11-6-90

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

NOV 6 1990

MEMORANDUM

SUBJECT: PP#4F3013/FAP#4H5421 (CBTS #6971). Thiodicarb on Tomatoes. Amendment dated 8/10/90 concerning a Tomato Processing Study. (MRID #40049101).

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THRU: Elizabeth Haeberer, Section Head Elizabeth Haeberer
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TO: Dennis Edwards, Product Manager #12
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A letter dated 8/10/90 and a tomato processing study dated 12/17/86 (MRID #40049101) have been forwarded to CBTS.

MRID #40049101 has been reviewed by CBTS previously (PP#4F3013/FAP4H5421, V.F. Boyd, 4/24/87).

Other previous reviews of PP#4F3013/FAP#4H5421 were dated 7/26/84 and 2/25/85 (both by V.F. Boyd).

Since several years have elapsed since the last CBTS review of thiodicarb on tomatoes and since petitions on other commodities which have been reviewed in the interim affect the status of the conclusions made in the original tomato review of PP#4F3013/FAP#4H5421 dated 7/26/84 (V.F. Boyd), CBTS herein repeats the deficiencies which were listed in the 7/26/84 review and indicates the current status of the issues.

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Conclusions

No additional information for CBTS review has been provided with the 8/10/90 submission. CBTS has summarized the current status of the deficiencies concerning tomatoes below. (Numbering of conclusions 1a-4c is consistent with CBTS's 7/26/84 review.)

1a. Acetamide has not been detected as a metabolite of thiodicarb in plants. Thiodicarb and its metabolite methomyl are the residues to be regulated in plants.

1b. The nature of the residue in ruminant tissues and milk has been adequately delineated. The residue consists of acetamide and acetonitrile, which are not currently regulated for thiodicarb uses.

"The Health Effects Division Peer Review Committee memorandum of May 29, 1990 states that the toxicity data available are inadequate to quantify the risk for acetamide and recommends that no new tolerances be established until certain toxicology studies have been satisfactorily completed. The Toxicology Branch decision on the safety of acetonitrile awaits the conclusion of ongoing oncogenicity studies by the National Toxicology Testing program."

2b. Since ^{14}C-thiodicarb metabolism studies on plants have indicated that acetamide is not a plant metabolite, acetamide is not included in the tolerance expression and, therefore, an enforcement method for acetamide on tomatoes is not needed.

2c. If TOX concludes that acetamide and acetonitrile need to be regulated in meat, milk, poultry and eggs, then validated analytical methods for acetamide and acetonitrile in animal products will be needed. A method validation by an independent laboratory and then an EPA method validation would be needed. Multiresidue method testing for acetamide and acetonitrile would also be needed.

3a. Current proposed labels for Larvin 80DF and Larvin 3.2 AF on tomatoes should be provided. These labels should include a 1-day preharvest interval for tomatoes.

3b. The tomato processing study dated 12/17/86 (MRID #40049101) was reviewed and found inadequate (PP#4F3013/FAP4H5421, V.F. Boyd, 4/24/87). Therefore, the deficiency #3b above remains outstanding until another processing study is provided. This requested processing study should process tomatoes containing weathered residues $\geq$3 ppm, which are distributed in the fruit as representative of the proposed use.

4a. Feeding studies on lactating cows and laying chickens are available. However, the residue levels of acetamide and

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acetonitrile in animal commodities cannot be determined until the residue level in dried tomato pomace is determined.

4c. CBTS continues to defer to Toxicology Branch on the toxicological significance of the metabolites acetamide and acetonitrile.

5. Thiodicarb and methomyl have been tested through FDA's multiresidue protocols. The petitioner's data was forwarded to FDA on July 25, 1989.

6. The following information is now required for residue studies. These issues were not discussed/specified in the Dec. 1983 submission (Accession #072237). Additional residue studies may be needed to fill the following data gaps:

a. Residue data are now required for both cherry tomatoes and large tomatoes. These data are needed because the difference in surface to volume ratio may affect residue levels.

b. Since the label allows both aerial and ground applications, residue data reflecting both aerial and ground applications are needed. [The application method was not specified in the 1983 submission (Accession #072237)]. Alternatively, the label could restrict the application method to ground or aerial application.

c. The type of application equipment used in field trials should be indicated. Commercial application equipment (ex. tractors and airplanes) should be used. Some trials may include application by back-pack sprayers provided sufficient data are available to show that residue levels are similar to those from commercial application equipment.

d. The maximum number of applications, the minimum interval between applications, and the maximum number of pounds active ingredient per acre per season should be stated on the labels. (These should all be supported by available residue data.)

e. The spray volume in gallons per acre should be provided for the residue studies in Accession #0722371 and for any additional studies which are conducted. Residue studies should reflect the minimum spray gallonage which is specified on the label for both ground and air applications.

f. Representative chromatograms of treated samples, controls, and recoveries which were obtained at the time of field trial sample analysis for the residue studies in Accession #0722371 should be submitted if available. Any additional residue or processing studies which are submitted should include such raw data.

