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

JUN 12 1984

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#OF2413/FAP#OH5275: PP#3F2793/FAP#3H5378.
Thiodicarb in Cotton and Soybeans. Amendment
of May 10, 1984.

FROM: Alfred Smith, Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

EXPEDITE

THRU: Charles L. Trichilo, Ph.D., Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

TO: Jay Ellenberger, PM Team No. 12
Registration Division (TS-767)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

Note: This review was expedited by the written request of Douglas D. Campt, Director, Registration Division (see memo of 5/25/84).

The Union Carbide Agricultural Products Company, Inc., has submitted a position paper, "Evaluation of Thiodicarb under FDA's Sensitivity of Methods Procedures," as a basis for the establishment of tolerances for thiodicarb on cotton (PP#0F2413/FAP#OH5275) and soybeans (PP#3F2793/FAP#3H5378).

In the Sensitivity of Methods Procedures (SOM), the minimum acceptable level for residue components (in the present case, acetamide or acetonitrile) in animal tissue, eggs, or milk is first established. An analytical method is then developed which is capable of detecting and determining the residue components at and above the established levels. If no residues are detected, it can be concluded that the concentration of the residue component in the total daily diet of humans will not exceed an acceptable upper limit.

A table of detection limits for the metabolite acetamide and its precursor component acetonitrile has been compiled from data in the above Pesticide Petitions for cotton and soybeans. The table is reproduced below.

Target Tissue	Marker Residue	Required Detection Limit (PPM)
1. milk milk	acetamide acetonitrile (alternate)	0.005 4.0
2. eggs eggs	acetamide acetonitrile (alternate)	0.035 0.15
3. liver, cattle	acetamide	0.80
4. liver, poultry	acetamide	0.28

The paper states that Union Carbide is now developing the analytical methods and anticipates submitting them to the EPA for validation in the near future.

Conclusion

RCB has no objection to the analytical rationale developed in this paper. However, RCB defers to toxicology on the detection limits proposed by the petitioner. The adequacy of the analytical methods cannot be fully evaluated until RCB receives the methods. The methods will then be reviewed and, if necessary, method trials will be conducted by EPA to determine the method's adequacy for enforcement purposes.

Background

Pesticide Petitions have been submitted by Union Carbide which requested that tolerances for combined residues of the insecticide thiodicarb (LARVIN®), dimethyl N, N'-[thiobis[(methyl-imino)carbonyloxy]]bis[ethanimidothioate], and its metabolite

methomyl, S -methyl N-[(methylcarbamoyl)oxy] thioacetimidate, in or on cottonseed at 0.4 ppm; soybeans at 0.1 ppm; soybean straw at 0.2 ppm; cottonseed hulls at 0.8 ppm (food additive tolerance); soybean hulls at 0.4 ppm (food additive tolerance).

RCB recommended for the establishment of the proposed tolerances (PP#0F2413/FAP#0H5275).

TOX indicated no toxicological concern regarding the metabolite acetonitrile, but indicated that the metabolite acetamide had been shown to be an animal carcinogen. TOX also indicated that the TMRC for acetamide would be determined and risk assessments would also be determined. The assessments would then be deferred to the Administrator for an RPAR decision.

TOX performed a risk assessment and recommended "that the residues of acetamide in the commodities found did not require further regulation or inclusion in the tolerance of thiodicarb (memo of W. Dykstra, 7/ 8/81). TOX later recommended for the proposed tolerances (memo of 4/30/82).

In a subsequent review of the tolerance proposals for thiodicarb in soybeans (PP#3F2793/FAP#3H5378, memo of 3/7/83), RCB deferred to TOX on the question of the metabolite acetonitrile and the suspected carcinogenicity of the metabolite acetamide and if such components needed to be regulated. RCB further indicated that if acetonitrile and acetamide were considered to be toxicologically significant and should be regulated, then validated analytical methods would be needed to determine these components. (RCB has not yet received TOX's response to these questions.)

RCB recommended against the soybean tolerances and made a favorable recommendation contingent upon the resolution of questions concerning the metabolites acetonitrile and acetamide.

The petitioner's position paper is in response to RCB's recommendation.

cc: R.F, Circu, Reviewer: TOX, EAB, EEB, PP#0F2413/PP3F2793
FDA: Robert Thompson
RDI: J. Onley:6/5/84:R.D. Schmitt:6/5/84
TS-769:A. Smith:wh:6/11/84:CM#2:RM810:X77377

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