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

SEP 7 1984

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#0F2413/OH5275: Thiodicarb in Cotton and Soybeans. Letter of 8/7/84.

FROM: Richard D. Schmitt, Deputy Chief
Residue Chemistry Branch
Hazard Evaluation Divison (TS-769)

and

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

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

TO: Jay Ellenberger, PM Team #12
Registration Division (TS-767)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

The Union Carbide Agricultural Products Company, Inc., has submitted a letter (J. S. Lovell, 8/7/84) which contains a summary of points discussed at the conference with EPA personnel on Friday, July 27, 1984. The points which pertain to RCB are quoted below with RCB's responses to these points.

"EPA agrees with Union Carbide's choice of liver, milk, and eggs as target tissues".

EPA agrees that under the FDA's Sensitivity of Methods (SOM) procedure the above tissues would be logical choices as target tissues.

"EPA agrees with Union Carbide's choice of acetamide as the marker residue in meat, milk, and eggs, but is unsure of use of acetonitrile as an alternative marker residue in milk, due to limited data establishing the quantitative relationship between acetonitrile and acetamide. EPA asks for additional information to establish that the relative ratio of acetonitrile to acetamide in milk was conservatively estimated." The following discussion also applies to the statement immediately following this one in the letter.

RCB discussed this point in general terms, but no definite agreements were made. RCB does conclude that under the SOM procedure acetamide is the logical choice for a marker residue in meat, milk, and eggs. RCB also indicated that the use of acetonitrile as an alternative marker residue is contingent upon the submission of data by Union Carbide which establishes a quantitative relationship between acetonitrile and acetamide. RCB would evaluate the data and then reach a conclusion.

The PM should note that the acceptance by the Agency of the target tissues and marker residues as defined in the SOM procedures will result in a metabolite of concern (acetamide) in muscle and milk at levels below the limit of detection of available analytical methods. Normally, the Agency requires an analytical method capable of detecting all metabolites at the level of toxicological concern.

"EPA agrees with Union Carbide that dosed tissue samples are not useful and therefore not necessary, especially in light of endogenous acetamide in liver or eggs at up to 250 times higher concentration than from thiodicarb use".

Union Carbide indicated that recently samples of liver had been purchased from a retail market, analyzed for acetamide, and very high levels were present. Union Carbide concluded that such residues were due to naturally-occurring (endogenous) acetamide. Union Carbide stated that it had no other historical data on the purchased samples and, therefore, could not validly conclude that the acetamide residues were endogenous.

RCB indicated that when these data were submitted, an evaluation would be made, and conclusions could then be made. RCB made no agreements on the point of endogenous acetamide in the samples or on the need for additional feeding studies to test the analytical method on dosed tissue samples.

RCB concurs on the final three points cited below.

"EPA will accept recovery levels that are near the range established by FDA."

"EPA will accept 95% confidence limits for the analytical curve."

"EPA agrees with use of GCMS as a confirmatory method."

cc:R.F., Circu, Reviewer, TOX, EAB, EEB, PP#OF2413/OH5275
FDA, Robert Thompson
RDI:J. Onley:8/31/84:R. D. Schmitt:9/4/84
TS-769:RCB:CM#2:RM810:X7377:A Smith:wh:9/4/84

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