3-7-85

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

MAR 7 1985

EXPEDITE

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#0F2413/FAP#0H5275 and PP#3F2793/FAP#3H5378 [RCB Nos. 709, 710, 711, 712]. Thiodicarb (Larvin®) on Cotton and Soybeans. Evaluation of Amendment Dated February 26, 1985 (Accession Numbers 146057, 146058, 146059, 146060 - Recorded on RD Data Review Record Only).

FROM: Michael P. Firestone, Ph.D., Chemist
Tolerance Petition Section II
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Hazard Evaluation Division (TS-769)

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

TO: Jay S. Ellenberger, Product Manager No. 12
Insecticide-Rodenticide Branch
Registration Division (TS-767)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

Note: This review has been expedited per the request of Mr. Douglas D. Campt, Director of Registration Division (see memo of 2/28/85).

Introduction

Union Carbide Agricultural Products Company, Inc. has submitted this amendment, consisting of a discussion of the "acetamide in liver" method trial performed in part at Union Carbide's laboratory at Research Triangle Park (RTP), NC and all raw data and calculations used to generate data re: ubiquitous acetamide in milk and eggs, in response to issues raised in RCB's method trial evaluation (see M. Firestone memo of 1/29/85) and review of a 1/22/85 amendment (see M. Firestone memo of 2/4/85). These issues will be restated below followed by the petitioner's response and RCB's new evaluation/ conclusions.

Issue 1 - RCB Method Trial Evaluation (1/29/85 Memo)

Because of the very low recoveries at the 1.0 ppm fortification, RCB considers the method questionable for the determination of acetamide in liver.

Petitioner's Response

"The Registration (sic) Chemistry Branch (RCB) of the EPA submitted Union Carbide Agricultural Products Company's proposed method of analysis for acetamide in liver to the Analytical Chemistry Section (ACS) for validation. One set of samples was prepared by ACS which they were unable to analyze because of unavailability of the specified equipment. Therefore, the samples were brought to Union Carbide for analysis on its equipment by Union Carbide chemists. The raw data and GLC chromatograms were given by Union Carbide to ACS chemists. ACS complied its report and sent it to RCB for evaluation. RCB has reviewed the data and has expressed concern over the low recoveries obtained. The following comments are intended to clarify for RCB some of the reasons the recoveries were somewhat low. Samples used by EPA's Beltsville Laboratory in the validation of the ACETAMIDE-NPD-POULTRY LIVER method of analysis were of questionable value. Comments were written by Union Carbide chemists on the raw data sheets submitted to ACS. As noted on the raw data sheets, large quantities of gases (probably carbon dioxide) were dissolved in the samples. This most likely resulted from the samples being packed on dry ice for transport from Beltsville to RTP. Also, the samples had been diluted to 25 mL making them too dilute for GC analysis. The samples were allowed to warm at room temperature for several hours. They were then placed in an ultrasonic water bath to remove the dissolved gases. About five mL of the Reagent Blank Liver-1 sample was lost when the dissolved gases caused sudden eruption of the sample from the 25 mL volumetric flask. Twenty mL from each sample (all of the above reagent blank) were concentrated to 5 mL on a rotary evaporator at 30°C. The final effective analytical volume for each sample was 6.25 mL (25 ÷ 4). The method sensitivity was calculated from the lowest standard used: (0.1 ug/mL x 6.25 mL) ÷ (5g) = 0.12 ppm.

Additionally, only a single analytical run of the procedure was attempted by the Beltsville Lab. Analysis of a single set of recoveries by even the most competent residue laboratory rarely results in satisfactory data in the first attempt to test the procedure. This, in conjunction with the above mentioned problems with the samples, suggests that the low

recovers (sic) observed were not due to a flaw in the method, but rather in the method trial process. This is supported by the fact that the procedural standards were only 75% and 52% of nominal. It is surprising that the Beltsville Laboratory did not analyze an additional set of samples before reporting the results to RCB."

RCB's Comments/Conclusions

Based on the good recoveries obtained by the petitioner (average of 12 trials = 100%) for analysis of acetamide in beef and poultry liver (see M. Firestone review of 12/6/84), and the petitioner's account of the method trial's sample histories, RCB now considers the methods for analysis of acetamide in beef and poultry liver adequate. Issue 1 has been resolved.

Issue 2 - RCB Method Trial Evaluation (1/29/85 Memo)

Due to the determination of acetamide (0.07 ppm) in reagent blanks by EPA's chemists, RCB is unable to determine the validity of the data on endogenous or ubiquitous acetamide in animal commodities. The petitioner should submit raw data and calculations re: analysis of solvents (i.e., acetone) used for residue extraction.

Petitioner's Response

"The levels of 'acetamide' found in the reagent blank (acetone) from Beltsville by Union Carbide chemists are also of little values since they were part of the same set of sample discussed above. Since acetamide residue analyses have not previously been performed by the Beltsville Laboratory, there is no assurance that this 'acetamide' is not general laboratory contamination. Very high levels of acetamide have been found in reagent and pesticide grade acetonitriles in Union Carbide's laboratory. Therefore, caution must be observed when attempting to analyze for part per billion levels of acetamide in a residue laboratory where large amounts of acetonitrile are used. The procedures at RTP were carefully controlled by Union Carbide chemists to avoid such contamination."

