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

DEC 14 1990

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: PP#9F3714. EPA Reg. No. 8340-GI. Fenoxaprop-ethyl (Tiller) in or on Wheat. Amendment of 4/18/90. Petitioner's Response to DEB's 2/2/90 Review of Amendments of August 21, 1989. MRID No. 414585-01 DEB Nos. 6587 and 6743

FROM: Joel Garbus, Ph.D., Chemist
Tolerance Petition Section III
Chemistry Branch, Tolerance Support
Health Effects Division (H7509C)

THRU: P. Errico, Head
Tolerance Petition Section III
Chemistry Branch, Tolerance Support
Health Effects Division (H7509C)

TO: J.Miller/E. Wilson, PM-23
Fungicide - Herbicide Branch
Registration Division (H7505C)

Hoechst Celanese Corporation has responded to DEB's review of February 2, 1990 regarding amendments to the petitioner's request for the registration of a formulation of fenoxaprop-ethyl specifically for use on wheat (Tiller) and the concurrent establishment of wheat grain and straw tolerances.

Summary of Remaining Deficiencies

3b. The petitioner should propose tolerances at the limit of detection (0.01 ppm) for meat, meat by-products, and milk resulting from the use proposed in this petition.

3d. A method validation of the proposed enforcement method AL 06/84 for residues in meat and milk is required. However, before an Agency validation can be conducted the petitioner will need to submit a complete description of the methodology which includes representative chromatograms and validation data of fortified

samples. An independent laboratory validation is also needed.

Summary of Petitioner's Response

The petitioner has satisfactorily responded to Conclusions 3c, 4a, 5b, and 5c. (See below.) However, in the submitted material the petitioner has taken exception to conclusions 3a and 3b (the need for tolerances for secondary residues in meat, meat by-products, and milk) and the need for the actions stemming from this conclusion as set forth in Conclusion 3d.

The petitioner asks that Conclusions 3a, 3b, and 3d be reconsidered in light of the submitted data and arguments that demonstrate that detectable residues would not accumulate in animal tissues or milk from the proposed use on wheat.

Recommendation

CBTS does not recommend for the proposed tolerances until remaining deficiencies 3b and 3d are satisfied.

Detailed Considerations

DEB's 2/2/90 review concluded that the proposed amendments addressed some of the deficiencies identified in the original review of the petition but that the substantial issue of the need for secondary tolerances in meat , milk, and meat by-products remained. DEB concluded that:

> 3a. The presence of residues in milk and tissues at all feeding rates in the submitted feeding study demonstrates the potential for residues to transfer. We conclude that this is a Section 180.6(a)(2) situation with respect to secondary residues in meat, milk, poultry, and eggs.
>
> 3b. The petitioner should propose tolerances at the limit of detection (0.01 ppm) for meat, meat by-products, and milk resulting from the use proposed in this petition.
>
> 3c. A method validation for a proposed enforcement method (HRAV-4)is needed for wheat grain and straw. The method validation has been requested of the Agency's Analytical Chemistry Branch.
>
> 3d. A method validation of the proposed enforcement method AL 06/84 for residues in meat and milk is required. However, before an Agency validation can be conducted the petitioner will need to submit a complete description of the methodology which includes representa-

tive chromatograms and validation data of fortified samples.

4a. The site of the ^{14}C label used in the goat metabolism study submitted in this amendment was not identified. Presumably it is located in the benzoxazol ring. Acceptance of this study for the proposed use on wheat is predicated on the petitioner verifying that the labeled site is in the benzoxazol ring. Provided that this is the case the residues of concern in ruminants and hogs are fenoxaprop-ethyl, its free acid, fenoxaprop, and 6-chloro-2,3-dihydrobenzoxazol-2-one.

4b. For any future tolerance requests on potential livestock feed items which can lead to higher livestock exposure to regulated residues of fenoxaprop-ethyl, the unidentified residues in tissues and milk, except kidney, from the goat metabolism study must be characterized/-identified. Both rings of fenoxaprop-ethyl should be labeled.

