppm), and liver (0.02-0.03 ppm) were not characterized.

Discussion

Ninety-two percent of the radioactive residues in milk and 88% of the radioactive residues in kidney resulting from dosing goats with 5-^{14}C-pyridine-labelled DE-498 were identified as parent.

Residues in muscle, fat, and liver were not characterized. However, if residues are found to be nondetectable or very low in feed items, no characterization of these tissues will be required since the total ^{14}C-residues in muscle, fat, and liver were low ($\leq$0.1 ppm) after dosing at an exaggerated feeding level (10 ppm). (See "Guidance on When and How to Conduct Livestock Metabolism Studies", Richard D. Schmitt, 7/25/89, page 2, paragraph 4.)

Poultry

Fifteen hens (in groups B, C, and D) were fed 5-[^{14}C]pyridine-labelled DE-498 in capsules for ten consecutive days (MRID #419317-17). Five control hens (Group A) were included in the study. The dosage was 2.1 mg/day (15 ppm in feed). The test substance had a radiochemical purity of 99.9%. The specific activity of the test substance was 3.50 mCi/mmol (23,900 dpm/ug.) Animals were sacrificed six hours after the last dose. Samples were stored frozen between sampling and analysis. Combustion of tissues, excreta and eggs was conducted within 1 month of sampling. Excreta and kidney were extracted and analyzed within 22 months of

sampling. The distribution of radioactivity in laying hens (in XRD-498 equivalents) was reported as follows:

tissue	Group B ppm	Group C ppm	Group D ppm
kidney	0.052-0.057	0.056	0.099-0.108
liver	0.008	0.007	0.004
thigh muscle	ND	ND	ND
breast muscle	ND	ND	ND
fat	ND	ND	ND
skin	ND	ND	0.009
gastrointestinal tract	2.53	0.989	1.16
gizzard	0.017	0.017	0.021
blood	0.016	0.016	0.018
egg white	ND	ND	ND
egg yolk	ND	ND	ND
excreta	11.2	12.1	10.9

Residues in kidney were characterized. Acetone extracted an average of 89% of the radioactivity from kidney. (Average recovery from spiked controls was 103%.) After concentration of the acetone extract, 74% of the total radioactivity in kidney tissue remained in the acetone and 14% was in an oil and precipitate which were formed during concentration. Reversed phase liquid chromatography of the concentrated extract identified by similar retention times parent (46% of the total radioactivity in kidney tissue) and the 5-hydroxymethyl metabolite (24% of the total radioactivity in kidney tissue).

Residues in excreta were also characterized. Radioactivity was extracted from excreta with various solvents including 50% aqueous acetone (96% extracted), a sequence of acetonitrile, acetone, and 50% aqueous acetonitrile (93% extracted), and acetonitrile followed by 50% aqueous acetone (99% extracted). (Recovery from a spiked control was 101%.) Reversed phase liquid chromatography, ultraviolet spectroscopy, and mass spectroscopy of the extracts identified parent (61-81%) and the 5-hydroxymethyl metabolite (14-18%).

Discussion

Seventy percent of the residues in kidney resulting from dosing hens with 5-^{14}C-pyridine-labelled DE-498 were identified as parent (46%) and the 5-hydroxymethyl metabolite (24%).

Residues in muscle, fat, liver, and eggs were not characterized. However, if residues are found to be nondetectable or very low in feed items, no characterization of these tissues will be required since the total ^{14}C-residues in muscle, fat, liver,

and eggs were low (≤0.1 ppm) after dosing at an exaggerated feeding level (15 ppm). (See "Guidance on When and How to Conduct Livestock Metabolism Studies", Richard D. Schmitt, 7/25/89, page 2, paragraph 4.)

Conclusion

The nature of the residue in animals is adequately defined for this proposed use provided that no detectable or very low residues are found in feed items. The residue of concern in ruminants is DE-498 per se. The residues of concern in poultry are DE-498 per se and the 5-hydroxy metabolite. Provided that no detectable or very low residues are found in feed items, tolerances will not be required on animal commodities.

