C. Thrlow
PTB/FOD

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

DEC 13 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#9F3743 - Clethodim (Select®) in/on Soybeans, Cottonseed, and Animal Commodities. Review of October 17 and November 13, 1990 Amendments. (MRID No. 416850-01) [DEB Nos. 7255 and 7299] {HED Project Nos. 1-0175 and 0-0190}

FROM: Francis D. Griffith, Jr., Chemist
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Francis D. Griffith Jr.

TO: Joanne I. Miller, Acting PM 23
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Registration Division (H7505C)

and

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

THRU: Robert S. Quick, Section Head
Tolerance Petition Section I
Chemistry Branch I - Tolerance Support
Health Effects Division (H7509C)

RSQ

Valent U.S.A. Corporation has submitted these amendments consisting of cover letters and supplementary Section D (revised analytical method and secondary laboratory validation data) in response to deficiencies outlined and summarized in our May 4, 1990 review by M. J. Nelson and the November 9, 1990 review by F.D. Griffith, Jr. The deficiencies are listed and repeated in the body of this review in the order they appeared in our November 11, 1990 review followed by the petitioner's responses, then CBTS comments. Our conclusions and recommendations follow.

EXECUTIVE SUMMARY OF CHEMISTRY DEFICIENCIES

1. Run a Petition Method Validation (PMV) on the proposed enforcement method and the confirmatory method.

2. Resubmit the compound-specific confirmatory procedure revised in accordance with our suggestions.

3. Address Product Chemistry deficiencies.

4. Submit a quantity of the internal standard (cloproxydim sulfoxide) to the Pesticides and Industrial Chemicals Repository, Research Triangle Park, NC.

CONCLUSIONS

1. Chemistry Branch (CB) Conclusions on **Residue Analytical Methods**

   a. We have requested ACB/BEAD conduct a new PMV on the revised version of Analytical Method RM-26B-2 (MRID No. 416234-01), the proposed primary enforcement method (see memorandum F.D. Griffith, Jr. to D.A. Marlow, October 23, 1990). We defer judgment on the method being an enforcement method pending review of a new ACB/BEAD PMV report. The deficiency remains unresolved and continues outstanding.

   b. The petitioner needs to resubmit the compound-specific confirmatory method further revised in accordance with our eight concerns as noted in the body of our November 11, 1990 review. The deficiency remains unresolved and continues outstanding.

   c. The petitioner has provided the requested second laboratory validation data and has satisfactorily explained why diazomethane is needed as the methylating agent in the method. These parts of the deficiency are resolved.

   d. The petitioner needs to submit a quantity of the internal standard cloproxydim sulfoxide (reference grade) along with supporting documentation, i.e., the Material Safety Data Sheet (MSDS), to EPA's Pesticides and Industrial Chemicals Repository. The deficiency continues to be unresolved and remains outstanding.

2. CB Conclusion on **Proposed Tolerances**

   Judgment on the adequacy of the proposed tolerances is deferred until there have been successful PMVs. CB tentatively concludes that residues of total clethodim are not expected to exceed the proposed tolerances from the

proposed conditions of use of Select® Herbicide. The deficiency continues unresolved and remains outstanding.

3. CB Conclusion on **Product Chemistry**

The deficiencies associated with the product chemistry of clethodim will need to be resolved prior to the establishment of the proposed tolerances in this petition. These deficiencies are discussed in CB's (aka DEB) companion review titled "PP#9F3743. Clethodim Product Chemistry Data Submitted in Support of Registration" by M.J. Nelson dated March 12, 1990, DEB No. 5681, which see for details. The deficiency remains unresolved and continues outstanding.

RECOMMENDATION

At this time, CB recommends against the establishment of the proposed clethodim plus its metabolites containing the 2-cyclohexen-1-one moiety tolerances in or on the commodities of this petition for the reasons cited in our Executive Summary and further explained in our Conclusions 1, 2, and 3 above.

For further consideration of the proposed tolerances, the petitioner should be advised to resolve the deficiencies noted above.

