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

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: PP#7F3560/7H5543, PP#1F3952/1H5607, FAP#0H5599, PP#1F03985. Lambda-Cyhalothrin. Tolerance Petitions For Residues In Or On Various Raw Agricultural and Processed Commodities. Toxicology Branch Analysis of Residues of Concern.

Tox. Chem. No. 725C

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Health Effects Division (H7509C)

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Pamela M. Hurley 11/11/91

THRU: Roger L. Gardner, Section Head
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Roger Gardner 11/13/91

Background and Request:

The Chemistry Branch I has requested that the Toxicology Branch I (TB-I) examine the available residue data on lambda-cyhalothrin and its metabolites in a variety of raw commodities and determine from a toxicological standpoint if there are any residues of concern which should be included in the tolerance expression. The raw commodities are those for which tolerances have been requested by the Registrant and include: head lettuce, sweet corn forage, sweet corn, broccoli, cabbage, tomatoes, meat, milk, eggs, poultry and dried hops. The metabolites which are to be considered by TB-I include cis-PP890 (CPA), trans-PP890, 3-PB Acid and 3-PB alcohol. The structures of these metabolites are given at the end of this memorandum.

Toxicology Branch Response:

Conclusion:

Due to lack of testing data, the Toxicology Branch (TB-I) examined the above listed metabolites for potential toxicological concern on the basis of structure-activity comparisons. TB-I has a potential concern for the 3-PB-alcohol and suggests that it be

listed in the tolerance expression. For the other metabolites in the raw commodities listed above, TB-I was not able to support a concern from a toxicological standpoint. In the past, when no toxicology data are available on the metabolites, TB-I has suggested metabolites that are to be listed in the tolerance expression on the basis of quantity. The following paragraphs discuss our conclusions and provide the general "rule of thumb" that TB-I has used for determining which metabolites are to be listed. Using this method, both PP890 and the 3-PB acid could be included in the tolerance expression, although the 3-PB acid is borderline.

The Toxicology Branch has examined the above listed metabolites from a potential toxicological standpoint. To our knowledge, there are no actual toxicological data any of these metabolites. Therefore, we examined them on the basis of structure-activity considerations (i.e. we compared them to other compounds of similar structure for which testing data are available).

The parent compound is similar to other pyrethroids for which data are available. However, since the parent compound is already being included in the tolerance expression, TB-I will not consider it in this memorandum.

To our knowledge, no actual toxicological data are available on metabolites of other pyrethroids that are registered with OPP. Therefore, no comparisons could be conducted with OPP data. TB-I accordingly searched sources outside of OPP for a possible SAR analysis. Again, there was no testing data on structural analogues of either CPA or trans-PP890 for which an SAR anaysis could be conducted. One paper based on quantum mechanical considerations indicates that if the double bond between the trifluoro-chloro carbon could be epoxidized, then the compound may be carcinogenic. However, there are no data indicating that these two metabolites can be epoxidized.

There were no testing data available on structural analogues of 3-PB acid. For the 3-phenoxybenzyl alcohol (3-PB alcohol), it was suggested that if this could be oxidized to 3-phenoxy benzaldehyde (the C-OH to a CH=O), then there is some evidence (an available NTP bioassay on mice) that it may be a weak carcinogen. On the basis of this data and on the possibility that this metabolite may be further oxidized by the body to the benzaldehyde, TB-I suggests that the 3-PB alcohol be added to the tolerance expression.

In the past, when no toxicology data are available on metabolites, TB-I has suggested metabolites that are to be listed in the tolerance expression on the basis of quantity. As a general "rule of thumb", TB has not included metabolites in the tolerance expression if the requested tolerance is 0.1 ppm or

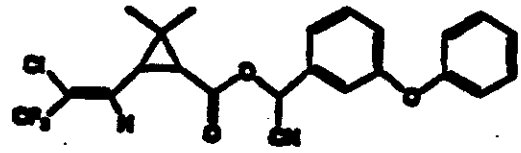
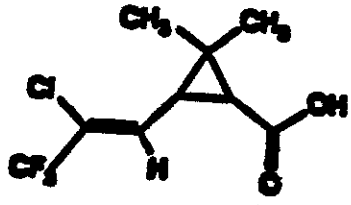
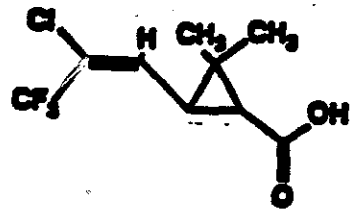
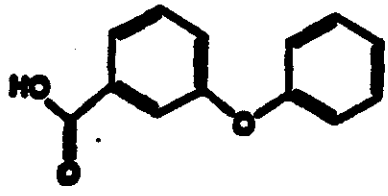
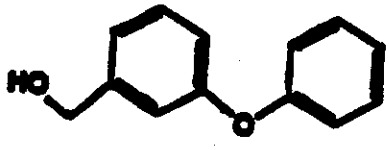
less and if the amount of the metabolite residue is less than 10% of the total residue in the commodity. For example, suppose one wanted to determine whether or not PP890 should be used in the tolerance expression for lettuce. Without other data, one could use Table I from the memorandum from Morales to LaRocca, dated 10/22/91 (Residues of Lambda-cyhalothrin and metabolites in Head Lettuce...) to make the calculations. The requested tolerance is for 2.0 ppm in lettuce. Already the first rule is satisfied for including PP890 in the tolerance expression - 2.0 ppm is greater than 0.1 ppm. In using the table in this memorandum, unless other data are available, one has to assume that the total residue in the commodity is the sum of all the residues of parent and metabolites in that commodity for that trial. For PP890, if one picks Arizona using the EC and New Jersey using the EC, one would do the following calculations:

Arizona: 0.68 + 0.09 + 0.25 + 0.07 = 1.09 ppm total residue in lettuce (all residue values added together for Arizona). 0.25 (residue for PP890) divided by 1.09 = .229 or 22.9% of the total residue. Since recovery data indicated that the recovery of the parent compound was 84-86% for a spiked sample, one may wish to include that in the calculation. The result would be 20% of the total residue. Therefore, in this case, TB-I would include PP890 in the tolerance expression.

New Jersey: 1.10 + 0.10 + 0.19 + 0.09 = 1.48 total residue. 1.48 divided by 0.19 = .128 or 12.8% of the total residue. PP890 would be included in the tolerance expression.

The preceeding calculations are to be considered to be rough estimates. In past actions, the calculations have been reconsidered using more accurate data when available.

Attachment 1.

Names	Structure
PP321 ICIA0321 Lambda-cyhalothrin	
Compound Ia cis-PP890 (CPA) cis-1-RS-3-(ZE-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid	
Compound Ib trans-PP890 trans-1RS-3-(ZE-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid	
3-PB Acid 3-phenoxybenzoic acid	
3-PB Alcohol 3-phenoxybenzyl alcohol	

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Chemical:	**Cyclopropanecarboxylic acid, 3-(2-chloro**
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