For uses which may result in detectable residues in feed items, additional animal metabolism data on ruminants and poultry may be required.

Analytical Methods

Plants

Soybeans

A method for analysis of residues of DE-498 per se in soybeans ("Determination of Residues of DE-498 in Soybeans by Capillary Gas Chromatography/Mass Spectrometry", Method No. ACR 91.6) has been submitted (MRID #419521-04). This is the proposed enforcement method for soybeans.

The method involves extraction with 90% acetone/10% 0.1 N hydrochloric acid. After evaporation of the acetone, the residue is diluted with 0.005 N HCl. The residue is washed with hexane and purified using C_{18} and alumina solid-phase extractions. The eluant is evaporated to dryness. The residue is reconstituted in acetonitrile and derivatized with methyl iodide to form the N-methyl derivative. The solution is evaporated to dryness, reconstituted in 5% NaCl (aq.), and partitioned into methyl tert-butyl ether. After evaporation to dryness, the residue is reconstituted with toluene containing N-d_3-methyl DE-498 as an internal standard. The residue is analyzed by capillary gas chromatography/mass spectrometry (GC/MS). The limit of quantitation of the method is 0.005 ppm (5 ppb). The following recoveries were reported:

ppb DE-498 Added	% Recoveries
5	90-107 (av. 99)
10	75- 99 (av. 89)
25	77- 97 (av. 88)
50	84-100 (av. 92)

No detectable residues were found in controls.

Soybean forage samples from metabolism studies containing radioactive residues ranging from 0.03 to 0.10 ppm DE-498 equivalents were analyzed by Method 91.6 to determine extraction efficiency. Results were reported as follows:

Soybean Forage Samples Sample Number	DE-498, ppm	
	^{14}C	GC/MSD
90046-08C	0.099 ± 0.006	0.140 ± 0.040
90046-12A	0.046 ± 0.023	0.033 ± 0.004
90046-12D	0.050 ± 0.026	0.036 ± 0.006

An independent lab validation for Method No. ACR 91.6 on soybeans was conducted by A & L Great Lakes Laboratories, Inc. (MRID #419521-05). The lab fortified soybeans at 5.0 and 25.0 ppb. Average recoveries were 90% and 121% at the 5.0 and 25.0 ppb fortification levels, respectively. The analysis of six samples (two controls, two fortifications at 5.0 ppb, and two fortifications at 25.0 ppb) required 30 person-hours and 4 calendar days.

Field Corn

The petitioner indicates that the method in MRID #419521-04 for soybeans can be used as the enforcement method on corn grain, forage, and fodder with minor modifications. However, the modifications and validation data (ie. recoveries, limit of quantitation of the method, chromatograms, etc.) are not provided.

Conclusion

The analytical methodology for soybeans and field corn is not adequate as submitted. The following additional information is needed:

a) The source/supplier of methylene chloride should be included in the method.

b) The complete method for field corn including the minor modifications to the method which are made for analysis of field corn grain, forage, and fodder and validation data (ie. recoveries,

limit of quantitation of the method, and chromatograms) should be submitted.

c) An independent laboratory validation of the method for field corn may be required depending upon how the method differs from the soybean procedure.

d) Method No. ACR 91.6 uses an internal standard. Generally, an enforcement method cannot use an internal standard. However, the deuterated standard is expected to behave the same chemically as the DE-498. This internal standard is acceptable in the enforcement method provided that the deuterated internal standard is made available along with the DE-498 analytical standard to RTP and enforcement labs.

e) Enforcement methods should require a maximum of 24 hours for completion, whereas this method took the validating lab 30 person-hours and 4 calendar days. Efforts should be made to shorten the method for enforcement purposes.

f) A confirmatory method should be provided for enforcement purposes.

g) An interference study should be conducted to determine if other pesticides registered on corn and soybeans would interfere with the method. This specificity study is needed for enforcement purposes.

h) Analytical reference standards for DE-498 including the deuterated analog and other residues of concern, if any, should be sent to the Pesticide and Industrial Chemicals Repository (MD8), U.S. Environmental Protection Agency, Research Triangle Park, North Carolina 27711. Two grams each of the purified analytical standards should be provided for the pesticide and principal degradation products or metabolites. The Material Safety Data Sheets should be included as required by OSHA in 29 CFR 1910.1200. A letter of transmittal accompanying the standards should include the following: the purity of the standards; analytical methods used to assay the standards; a statement of principal impurities; purification procedures; storage requirements; and special precautions for safe handling.

i) When the necessary information is provided, CBTS will request an EPA lab to perform a method validation for Method No. ACR 91.6 on corn and soybeans.