Recommendations

CBTS continues to recommend against establishing the proposed 3 ppm thiodicarb tolerance on tomatoes for reasons given in Conclusions #1b, 2c, 3a, 3b, 4a, 4c and 6 (a through f) above.

Besides Subdivision O of the Pesticide Assessment Guidelines, CBTS recommends that the petitioner refer to the following 1985-1988 EPA publications concerning processing studies and residue studies which are available from the National Technical Information Service (NTIS):

	NTIS #
Addendum 4 on Data Reporting	PB88-117270
HED's Standard Evaluation Procedure, Magnitude of the Residue: Processed Food/Feed Studies	PB88-243209
Addendum 2 on Data Reporting	PB86-248192
HED's Standard Evaluation Procedure, Magnitude of the Residue: Crop Field Trials	PB86-129426

Although not required, CBTS recommends that protocols be submitted to CBTS for review before any additional studies are begun.

DETAILED CONSIDERATIONS

CBTS repeats the deficiencies which were listed in the 7/26/84 review and indicates the current status of the issues below:

CBTS's Deficiency #1a

"The major residues of concern for thiodicarb on plants have been considered to be thiodicarb, per se, methomyl and methomyl oxime. It has recently come to our attention, however, that the carcinogen, acetamide, may also be a metabolite. Residue data for acetamide on tomatoes are needed."

CBTS's Conclusion #1a

In reply to a TOX memo of 10/22/87, CBTS stated that acetamide has not been detected as a metabolite of thiodicarb in plants (PP#7F3516, M.J. Nelson, 6/7/88). Thiodicarb and its metabolite methomyl are the residues to be regulated in plants. (See PP#7F3526/FAP#7H5538, J. Stokes, 1/12/88.)

Deficiency #1a is resolved.

CBTS's Deficiency #1b

"In livestock and poultry, the metabolic pathway would include residues of thiodicarb, methomyl, methomyl oxime, acetamide and acetonitrile. TOX has expressed concern over residues of acetamide and acetonitrile in meat, milk, poultry and eggs.

CBTS defers to the Toxicology Branch on the toxicological significance of acetamide and acetonitrile in these commodities and their need to be regulated."

CBTS's Conclusion #1b

As stated in PP#OF3833 (M. Bradley, 7/2/90), "the nature of the residue in ruminant tissues and milk has been adequately delineated. The residue consists of acetamide and acetonitrile which are not currently regulated for thiodicarb uses."

"The Health Effects Division Peer Review Committee memorandum of May 29, 1990 states that the toxicity data available are inadequate to quantify the risk for acetamide and recommends that no new tolerances be established until certain toxicology studies have been satisfactorily completed. The Toxicology Branch decision on the safety of acetonitrile awaits the conclusion of ongoing oncogenicity studies by the National Toxicology Testing program."

CBTS's Deficiency #2b

"A validated analytical method is needed for the determination of residues of acetamide in/on tomatoes."

CBTS's Conclusion 2b

Since ^{14}C-thiodicarb metabolism studies on plants have indicated that acetamide is not a plant metabolite, acetamide is not included in the tolerance expression and, therefore, an enforcement method for acetamide on tomatoes is not needed.

Deficiency #2b is resolved.

CBTS's Deficiency #2c

"If TOX concludes that acetamide and acetonitrile need to be regulated in meat, milk, poultry and eggs, then validated analytical methods will be needed for animal products."

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CBTS's Conclusion #2c

Deficiency #2c remains outstanding.

If TOX concludes that acetamide and acetonitrile need to be regulated in meat, milk, poultry and eggs, then validated analytical methods for acetamide and acetonitrile in animal products will be needed. A method validation by an independent laboratory and then an EPA method validation would be needed. Multiresidue method testing for acetamide and acetonitrile would also be needed.