DETAILED CONSIDERATIONS

RESIDUE ANALYTICAL METHODS

Deficiency (1b. from our November 9, 1990 review)

CBTS has requested ACB/BEAD conduct a new PMV on the revised version of the Analytical Method RM-26B-2 (MRID No. 416234-01), the proposed primary enforcement method (see memorandum by F.D. Griffith, Jr. to D.A. Marlow, October 23, 1990). CBTS defers judgment on the method being an enforcement method pending review of a new ACB/BEAD PMV report. The deficiency remains unresolved and continues outstanding.

CB Comments

The petitioner is not expected to respond. CB notes the PMV is in process (telecon D. Griffith to E. Greer, November 28, 1990). However, the deficiency remains unresolved and continues outstanding.

Deficiency (1d. from our November 9, 1990 review)

The petitioner needs to resubmit the compound-specific confirmatory method further revised in accordance with our 8 concerns as noted in the body of our November 9, 1990 review. This deficiency overall remains unresolved and continues outstanding.

Petitioner's Response

The petitioner did not respond.

CB Comments

CB reiterates the deficiency noted above. It continues unresolved and remains outstanding.

Deficiency (1c. from our November 9, 1990 review)

CBTS reiterates that the petitioner needs to submit a quantity of the internal standard cloproxydim sulfoxide (reference grade) along with the supporting documentation, i.e., the MSDS, to EPA's Pesticides and Industrial Chemicals Repository. The deficiency remains unresolved and continues outstanding.

Petitioner's Response

The petitioner has not responded.

CB Comments

In a telecon (D. Griffith to P. Bayer at the Repository on December 4, 1990) CB confirmed the internal standard cloproxydim sulfoxide is not presently at the Repository. We were informed that Valent also knows this standard is not at the Repository.

Valent has sent a small portion of this standard (100-500 mg) to EPA's Analytical Chemistry Laboratory at Beltsville, MD (telecon D. Griffith to E. Greer, November 28, 1990). CBTS had previously suggested a portion of the standard be sent directly to the lab so that the PMV may move forward. However, ACB/BEAD is not in the business of supplying Federal and State enforcement labs with small portions of analytical reference standards for tolerance enforcement. Distribution of standards is a function of EPA's Repository.

The deficiency remains unresolved and continues outstanding.

Deficiency (from our November 9, 1990 review)

As for the concerns expressed in CB's May 4, 1990 review on the confirmatory method, the petitioner still needs to provide

independent lab validation of the method and also explain why diazomethane is needed as the methylating agent in the method.

Petitioner's Response (See MRID No. 416850-01)

For justification of the use of diazomethane, the petitioner presented a copy of a September 4, 1990 memorandum from Chevron Chemical Company titled "Clethodim Confirmatory Method RM-26D-1 Diazomethane Use Justification."

The petitioner presented independent laboratory validation data for the confirmatory method in a study titled "Validation of the Confirmatory Method for Determination of Clethodim Metabolites in Soybean Seed, Cotton Fuzzy Seed, and Bovine Liver" by J.F. Kruplak and B. Ho dated October 31, 1990 and coded 9012643.

CB Comments

The petitioner tried two other methylating agents, methyl iodide and dimethyl sulfate. After 4 hours of reacting dimethyl sulfate with clethodim, the yield of the enol ranged from 59 to 73 percent. Also, after reacting methyl iodide for 4 hours with clethodim, the yield of the enol was about 33 percent. In both methylations, 15 to 25 percent, respectively, of unidentified products were present. Additional heat does not help as clethodim is heat sensitive undergoing a Beckman Rearrangement to form dihydrobenzoxazolone.

We agree the methylation yield is too low and the amount of unidentified material formed is too high, thus the use of diazomethane as a methylating is acceptable for this reaction. The petitioner tried alternate methylating agents and presented an acceptable argument for the use of diazomethane. This part of the deficiency is resolved.