Multiresidue Methods

The petitioner has submitted some data for Multiresidue Protocols B and C on soybeans (fatty food) and wheat grain (non-fatty food) (MRID #419938-02).

Conclusion

CBTS will forward the submitted data on Protocols B and C to FDA for review to determine sufficiency.

The petitioner should explain why testing through Protocols D and E was not submitted. Testing through Protocol A is not required because DE-498 does not contain the N-methylcarbamate structure.

Animals

No analytical methods have been submitted for animal commodities.

Conclusion

Analytical methods for animal commodities will not be required provided that no detectable or very low residues are found in feed items and no detectable residues are expected to occur in animal commodities as a result of the proposed use.

Residue Data

Storage Stability

Soybeans

An interim report for frozen storage stability of DE-498 per se on soybeans was submitted (MRID #419317-18). (The study will be continued for at least two years.) Analytical method ACR 91.6 , with modifications, was used. Samples of soybeans were ground and fortified with 1.0 ppm DE-498 and stored below -15°C. Storage stability (corrected for recoveries of 83-104% from spiked controls analyzed at the time of analysis) were reported as follows:

Storage Time (days)	ppm Found (Corrected for Recoveries)
0	1.05
64	1.03
124	1.04
187	0.99
411	0.93

Conclusion

DE-498 in soybeans in frozen storage is fairly stable for at least 411 days, with a possible loss of ≤11% DE-498.

Corn

A frozen storage stability study on corn is in progress, as indicated in MRID #419317-21. Field corn forage, fodder, and grain were fortified with 0.251 ppm DE-498. Storage stability data in the form of a table are available for forage and fodder stored 105 days and for grain stored 92 days as follows:

Matrix	Storage Time (Days)	Average ppm Found
forage	0	0.237
	105	0.220
grain	0	0.237
	92	0.238
fodder	0	0.237
	105	0.211

Conclusion

CBTS cannot determine storage stability of DE-498 on corn based on a table alone. The interim and then the complete storage stability study on corn should be submitted for evaluation instead of just a table. Storage stability data for a period equal to or exceeding the actual storage time of the residue samples will be needed to support the residue data on corn discussed below. (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981; a Position Document: "Effects of Storage (Storage Stability) on Validity of Pesticide Residue Data", NTIS #PB88-112362; and "Storage Stability Study", Addendum on Data Reporting.)

Field Corn

Studies were conducted on field corn at 16 locations in the 13 states of GA (1), IL (2), IN (1), IA (2), KY (1), MI (1), MN (2), MO (1), NE (1), NC (1), OH (1), WI (1), and MS (1) (MRID #419317-21). At each location, one preplant incorporated soil application was made on a plot, and one postemergence application was made on a different plot. The formulation XRM-5019 was applied at the rate of 0.08 lb XRM-5019/A (0.06 lb ai/A). At three locations (IL, IA, and MS) on additional plots, a rate of 0.24 lb XRM-5019/A (0.18 lb ai/A) was applied postemergent. Applications were made with ground equipment. (Backpack sprayers were used at six locations. Tractor mounted sprayers were used at eight locations. "Plot sprayers" were used at two locations.) Most applications were made in approximately 20 gallons spray per acre. All postemergence sprays included 0.25% (v/v) Ortho X-77, a non-ionic surfactant. Forage, grain, and fodder were sampled at harvest and frozen in polyethylene bags. Grain was not ground before storage. Forage and fodder were cut but not ground. Samples were analyzed within