5a. We conclude that the 0.05 ppm proposed for wheat grain most likely would be accommodated by the proposed revised label instructions and that the revised label giving application timing in terms of growth stages rather than fixed PHI's is acceptable.

5b. However, until additional data are submitted we cannot be certain that the proposed tolerance of 0.5 ppm for wheat straw will be sufficient to encompass the minimum interval from application to harvest. The maximum residue value (0.36 ppm) upon which the proposed tolerance of 0.5 ppm was based was obtained with a 70 days PHI. At present it remains only an assumption that the proposed tolerance would not be exceeded at a 60 day PHI.

5c. Therefore, the petitioner can submit growth-stage information for all varieties of wheat grown under all US cultural conditions so as to indicate the range of time that could elapse between application as per the label instructions and harvest.
The petitioner will need to relate the residue data previously submitted in terms of PHI's to wheat growth stages. When we are in possession of this additional information we can determine if the proposed tolerance of 0.5 ppm on wheat straw is adequate.

As an alternative to supplying the above information, the petitioner can submit a revised Section B that includes a 70 day PHI.

Response to Specific Deficiencies:

Below we summarize the specific deficiencies noted in the 2/2/90 memo, and give the petitioner's response and our comments and conclusions.

Conclusion 3c:

The need for EPA's validation of the proposed enforcement methodology for fenoxaprop-ethyl and its metabolites on wheat grain and straw.

Response.

The method has undergone a validation trial by EPA's Analytical Chemistry laboratory and appears to be satisfactory provided that the petitioner revises the description of the method to incorporate suggestions aimed at improving the method's efficiency.

Comment

The deficiency is partially resolved and will be completely resolved when the petitioner supplies a satisfactorily revised description of the method.

Conclusion 4a

The need to identify the site of the ^{14}C label used in the submitted goat metabolism.

Response

The labeled fenoxaprop-ethyl used in the goat metabolism study was uniformly labeled in the benzoxazol ring.

Comment

This deficiency is adequately resolved.

Conclusions 5b and 5c

If applications of Tiller were to be timed to growth stages,the need to include additional information on tillering of varieties grown under different conditions. Alternatively a fixed PHI of 70 days could be imposed.

Response

The proposed label has been revised to impose a PHI of 70 days. This interval is consistent with the proposed tolerance of 0.5 ppm for wheat straw.

Comment

This deficiency is satisfactorily addressed.

Conclusion 3a, 3b, and 3d.

The need for tolerances for secondary residues in meat, meat by-products, and milk resulting from the feeding of fenoxaprop-ethyl treated straw and the consequent need for validated analytical methods.

Response

The petitioner believes that no tolerances for milk, meat, and MBYP will be needed based on the following observations.

The dose used in the feeding study cited above (Conclusion 3a) was 12 times the tolerance proposed for wheat straw, 16 times the maximum residue found, and 36 times the "anticipated residue", for wheat straw and 2680 times the level expected at a feeding rate of 10% straw in cattle diets. Extrapolating linearly from the exaggerated rates of the metabolism study to the expected residue in wheat straw results in calculated residues in all tissues and milk considerably below the limit of detection of the enforcement methodology.

Comment

In this instance, the petitioner has submitted a ruminant feeding study originally submitted as a part of PP#8F3599.

In this study, lactating cattle were feed a 1:1 mixture of parent and 6-chloro-2,3-dihydrobenzoxazol-2-one. Calculations based upon theoretical livestock diets consisting of feedstuffs containing tolerance level amounts of fenoxaprop-ethyl showed that the maximum amount for lactating cattle would be 3 mg per animal per day based on a 600 kg bodyweight. Consequently animals were fed, as part of a normal ration, 3 mg of the parent and 3 mg of the substituted benzoxazolone for 28 days. Other groups of animals received 9 and 30 mg respectively. Milk was collected through out the feeding study; animal tissues were obtained at sacrifice 28 days after the study was initiated. Milk and tissues were analyzed by method AL 06/84 that converts residues to the common moiety of the substituted benzoxazolone. The limit of detection of this method is reported as 0.01 ppm.