The independent laboratory validation of the confirmatory methods was performed by Analytical Development Corporation (ADC) of Colorado Springs, CO. ADC validated the original clethodim method RM-26C-1 reviewed in our March 12, 1990 memorandum. Control samples of soybean seeds and cottonseed were spiked with clethodim sulfoxide and 5-hydroxy clethodim sulfoxide, first at the proposed tolerance level and 2X proposed tolerance, then another set of spikes were run at EPA's suggested tolerance levels. The spike levels in soybeans ranged from 5 to 20 ppm and in cottonseed ranged from 0.5 to 10 ppm. Duplicate analyses were conducted for reagent blanks, controls, and then spiked controls.

ADC followed the method RM-26C-1 as written. They did not have to contact the petitioner to complete the trial. A few very minor modifications were made to the procedure such as use of a stainless steel blender jar instead of a 1 pint Mason jar, the IS concentration was 50.5 ug/mL instead of 50.0 ug/mL, prerinse the Na_2SO_4 with CH_2Cl_2, and change in HPLC elution gradient. CB

considers these to be routine for local conditions that would be done by any enforcement lab using the procedure.

Recoveries of 5-hydroxy clethodim sulfoxide ranged from 75 to 120 percent in cottonseed and from 73 to 105 percent in soybean seed. Recoveries of clethodim sulfoxide ranged from 75 to 104 percent in cottonseed and from 70 to 97 percent in soybean seed. The petitioner (from ADC) has supplied extensive supporting chromatographic data to confirm these findings.

Revised method RM-26D-1 was validated by ADC for clethodim sulfoxide in bovine liver. Beef liver was spiked at 0.2 and 0.5 ppm. Analyses were done in duplicate for controls and each spike level.

ADC followed the revised method RM-26D-1 as written. They did not have to contact the petitioner to complete the trial. A few very minor modifications were also made to this method such as substitution of filter paper and microfilter, slower centrifuge speed, and different shape flasks. CB also feels these changes are routine to reflect local conditions that would be done by any enforcement lab using the procedure.

Recoveries of clethodim sulfoxide in bovine liver ranged from 70 to 82 percent. The petitioner (from ADC) has supplied adequate supporting chromatographic data to confirm the results.

The steps identified as critical were immediate alkaline precipitation following extraction and immediate addition of acid to the filtrate following precipitation. ADC had several suggestions on filtration and calculations that need to be incorporated by the petitioner into his revised method. CB notes that ADC took 5 days lapse time with 26 hours run time to complete the plant PMV (13 samples/5 days) and 4 days lapse time with 17 hours to complete the animal tissue PMV (6 samples/4 days). These lapse (run) times are not acceptable for enforcement purposes. However, the petitioner has provided adequate independent lab validation data for the confirmatory method. This part of the deficiency is resolved.

PROPOSED TOLERANCES

Deficiency (No. 5 of our November 9, 1990 review)

Judgment on the adequacy of these tolerances is deferred until there have been successful PMVs. CB tentatively concludes that residues of total clethodim are not expected to exceed the proposed tolerances from the proposed conditions of use of Select® Herbicide.

CB Comments

The petitioner is not expected to respond at this time. CB reiterates the above deficiency.

PRODUCT CHEMISTRY

Deficiency (No. 6 of our November 9, 1990 review)

CB reiterates that the deficiencies associated with the product chemistry of clethodim will need to be resolved prior to the establishment of the proposed tolerances of this petition. These are discussed in CB's (aka DEB) companion review titled "PP#9F3743. Clethodim Product Chemistry Data Submitted in Support of Registration" by M. Nelson, DEB No. 5681 dated March 12, 1990, which see, for details.

Petitioner's Response

The petitioner did not respond.

CB Comments

CB reiterates the above deficiency. It continues unresolved and remain outstanding.

cc: R.F., Circu (7), Reviewer (FDG), PP#9F3743, D.A. Marlow (ACB/BEAD), C. Furlow (PIB/FOD), R.D. Schmitt, Ph.D., Chief.

H7509C:CBTS:Reviewer (FDG):CM#2:RM 814B:557-0826:JOB: 55971:I:WP5.0:C.Disk:KENCO:12/10/90:DD:VO:EK:CL:ed:fdg:12/12/90.

RDI:SecHd:RSQuick:12/12/90:BrSrSci:RALoranger:12/12/90.