11 months. The analytical method was #ACR 91.6 with minor modifications. The limit of quantitation of the method was 0.005 ppm. All control values for forage, fodder, and grain were 0.000 ppm. Average recoveries from control samples of field corn fortified with 0.005 to 0.05 ppm DE-498 were 92% for forage, 97% for grain, and 91% for fodder. No detectable residues (<0.0025 ppm) were found in field corn grain, forage, and fodder as reported in the following table:

Sample	Application Rate Rate (lb ai/A)	PHI (days)	# of Sites	ppm
forage[a]	0.06	72-121	16	ND
forage[b]	0.06	43- 80	16	ND
grain[a]	0.06	120-169	16	ND
grain[b]	0.06	88-134	16	ND
grain[b]	0.18	102-127	3	ND
fodder[a]	0.06	120-169	16	ND
fodder[b]	0.06	88-134	16	ND

a/ preplant incorporated
b/ postemergence

Residue data on silage are not needed since residue data on forage and fodder will be available.

CBTS concludes that the residue data on field corn are not adequate for reasons a-e and g below: (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981; "Magnitude of the Residue: Crop Field Trials", Standard Evaluation Procedure, NTIS #PB86-129426; and "Magnitude of the Residue: Crop Field Trials", Addendum #2 on Data Reporting, NTIS # PB86-248192.)

a) Adequate geographic representation is not provided. Additional residue data should be obtained from TX, CA, MD, and WA.

b) The following information is needed to evaluate the adequacy of the residue data: the maximum number of applications, the maximum pounds ai/A/yr for postemergence uses, the maximum pounds ai/A/yr for all uses combined (preplant incorporated, preemergence, and postemergence), the minimum interval between applications, and

the minimum interval between the last application and harvest (preharvest interval).

c) The label indicates that field corn can be treated up to the height of 12 inches. The height of the corn at treatment in all field trials should be indicated. Since the highest residues would be expected to result from postemergence treatment of corn which was 12 inches high, that use pattern must be adequately represented.

d) The label indicates that postemergence applications can be made with a crop oil concentrate at 1% v/v (1 gal/100 gal) or a non-ionic surfactant at 0.25% v/v (1 qt/100 gal) in the spray. No residue data were submitted reflecting use of the crop oil concentrate. (All sprays included a non-ionic surfactant.) Therefore, references on the label to the crop oil concentrate should be deleted or additional residue data should be submitted reflecting use of the crop oil concentrate.

e) The petitioner has indicated that samples were stored frozen. Storage temperature should be specified.

f) Residue data on silage are not needed since residue data on forage and fodder will be available.

g) Adequate storage stability data on corn have not been provided. (See "Storage Stability" above).

Processing Study

No processing study was conducted on field corn grain. No detectable residues (<0.0025 ppm) were found in field corn treated postemergence at the rate of 0.18 lb ai/A (3X the proposed postemergence application rate). No detectable residues (<0.005 ppm) were found in corn grain in metabolism studies at 0.18 lb ai/A (3X). However, dent corn contains 3.6-4.0% fat (Pesticide Analytical Manual, Vol. 1, Section 202.25). This means that the theoretical concentration factor from corn grain to corn oil is 28X. However, the petitioner should apply the maximum practical exaggerated foliar application rate, which would be considered to be 5X or less if phytotoxicity occurs at 5X. Even if no detectable residues were found in corn grain after postemergence treatment at 5X, the corn grain should be processed. If no detectable residues are found in the processed products, then no food additive tolerance would be required. Processed commodities from field corn are starch, crude oil and refined oil from wet milling; and grits, flour, meal, crude oil and refined oil from dry milling. Grain dust residue data are not required for this use on corn since applications are preplant incorporated, preemergence, and early postemergence. "The grain dust data are needed only in those cases in which detectable, primarily surface residues are found on the grain." ("Overview of Residue Chemistry Guidelines", R.D.

Schmitt, 10/10/89). (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981; "Magnitude of the Residue: Processed Food/Feed Studies", Standard Evaluation Procedure, NTIS #PB88-243209; and "Magnitude of the Residue: Processed Food/Feed Study", Addendum on Data Reporting, NTIS #PB88-117270.)

