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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **PP#7F3560/7H5543.** Lambda-cyhalothrin in/on Wheat, Sweet Corn and Sunflowers.

PP#1F3952/1H5607. Lambda-cyhalothrin in/on Broccoli, Cabbage and Tomatoes.

FAP#0H5599. Lambda-cyhalothrin in/on Imported Dried Hops.

PP#9F3770. Lambda-cyhalothrin for Dermal Application to Beef Cattle.

DP Barcodes: D173946-D173950, D173956-D173957.
CBTS#'s 9317 through 9323.
MRID #'s 421723-01 through 421723-08, 421823-01, 41823-02.

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Introduction

The present submission is ICI's response to our reviews dated 9/19/91 and 4/17/91 (for dermal application). A large part of this submission has already been reviewed under a concurrent submission for FAP#0H5599. That review (expedited), dated 3/23/92, should be consulted.

1/12

Conclusions (including those from our 3/23/92 memo for FAP#0H5599)

1a. The correct Chemical Abstracts name for lambda-cyhalothrin is [1α(S*),3α(Z)]-(±)-cyano(3-phenoxyphenyl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate. The correct Chemical Abstracts name for the epimer of lambda-cyhalothrin is [1α(R*),3α(Z)]-(±)-cyano(3-phenoxyphenyl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate.

1b. CBTS recommends that the IUPAC names for lambda-cyhalothrin and its epimer -- rather than the Chemical Abstract names -- appear in the regulation. In our opinion, a practicing chemist can more readily relate the IUPAC name to the structure.

The IUPAC name for lambda-cyhalothrin is --

A 1:1 mixture of

(S)-α-cyano-3-phenoxybenzyl-(Z)-(1R,3R)-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate

and

(R)-α-cyano-3-phenoxybenzyl-(Z)-(1S,3S)-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate

The IUPAC name for the epimer of lambda-cyhalothrin is a 1:1 mixture of the (S,S,S) and (R,R,R) isomers.

[Conclusions 1a and 1b from our 3/23/92 memo, as modified in our 4/7/92 memo for FAP#0H5599.] The registrant has changed the proposed nomenclature according to our recommendation.

2a. The nature of the residue in plants is adequately understood. The residue to be regulated is lambda-cyhalothrin and its epimer.

2b. The nature of the residue in ruminants and poultry is adequately understood. The residue to be regulated will include lambda-cyhalothrin and its epimer. However, the ruminant and poultry metabolite 3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2-hydroxymethyl-2-methylcyclopropanecarboxylic acid (HO-CPA) was not

analyzed in the urine or feces of rat, although studies on similar compounds imply that HO-CPA should be a rat metabolite. A residue transfer study in which lambda-cyhalothrin was fed to beef cattle and tissue of liver and kidney analyzed for HO-CPA has been completed, but a final report has not been submitted. If residues of the metabolite in beef are found only at low levels, it may not be necessary to include this metabolite in the tolerance expression.

3a. ICI Method 81 for residues of lambda-cyhalothrin, per se, in plant matrices and Method 86 for these residues in animal matrices have undergone successful EPA method validation. Because of similar structure, there is no need for EPA validation of these methods for the epimer.

3b. Should it be necessary to include HO-CPA in the tolerance expression, the analytical method for this compound must undergo independent lab validation and EPA lab validation.

4. Recoveries have been determined for cyhalothrin (which consists of lambda-cyhalothrin and its epimer), and metabolites CPA and 3-PBAcid under FDA's multiresidue protocols. Reports of recoveries of 3-PBAlcohol and 4'-OH-3-PBAcid have been submitted and are being forwarded to FDA. Because the regulatory status of HO-CPA is uncertain at this time, recovery data for this metabolite may be required.

5. Storage stability data for lambda-cyhalothrin support the residue analyses in plant and animal matrices. Storage stability data for CPA, 3-PBAcid and 3-PBAlcohol are being developed. Storage stability data for lambda-cyhalothrin, epimer and metabolites is available for four months, and the current study is being extended. To completely support the submitted residue analyses, storage stability of metabolites needs to be demonstrated for periods up to two years. Similarly, forthcoming residue analyses for HO-CPA must be supported by storage stability data.

6a. ICI has proposed tolerances of 5.0 ppm for residues of lambda-cyhalothrin in/on corn forage and 0.05 ppm for these residues in/on sweet corn (K + CWHR). A revised Section F should be submitted in which respective tolerances of 6.0 ppm and 0.05 ppm are proposed for the combined residues of lambda-cyhalothrin and its epimer.

6b. The proposed tolerance of 0.4 ppm for residues of lambda-cyhalothrin in/on broccoli is appropriate, but

3

ICI should submit a revised Section F in which the epimer is included in the tolerance expression. The numerical value of the tolerance need not be changed.

6c. ICI has proposed a tolerance of 0.4 ppm for residues of lambda-cyhalothrin in/on cabbage. A revised Section F should be submitted in which the epimer is included in the tolerance expression. The numerical value of the tolerance need not be changed.