CBTS's Deficiency #3a

"Residues of thiodicarb, methomyl and methomyl oxime in tomatoes are not expected to exceed the proposed tolerance of 3.0 ppm, under the proposed conditions of use, provided a 1-day PHI is imposed on the label. (This is the shortest interval for which there is residue data.)"

CBTS Conclusion #3a

Current proposed labels for Larvin 80DF and Larvin 3.2 AF on tomatoes should be provided. These labels should include a 1-day preharvest interval for tomatoes.

CBTS's Deficiency #3b

"The adequacy of the food additive tolerance of 5.0 ppm for tomatoes paste, as proposed, cannot be substantiated by the processing study because of the low residue level (0.13 ppm) in the tomatoes used for processing. A study using tomatoes containing residues at or near the proposed 3.0 ppm level is required. Analysis should be conducted for paste, puree, catsup and dried pomace."

CBTS's Conclusion #3b

The tomato processing study dated 12/17/86 (MRID #40049101) was reviewed and found inadequate (PP#4F3013/FAP4H5421, V.F. Boyd, 4/24/87). Therefore, the deficiency #3b above remains outstanding until another processing study is provided. This requested processing study should process tomatoes containing weathered residues $\geq$3 ppm, which are distributed in the fruit as representative of the proposed use.

CBTS's Deficiency #4a

CBTS is withholding its conclusions with respect to residues in meat and milk until the questions raised in Conclusion 3b above are resolved.

CBTS's Discussion #4a

Feeding studies on lactating cows and laying chickens are available (PP#0F2413/FAP#0H5275, Al Smith, 1/21/81; PP#7F3526/FAP#7H5538, reviews by J. Stokes dated 1/12/88 and W.T. Chin dated 3/16/89).

CBTS's Conclusion #4a

Deficiency #4a remains outstanding.

Feeding studies on lactating cows and laying chickens are available. However, the residue levels of acetamide and acetonitrile in animal commodities cannot be determined until the residue level in dried tomato pomace is determined.

CBTS's Deficiency #4c

"The metabolites of thiodicarb will occur in meat and milk. CBTS defers to TOX on the toxicological significance of the metabolites, acetamide and acetonitrile. Their estimated levels in meat and milk cannot be determined at this time but will be based on the residue level in dried tomato pomace. (See Conclusion 3b above.)"

CBTS's Conclusion #4c

CBTS continues to defer to Toxicology Branch concerning the toxicological significance of the metabolites acetamide and acetonitrile.

Other Considerations

A. As stated by CBTS in connection with PP#0F3833 (M.J. Bradley, 7/2/90), thiodicarb and methomyl have been tested through FDA's multiresidue protocols. The petitioner's data was forwarded to FDA on July 25, 1989.

B. The following information is now required for residue studies. These issues were not discussed/specified in the Dec. 1983 submission (Accession #072237). Additional residue studies may be needed to fill the following data gaps:

a. Residue data are now required for both cherry tomatoes and large tomatoes. These data are needed because the difference in surface to volume ratio may affect residue levels.

b. Since the label allows both aerial and ground applications, residue data reflecting both aerial and ground applications are needed. [The application method was not specified in the 1983 submission (Accession #072237)]. Alternatively, the label could

restrict the application method to ground or aerial application, depending upon the mode of application in the field studies.

c. The type of application equipment used in field trials should be indicated. Commercial application equipment (ex. tractors and airplanes) should be used. Some trials may include application by back-pack sprayers provided sufficient data are available to show that residue levels are similar to those from commercial application equipment.

d. The maximum number of applications, the minimum interval between applications, and the maximum number of pounds active ingredient per acre per season should be stated on the labels. (These should all be supported by available residue data.)

e. The spray volume in gallons per acre should be provided for the residue studies in Accession #0722371 and for any additional studies which are conducted. Residue studies should include studies which use the minimum spray gallonage which is specified on the label for both ground and air applications.

f. Representative chromatograms of treated samples, controls, and recoveries which were obtained at the time of field trial sample analysis for the residue studies in Accession #0722371 should be submitted if available. Any additional residue or processing studies which are submitted should include such raw data.

cc: RF, SF, PP#4F3013/FAP4H5421, Circu(6), N.Dodd(CBTS), E. Haeberer (CBTS), PIB/FOD (Furlow), R.D. Schmitt

H7509C:CBTS:CM#2:Rm800D:X1681:N.Dodd:nd:11/06/90
RDI:E. Haeberer:11/05/90:R.Loranger:11/06/90