CBTS concludes that, for the temporary tolerance, no processing study is needed since no detectable residues were found at the 3X application rate.

CBTS also concludes that, for the permanent tolerance, a processing study is needed and food additive tolerances may be needed for processed fractions of corn grain. The theoretical concentration factor from corn grain to corn oil is 28X. However, the petitioner should apply the maximum practical exaggerated foliar application rate, which would be considered to be 5X or less if phytotoxicity occurs at 5X. Even if no detectable residues were found in corn grain after postemergence treatment at 5X, the corn grain should be processed. If no detectable residues are found in the processed products, then no food additive tolerance would be required. Processed commodities from field corn are starch, crude oil and refined oil from wet milling; and grits, flour, meal, crude oil and refined oil from dry milling. Grain dust residue data are not required for this use on corn since applications are preplant incorporated, preemergence, and early postemergence. "The grain dust data are needed only in those cases in which detectable, primarily surface residues are found on the grain." ("Overview of Residue Chemistry Guidelines", R.D. Schmitt, 10/10/89). (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981; "Magnitude of the Residue: Processed Food/Feed Studies", Standard Evaluation Procedure, NTIS #PB88-243209; and "Magnitude of the Residue: Processed Food/Feed Study", Addendum on Data Reporting, NTIS #PB88-117270.)

Soybeans

Residue studies on soybeans were conducted in 1988 (MRID #419521-06). Studies were conducted at 18 locations in the 13 states of AR (2), GA (1), IL (2), IN (2), IA (2), LA (1), MI (1), MN (2), MS (1), MO (1), NE (1), NC (1), and OH (1). The formulation was XRM-4950R, an aqueous suspension concentrate of DE-498 containing 1 lb ai/gallon. At each location, one preplant incorporated soil application was made on a plot, and one postemergence application was made on a different plot. The preplant application was made at the rate of 0.75 pt. XRM-4950R/A (0.09 lb ai/A, 1.3X the maximum preemergence application rate). The postemergence application was made at the fifth to seventh trifoliate stage at the rate of 0.25 pt. XRM-4950R/A (0.03 lb ai/A, 2X the maximum postemergence application rate). At three locations (MI, IL, and MS) on additional plots, one postemergence application was made at the rate of 0.75 pt. XRM-4950R/A (0.09 lb ai/A, 6X the

maximum postemergence application rate). Applications were made with ground equipment. (Backpack sprayers were used at 8 locations. Tractor mounted sprayers were used at 6 locations. Other ground sprayers were also used [ie. plot sprayer (1 location), Ford sprayer (1 location), ground research sprayer (1 location), and bicycle sprayer (1 location)]. Most applications were made in approximately 20 gallons spray per acre. None of the studies included nonionic surfactant or crop oil concentrate in the DE-498 spray solution. Threshed seeds were harvested at maturity (114-166 days after preplant incorporated application; 79-132 days after postemergence application at the rate of 0.03 lb ai/A and 104-132 days after postemergence application at the rate of 0.09 lb ai/A). Samples of soybeans were stored frozen in polyethylene bags. The samples were analyzed 4 1/4- 32 1/2 months after sampling. Samples were analyzed using two methods. One was method ACR 91.6, a GC/MS method with a limit of quantitation of 0.005 ppm. The other method was a gas chromatography/mass spectroscopy (GC/MS) method with a limit of quantitation of 0.010 ppm. (This second method is described as "slightly different" than method ACR 91.6. "Instead of the dual S-P-E purification followed by derivatization with methyl iodide, a liquid/liquid extraction using diethyl ether was used prior to methylation with diazomethane. The GC/MSD conditions were also similar; however, quantitation was based only on the peak area response of the m/z 134 ion because an internal standard was not used.") All control values were 0.000 ppm. Recoveries from controls fortified with 0.005-0.10 ppm DE-498 were 79-113%; however, the method used to obtain this data was not specified. No detectable residues of DE-498 (ie. less than one-half the lower limits of quantitation of the methods) were found.