The daily dose of 3 mg parent plus 3 mg 6-chloro-2,3-dihydrobenzoxazol-2-one did not result in any detectable residues in milk, kidney, or fat. In 1 of 3 liver samples 0.02 ppm was detected; in 1 of 9 muscle samples 0.02 ppm was detected. The petitioner believes that these results are anomalous and besides are at the limit of detection.

At the 10X rate of feeding 22 of 72 milk samples had residues of from 0.01 to 0.03 ppm. At this feeding level, residues in kidney were 0.04 to 0.09 ppm (n=3), in liver 0.10 to 0.20 ppm (n=3), and 0.01 ppm in 1 of 9 fat samples (residues in the remaining fat samples were below the limit of detection).

In its review of the feeding study DEB stated that the 3 mg of parent per animal rate was equivalent to 0.2 ppm based upon a daily consumption of 15 kg of feed on a dry weight basis. If wheat straw were the only component in the diet, the daily consumption would be 0.05 ppm (the tolerance level of 0.5 ppm at 10% of the diet). Thus the 1X feeding study was conducted at a rate 4 times that expected from the tolerance proposed for this RAC. The petitioner has pointed out in its reply that DEB overlooked the presence of the metabolite as a component of the fed material.

Having a mixture of the parent compound and a metabolite confounds the interpretation of results. The metabolism studies conducted with fenoxaprop-ethyl indicated that the feeding of the parent alone results in tissue levels of the parent and its free acid at least twice the concentration of the benzoxazol-2-one.

DEB agrees that it is reasonable to conclude that no detectable residues of fenoxaprop-ethyl or its metabolites would occur in milk or tissues of animals fed fenoxaprop-ethyl treated wheat straw at the tolerance level. However, the presence of residues in milk or tissues at all feeding rates in the feeding study demonstrates the potential for residues to transfer. In our opinion, Section 180.6(a)(2) regarding secondary residues applies in this situation. That is to say, that if fenoxaprop-ethyl is ingested at levels that exceed the proposed tolerance, finite and detectable residues could be found in animal tissues, milk, or eggs. It should be recalled that the 1 X feeding level in the study was based upon theoretical livestock diets consisting of feedstuffs containing tolerance level amounts of fenoxaprop-ethyl.

In its review DEB recommended that the petitioner propose tolerances at the limit of detection (0.01 ppm) for meat, meat by-products, and milk resulting from the use proposed in this petition. The petitioner would need to submit complete details including representative chromatograms of method Al 06/84 together with an independent laboratory validation. The Agency would need to conduct its own validation when the proposed enforcement methodology is received.

The specific issue of the need for the proposal of tolerances for secondary residues for this use of fenoxaprop ethyl on wheat and the general issue of the interpretation of 40CFR180.6 were discussed at a meeting with the petitioners on 5/6/90. It was agreed that an strict reading of this section would lead to the conclusion that the finding of a finite residue, however small, at a possible

feeding level that could be potentially encountered would mean that Section 180.6(a)(2) was applicable.

Tolerances have not been proposed in this submission. However, in a subsequent submission now under review, tolerances have been proposed for meat, meat by-products, and milk (MRID No. 416544-01).

Deficiencies 3b and 3d remain outstanding, pending our review.

Note: In our review of 2/2/90, DEB stated that it would require a copy of the accountability study titled: "HOE 033171-14-C: Nature of Residues in Milk and Tissues of Cows after Dosing 50 mg/Cow/Day at Three Consecutive Days." Authored by K. Krenzler, E. Dorn and H. M. Kellner. Hoechst Internal Report Fo 337/85, A30492.

A copy has been provided.

cc: PP9F3714, S. File, RF., Circ., Reviewer, FOD/ISB(Furlow)
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