6d. ICI has proposed a tolerance of 0.1 ppm for residues of lambda-cyhalothrin in/on tomatoes. A revised Section F should be submitted in which the epimer is included in the tolerance expression. The numerical value of the tolerance need not be changed.

Based on the determined concentration factor, ICI should submit a revised Section F in which a feed additive tolerance of 6.0 ppm is proposed for residues of lambda-cyhalothrin and its epimer.

7. ICI should submit a revised Section F in which the following tolerances for the combined residues of lambda-cyhalothrin and its epimer are proposed:

Meat and mbyp of cattle, goats, hogs, horses and sheep	0.2 ppm
Fat of cattle, goats, hogs, horses, and sheep	4.0 ppm
Meat, fat, mbyp and eggs of poultry	0.01 ppm
Milkfat (reflecting 0.2 ppm in whole milk)	5.0 ppm

Recommendation

CBTS recommends against the proposed tolerances for reasons given in Conclusions 3b, 4, 5 (status of HO-CPA); 5 (storage stability of metabolites); 6a, 6b, 6c, 6d, 7 (revised Section F).

Detailed Considerations

Most of ICI's responses to deficiencies listed in our 9/19/91 memo were reviewed in our concurrent memo for FAP#0H5599. In this memo we list only those deficiencies that either were not relevant to the petition for hops or were addressed but not completely resolved.

CBTS Deficiencies #4e, 5d, 10c (Conclusions 4e, 5d, and 10c from our 9/19/91 memo)

4

These deficiencies relate to the need for an analytical method, storage stability, and residue data for the animal metabolite HO-CPA. In an internal meeting held 4/11/91, CBTS and TB1 decided that unless the registrant could show that HO-CPA was a rat metabolite, residue data on this metabolite and a validated analytical method would be needed before a final decision could be made whether or not this metabolite should appear in the tolerance expression.

ICI Response and CBTS Comment

ICI's response was reviewed in our memo of 3/92. Our review of submitted articles showed that the hydroxymethyl cyclopropane analogues from permethrin and tefluthrin are rat metabolites. The cyclopropanecarboxylic acid moiety of tefluthrin is identical to that for lambda-cyhalothrin. We also stated that there was no direct analytical evidence that the hydroxymethylcyclopropane carboxylic acid was a rat metabolite of lambda-cyhalothrin.

Preliminary results from a residue transfer study in which beef liver and kidney were analyzed for HO-CPA indicate that levels of that metabolite do not exceed 0.01 ppm when cows were orally dosed with 8 ppm lambda-cyhalothrin -- the highest predicted level in the diet from all proposed uses.

In our 3/92 memo, we concluded that for purposes of FAP#0H5599, complete residue data on this metabolite would not be necessary because of the likelihood that levels resulting would be nondetectable in cattle tissue. The predicted concentration of lambda-cyhalothrin in the diet of cattle was only 0.05 ppm. We did conclude that our evaluation of the other pending petitions would not be complete before the relevant residue transfer study is reviewed. Therefore, these deficiencies remain for all pending petitions except PP#0H5599.

CBTS Deficiency #4f

Depending on the regulatory status of 4'-OH-3-PBAcid and HO-CPA, multiresidue testing of these compounds may be necessary.

ICI Response

Enclosed as ICI Volumes 121 and 122 are reports of the multiresidue testing for the following lambda-cyhalothrin metabolites: 4'-OH-3-phenoxybenzoic acid and 3-phenoxybenzyl alcohol (MRID #'s 421723-02, 421723-03).

CBTS Comment

These reports are being forwarded to FDA for evaluation. We note that CBTS and CB1 have determined that neither of the two

metabolites tested must appear in the tolerance expression for lambda-cyhalothrin. As noted above, the status of HO-CPA remains uncertain. Therefore, this deficiency remains.

CBTS Deficiency #5b

> CPA, 3-PBAcid and 3-PBAlcohol in various racs are stable for 3 months under frozen storage. This time period is insufficient to support the residue analyses; but, presumably, additional data will be reported at a later date.

ICI Response

Data to support storage stability of CPA[PP890], 3-PBAcid and 3-PBAlcohol in various racs are being developed. It is anticipated that 24-month storage data will be submitted during early 1992.