Another residue study on soybeans was submitted (MRID #419317-19). In this study, DE-498 was applied preplant incorporated to soybeans at the rate of 0.37 lb XRM-5019/A (0.28 lb ai/A, 4X) in IL, MI, and MS. Applications were made with ground equipment (tractor mounted sprayers). Threshed mature soybean seeds were collected at harvest (124-146 days after application). Samples were stored frozen in polyethylene bags until analysis. Samples were analyzed within 6-20 months. Samples were analyzed by method ACR 91.6 (GC/MS) and by a modification of ACR 91.6. The modification involved substituting a liquid/liquid extraction using diethyl ether for the dual solid phase extraction purification before methylation. The limit of quantitation of the method is 0.005 ppm. All control values were 0.000 ppm. Recoveries from controls fortified with 0.005-0.10 ppm DE-498 were 77-101%. No detectable residues of DE-498 (ie. less than one-half the lower limit of quantitation of the method) were found.

A formulation comparison study was conducted on soybeans in IL and MS to compare residues from postemergence applications of two different sprayable formulations of DE-498, XRM-5019 and XRM-4950R (MRID #419317-20). XRM-5019, a water dispersible granule formulation, was applied with ground equipment (a plot sprayer in

IL and a tractor mounted plot sprayer in MS) at the rate of 0.04 lb. XRM-5019/A (0.03 lb ai/A) in both states. XRM-4950R, an aqueous suspension concentrate, was applied at the rate of 0.24 pt. XRM-4950R/A (0.03 lb ai/A) in IL, but at the rate of 0.0032 pt/A (0.0004 lb ai/A) or 1.3% of that amount applied in MS due to error. Both formulations were applied to soybeans at the third or fourth trifoliate stage. Mature threshed soybeans were collected. PHI's were 89 days in IL and 108 days in MS. Samples were stored frozen. The analytical method was method ACR 91.6 (GC/MS) with a limit of quantitation of 0.005 ppm. Recoveries of DE-498 at fortification levels of 0.005-0.05 ppm were 75-107%. No detectable residues were found in soybean seeds from application of either formulation.

CBTS concludes that residue data on soybeans are not adequate for reasons b-g and i below: (Refer to the "Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry", NTIS #PB83-153981; "Magnitude of the Residue: Crop Field Trials", Standard Evaluation Procedure, NTIS #PB86-129426; and "Magnitude of the Residue: Crop Field Trials", Addendum #2 on Data Reporting, NTIS # PB86-248192.)

a) Adequate geographic representation is provided.

b) The following information is needed to evaluate the adequacy of the residue data: the maximum number of applications, the maximum pounds ai/A/yr for postemergence uses, the maximum pounds ai/A/yr for all uses combined (preplant incorporated, preemergence, and postemergence), the minimum interval between applications, and the minimum interval between the last application and harvest (preharvest interval).

c) Adequate bridging data for comparison of residues resulting from the proposed formulation XRM-5019 (a water dispersible granular formulation) and the experimental formulation XRM-4950R (an aqueous suspension concentrate) are not available. Although not required, CBTS recommends that a protocol for bridging data should be submitted before additional work is done.

d) The complete second method (ie. other than method ACR 91.6) which was used to analyze residues in soybeans (in MRID #419521-06) should be submitted.

e) The label indicates that soybeans can be treated up to the fifth trifoliate leaf stage of growth. The growth stage of the soybeans at treatment in all field trials should be indicated. Since the highest residues would be expected to result from postemergence treatment of soybeans which were at the fifth trifoliate leaf stage of growth, that use pattern must be adequately represented.

f) The label indicates that postemergence applications must be made with a non-ionic surfactant at 0.25% v/v (1 qt/100 gal) or a crop oil concentrate at 1% v/v (1 gal/100 gals) in the spray. No

residue data were submitted reflecting use of the crop oil concentrate or nonionic surfactant in the DE-498 spray solution. Therefore, references on the label to the crop oil concentrate and non-ionic surfactant should be deleted or additional residue data should be submitted reflecting use of the crop oil concentrate and the nonionic surfactant.

g) The petitioner has indicated that samples were stored frozen. Storage temperature should be specified.

h) Label restrictions against feeding soybean hay and forage are acceptable since these are considered to be under grower control and not routinely fed to livestock.

i) Available storage stability data (up to 411 days) do not support residue data on soybean samples stored longer (ie. up to 32 1/2 months). (See "Storage Stability" above.)

