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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#9F3714. EPA Reg. No. 8340-GI. Fenoxaprop-ethyl in or on Wheat. Amendment of October 12, 1990. Amended Section F and Analytical Methods for Meat and Milk. MRID Nos 416544-00 thru 416544-04. DEB No 7208.

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

In further response to CBTS's review of PP#9F3714 (J. Garbus, memo, August 8,1989) and its review (J. Garbus, memo, 2/2/1990) of an amended petition dated August 21, 1989, the petitioner has submitted a revised Section F requesting tolerances for meat, milk, and meat by-products and analytical methods to support the requested tolerances.

In its submission of April 18,1990, the petitioner satisfactorily responded to several of the deficiencies originally cited in our 1989 and 1990 memos.

Below the remaining deficiencies from our memos will be stated, followed by the petitioner's response and our comments.

Conclusions and Recommendations

1. All outstanding deficiencies have been resolved.

2. DEB recommends for the establishment of the proposed tolerances for the use of fenoxaprop-ethyl on wheat now that the enforcement

method for meat and milk has successfully undergone the Agency's method validation trial.

DETAILED CONSIDERATIONS:

Deficiencies 3a and 3b:

The presence of residues in milk and tissues at all feeding rates in the 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.

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.

Petitioner's Response:

The petitioner has submitted a revised Section F requesting the establishment of full tolerances for the combined residues of the herbicide fenoxaprop-ethyl:

(±)-ethyl 2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy] propanoate and

its metabolites:

2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy]-propanoic acid

and

6-chloro-2,3-dihydro-benzoxazol-2-one

each expressed as fenoxaprop-ethyl, in or on the following raw agricultural commodities:

Commodity	Parts Per Million
Wheat, grain	0.05
Wheat Straw	0.50
Cattle, fat	0.05
Cattle, meat	0.05
Cattle, mbyp	0.05
Goats, fat	0.05
Goats, meat	0.05
Goats, mbyp	0.05
Hogs, fat	0.05
Hogs, meat	0.05
Hogs, mbyp	0.05
Horses, fat	0.05
Horses, meat	0.05
Horses, mbyp	0.05

Commodity	Parts Per Million
Sheep, fat	0.05
Sheep, meat	0.05
Sheep, mbyp	0.05
Milk	0.02

Comment

With the proposal of adequate tolerances (limit of detection of proposed analytical methodologies for meat and for milk), the petitioner has resolved these deficiencies.

Deficiency 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.

Petitioner's Response

The petitioner has developed and independently validated a method for the quantitative determination of fenoxaprop-ethyl in animal tissues and milk.

Study Title

Gas Chromatographic Determination of Fenoxaprop-Ethyl [HOE-033171: Ethyl 2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy] propanoate] and its metabolites [HOE-053022: 2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy]-propanoic acid and HOE-054014 6-chloro-2,3-dihydro-benzoxazol-2-one] as Residues in Meat, Milk, and Meat By-Products.

Author

J. J. Czarnecki, Ph.D.

Performing Laboratory

Hoechst Aktiengesellschaft, Analytical Laboratory
6230 Frankfurt (M) 80

Report Date

Issued: August 2,1990 (as HRAV-8)
Reissued: September 10, 1990 (as HRAV-8a)

Two separate method validations are submitted.

Study No. 1:

Study Title

Method Validation for the HOE-033171, HOE-053022 (Free Acid) and HOE-054014 (Dihydrobenzoxazol Metabolite) in Animal Tissues

Authors

John W. James, Fred R. McKinney, and Frank B. Clayton

Performing Laboratory

EN-CAS Analytical Laboratories
2359 Farrington Point Drive
Winston-Salem, NC 27107

Report Date

October 4,1990 (as HRAV-8)

Study No. 2:

Study Title

Method Validation Ruggedness Trial for Hoechst-Roussel Agri-Vet (HRAV) Method HRAV-8, Gas Chromatographic Determination of Fenoxaprop-Ethyl [HOE-033171: Ethyl 2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy] propanoate] and its metabolites [HOE-053022: 2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy]-propanoic acid and HOE-054014 6-chloro-2,3-dihydro-benzox azol-2-one] as Residues in Meat, Milk, and Meat By-Products (Draft Version).

Authors

Alan D. Morris and Frank B. Clayton

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EN-CAS Analytical Laboratories
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Winston-Salem, NC 27107

Report Date

October 4,1990 (as HRAV-8)

The method is based upon the method (HRAV-4A) used with plant matrices and successfully validated by the Agency. Meat and milk samples are extracted by refluxing with acetonitrile/water/HCl. This has the effect of extracting fenoxaprop-ethyl and its metabolites of concern and converting them to 6-chloro-2,3-dihydrobenzoxazol-2-one (HOE 054014) by acid hydrolysis. The extracts are cleaned up, HOE 054014 is derivitized (acetylated) and determined by GC.

Limits of quantitation are given as 0.05 ppm for meat and meat by-products and as 0.02 ppm for milk. Recoveries from milk, muscle, liver, and fat for the parent and for each of the two metabolites range from 70 to 122%.

Two validation studies are submitted, both performed by EN-CAS Analytical Laboratories. The first study concludes:

> EN-CAS Analytical Laboratories modified and validated a method for the determination of HOE-033171 and its metabolites using HRAV-4A as a reference method. The modified method yields successful results for the determination in beef muscle, fat, liver, and milk.

The second validation study concludes:

> With the consideration of the above comments, [modifications to the method report are recommended to improve transfer of the techniques from one laboratory to another] EN-CAS analytical laboratory concludes that method HRAV-8 is valid for the determination of HOE-033171, HOE-053022 and HOE-054014 in milk,muscle,fat and liver.

Comment

The petitioner apparently contracted with EN-CAS Analytical Laboratories for a method to determine fenoxaprop-ethyl and its metabolites in animal tissues and milk. EN-CAS developed a method based upon an existing validated method (HRAV-4) for plant matrices that had originally been developed in the petitioners West German laboratory. The contract laboratory, conducted an independent validation of the animal tissue method in its own facility, following the guidelines of PR 88-4.

The petitioner's description of the method reports representative results of recoveries as given in the contract laboratory's first study. The recoveries for the parent and the two metabolites at 1X, 10X and 100x the requested tolerances range from 70 to 122% from milk, 77 to 107% from muscle, 81 to 113% from liver, and 79 to 102% from fat.

Initially, the validating laboratory at EN-CAS was unable to achieve satisfactory recoveries (70 to 120%) from milk, fat,

muscle, and liver. After consultations (reported as within the bounds of PR 88-4) with the developers of the method, modifications were introduced and a second attempt was made at satisfactory recoveries. This also failed in the case of fat, milk, and muscle. After further modifications, satisfactory results were achieved with all the animal matrices in a third attempt. The modifications have been incorporated in the petitioner's description of the proposed enforcement method (HRAV-8A).

The petitioner's cover letter accompanying this submission comments that: " the just validated wheat grain and straw method, as well as the previously validated rice grain and straw and soybean methods employ the same principals of extraction, clean-up and quantitation as the presently submitted meat and milk method. Thus the need for yet another validation by the Agency's Analytical Chemistry Branch would seem inappropriate to the petitioner."

Given the difficulties that the petitioner's contract laboratory had in satisfactorily validating a procedure developed in that laboratory and given the substantial differences between plant and animal matrices, we concluded that a validation by the Agency's Analytical Chemistry Branch was warranted. Therefore, we requested that the animal tissue method be validated by the Agency. The method was successfully validated (J. Garbus, memo, 4/08/91).

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