RCB's Comments/Conclusions

Based on RCB's analysis of raw data and chromatograms (including GC-MS data/chromatograms) submitted in the current amendment, it is concluded that the Union Carbide data re: acetamide in animal commodities is not significantly affected by any minor acetamide contamination of solvents. Issue 2 has been resolved.

Issue 3 - RCB Method Trial Evaluation (1/29/85 Memo)

The method for analysis of acetonitrile in milk and egg whites is inadequate due to extremely high reagent blank and control values. Thus, the determination of acetonitrile as a marker compound for acetamide in milk and eggs is not acceptable under FDA's SOM Policy.

Petitioner's Response

Union Carbide is now requesting a waiver of the requirement for regulatory analytical methods for analysis of acetamide in milk and eggs under FDA's sensitivity of methods (SOM) policy, since likely maximum acetamide residues in milk and eggs resulting from thiodicarb use would be much lower than ubiquitous levels and also much lower than levels which would result in a cancer risk of 10^{-6}.

RCB's Comments/Conclusions

Since the petitioner is no longer requesting that acetonitrile be used as a marker compound for acetamide, RCB is no longer concerned with the inadequacy of the methods for determination of acetonitrile.

Issue From RCB's 2/4/85 Memo re: Amendment 1/22/85

Since discrepancies exist between the results reported in the 11/19/84 amendment and the raw data submitted in the current amendment, since reagent blanks should be run (GC-MS) on the acetone used for acetamide extraction, and since the history of the milk and egg samples is unknown (i.e., these samples were purchased at local grocery stores); RCB is unable to reach any conclusions regarding the existance of endogenous/ ubiquitous acetamide in animal commodities.

Petitioner's Response

All requested raw data and calculations have now been submitted in the current amendment.

RCB's Comments/Conclusions

The petitioner has fully responded to RCB's request for all raw data and calculations, and has explained how all raw data were corrected for recoveries and converted to the data submitted in an 11/19/84 amendment.

The data are not adequate to support the conclusion that acetamide is endogenous to (i.e., produced within) animals, due in part to a lack of documented sample histories. However, RCB can conclude that the data demonstrate that acetamide is ubiquitous in milk and eggs at average levels of approximately 400 ppb and 170 ppb, respectively.

RCB's Current Evaluation of Acetamide in Animal Commodities

1. RCB considers previously submitted methods adequate for the analysis of acetamide in animal commodities (beef and poultry liver).

2. Ubiquitous acetamide levels have been found to range from about 275 to 500 ppb in milk (average = 400 ppb) and 70 to 350 ppb in eggs (average = 170 ppb).

3. The following chart tabulates a comparison of maximum expected levels of secondary acetamide residues in animal commodities resulting from the proposed uses on cotton and soybeans, allowable residue levels (Sm) calculated by TOX per FDA's SOM policy (see C. Chaisson memo of 9/21/84), the petitioner's reported lowest limit of reliable measurement (LLRM), and average ubiquitous acetamide levels in milk and eggs:

	Acetamide Residue Level			
Target Tissue	Maximum Expected (ppm)	Sm (ppm)	LLRM (ppm)	Ubiquitous (ppm)
milk	0.0003	0.04	---	0.40
eggs	0.00001	0.11	---	0.17
cattle liver	0.0018	1.84	0.8	----
chicken liver	0.00006	0.65	0.4	----

4. The petitioner has satisfied all current RCB concerns at this time.

Recommendations

RCB continues to recommend for establishment of the following proposed thiodicarb tolerances on cotton, soybeans, and their processed fractions, if TOX and EAB considerations permit:

soybeans	0.2 ppm
soybean hulls	0.8 ppm
cottonseeds	0.2 ppm
cottonseed hulls	0.4 ppm

Other Considerations

An International Residue Limit Status sheet is attached. Since there are no Codex, Canadian, or Mexican tolerances/ limits for thiodicarb on cotton and soybeans, there are no compatibility problems.

cc:R.F., Circu, Reviewer, TOX, EAB, EEB, PP#0F2413/FAP#0H5275 PP#3F2793/FAP#3H5378, Robert Thompson, FDA, Don Marlow, Anne Barton
RDI:JHOnley:3/6/85:RDSchmitt:3/6/85

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL: thiodicarb

PETITION NO.: 0F2413/0H5275
3F2793/3H5378

CCPR NO.:

REVIEWER: Michael P. Firestone

F. Hoes 3/6/85

Codex Status

☑ No Codex Proposal Step 6 or above

Residue (if Step 9):

Proposed U.S. Tolerances

Residue: thiodicarb and its metabolite methomyl

Crop(s)	Limit (mg/kg)

Crop(s)	Tol. (ppm)
soybeans	0.2
soybean hulls	0.8
cottonseeds	0.2
cottonseed hulls	0.4

CANADIAN LIMIT

Residue:

Crop(s)	Limit (ppm)
none	

MEXICAN TOLERANCIA

Residue:

Crop(s)	Tolerancia (ppm)
none	

Notes:

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