Processing Study

No processing study was conducted on soybeans. (Processed commodities from soybeans are meal, hulls, soapstock, crude oil, and refined oil.) No detectable residues (<0.005 ppm) were found in soybeans resulting from postemergence treatment at a 6X rate or preplant incorporated treatment at a 4X rate. Mature dry soybean seeds contain 17.7% fat (Pesticide Analytical Manual, Vol. 1, Section 202.25). This means that the theoretical concentration factor from soybean seeds to soybean oil is 6X. Since no detectable residues were found in soybeans after postemergence treatment at 6X, no processing study is required and no food additive tolerances are required. Grain dust residue data are not required for this use on soybeans since applications are preplant incorporated, preemergence, and early postemergence. "The grain dust data are needed only in those cases in which detectable, primarily surface residues are found on the grain." ("Overview of Residue Chemistry Guidelines", R.D. Schmitt, 10/10/89).
Note: Detectable radioactive residues (0.015 ppm) were found in mature soybeans in a metabolism study discussed above, in which soybeans were treated at the rate of 0.05 lb ai/A (3.3X the maximum postemergence rate) at the second and third trifoliate stage of growth. Detectable radioactive residues (0.02 ppm) were also found in soybeans in another metabolism study discussed above, in which soybeans were treated at the rate of 0.076 lb ai/A (5X the maximum postemergence rate) at the V5 to V6 growth stage. However, these radioactive residues resulting from use of an early season herbicide are not assumed to be residues of concern for purposes of determining the need for a processing study (ie. A processing study is not needed based on results of the cold study at 6X discussed above.)

CBTS concludes that a processing study and food additive tolerances are not needed for soybeans since no residues were found

in soybeans after postemergence treatment at 6X, the theoretical concentration factor for soybean oil.

CBTS also concludes that grain dust residue data are not required for this use on soybeans since detectable, primarily surface residues are not expected.

Meat, Milk, Poultry, and Eggs

No animal feeding studies have been conducted. Soybean seed, meal, hulls, soapstock, and grain dust; and corn grain, forage, fodder, silage and grain dust may be fed to livestock under this proposed use.

CBTS must reserve its conclusion regarding the need for animal feeding studies until questions regarding the proposed use, plant metabolism, plant analytical methods, and residue data are resolved. If no detectable residues are found in feed items, no animal feeding studies and no tolerances for animal commodities will be required.

Other Considerations

An International Residue Limits (IRL) Status Sheet is attached. (See attachment 4.) There are no Codex, Canadian, or Mexican tolerances for DE-498 (flumetsulam) on corn or soybeans. Therefore, no compatibility questions exist with respect to Codex.

Attachment 1: Distribution of C^{14} Residues in the Organic Extract of Soybeans
Attachment 2: Distribution of C^{14} Residues in the Acid Extract of Soybeans
Attachment 3: Tentative Metabolic Pathway for DE-498 in Soybeans
Attachment 4: International Residue Limit (Codex) Status Sheet
Attachment 5: Product Chemistry Chapter (Confidential Appendix A)
Attachment 6: Confidential Statement of Formula for DE-498 Technical (Confidential Appendix B)
Attachment 7: Confidential Statement of Formula for XRM-5019 (Confidential Appendix C)

cc with all attachments: SF (for DE-498 and Trifluralin), N. Dodd (CBTS), E. Haeberer (CBTS), PP#1G04006, PM#23, TOX (II), C. Furlow (PIB/FOD)

cc with Attachments 1, 2, 3, and 4 only: Circu.(7), RF

RDI:E. Haeberer:3/11/92:R. Loranger:3/12/92
H7509C:CM#2:Rm800D:X55681:N.Dodd:nd:3/25/92

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RIN # 4644-93 EFGW Review & Residue Chemistry Review for Flumetsulam (129016)

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____ Identity of product impurities.

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____ 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.

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