Two reports concerning the storage stability of lambda-cyhalothrin and metabolites in processed commodities have been submitted:

> "Interim Report on Storage Stability of ICIA0321 and R157836 in Processed Commodities;" P.S. Gillespie; October 4, 1991; ICI Western Research Center, Richmond, CA; Laboratory Study No. 0321-90-SS-01; Report No. RR 91-044B. (MRID # 421723-04)
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> "Interim Report on Storage Stability of Pyrethroid Metabolites in Processed Commodities;" P.S. Gillespie; October 24, 1991; ICI Western Reseach Center, Richmond, CA; Laboratory Study No. PYRE-90-SS-01; Report No. RR 91-043B. (MRID # 421723-05)

The first of these reports is a study of the stability of lambda-cyhalothrin and its epimer during storage at -20°C±10°C in the following commodities: dry apple pomace, sorghum flour, tomato juice, refined soybean oil, corn soapstock and sorghum starch. Samples were fortified at 0.10 µg/g with 91.1% pure cyhalothrin, which consists of 43.2% lambda-cyhalothrin and 56.8% epimer. Analysis of the commodities was by ICI Method 81, described in our 9/19/91 memo, with one exception. Soapstock was extracted by homogenization with acetone/water/conc. HCl. The solution was extracted with dichloromethane and the extract dried with sodium sulfate. The rest of the procedure is identical to that for the other analyses.

Over a four month period, lambda-cyhalothrin and epimer levels did not significantly change.

The second of these reports is a study of the stability of

b

PP890 (CPA), 3-PBAcid, 3-PBAlcohol and DCVA in the same commodities, excluding corn soapstock. DCVA is a metabolite of permethrin. All samples were fortified at 0.10 µg/g. Analysis was by a method similar to the analyses described in our 9/19/91 memo except that a reflux step using 2N HCl was omitted.

Over a four month period, none of the metabolite levels significantly changed.

CBTS Comment

The interim one-year report was submitted in PP#2F4100 (for dried bulb onions and garlic) and reviewed in our 3/92 memo for PP#0H5599. We concluded that although some decline was observed, the data supported the six month residue analyses on hops. We can also conclude that these data would support residue analyses in general for periods up to 12 months. However, stability up to two years must be demonstrated to support all the residue analyses on crops other than hops. Presumably, storage stability in processed commodities for periods longer than four months will be reported later.

This deficiency remains.

CBTS Deficiency #6

> Based on submitted data, proposed lambda-cyhalothrin tolerances of 0.02 ppm for sweet corn ears (i.e., sweet K + CWHR) and 6.0 ppm for sweet corn forage are adequate. However, because of analytical uncertainties at low levels, a tolerance of 0.05 ppm would be more appropriate for sweet corn (K + CWHR). (The tolerance should not be expressed as sweet corn ears.) The petitioner should submit a revised Section F in which this tolerance is proposed. CB and TOX will decide whether tolerances are necessary for metabolites and the epimer of lambda-cyhalothrin.

ICI Response

ICI has submitted a revised Section F in which the tolerance for sweet corn forage is proposed as 5.0 ppm and that for corn, sweet (K+CWHR) is proposed as 0.05 ppm.

CBTS Comment

As noted in our 3/92 memo, the tolerance expression must be for the combined residues of lambda-cyhalothrin, per se, and its epimer. Although a tolerance of 5.0 ppm would be appropriate for

lambda-cyhalothrin alone it is inadequate for the combined residues, for which a tolerance of 6.0 ppm is appropriate. ICI should submit a revised Section F in which this tolerance is proposed for the combined residues of parent and epimer. This deficiency remains.

CBTS and TB1 have decided that only parent and epimer need appear in the tolerance expression (see 1/3/92 memo from P. Hurley, PP#7F3560/7H5543).

CBTS Deficiency #7a

The proposed tolerance of 0.4 ppm for residues of lambda-cyhalothrin in/on broccoli is appropriate. Because no data reflecting aerial application have been submitted, the petitioner must either revise the use label or submit additional residue data from aerial application.

ICI Response

As noted in the Robert S. Quick's memo to Rick Holt dated December 6, 1991, the Agency's policy regarding the requirement for aerial data has changed... A copy of revised use directions for all pending uses of lambda-cyhalothrin will be submitted shortly. The revised directions will include the requirement for a minimum of 2 gallons per acre for aerial applications.

CBTS Comment

This deficiency is resolved pending change of the use label. However, as noted above the epimer must now appear in the tolerance expression. (This will not change the value of the tolerance.)

CBTS Deficiency #7b

The proposed tolerance of 0.4 ppm for residues of lambda-cyhalothrin in/on cabbage is appropriate. The rac is cabbage with wrapper leaves....

A revised Section F should be submitted for "cabbage" at 0.4 ppm. Any reference to wrapper leaves should be deleted.

Because no data reflecting aerial application have been submitted, the petitioner must either revise the use label or submit additional residue data from aerial application.

8

ICI Response

The revised Section F has been submitted. The same comment is made concerning aerial application.

CBTS Comment

This deficiency is resolved pending change of the use label. The tolerance expression must be revised to include epimer. (This will not change the value of the tolerance.)

CBTS Deficiency #7c

The proposed tolerance of 0.06 ppm for residues of parent in/on tomatoes is adequate, but to allow for analytical uncertainties at low levels we consider a tolerance of 0.1 ppm to be more appropriate. A revised Section F should be submitted in which this tolerance is proposed.

Because no data reflecting aerial application have been submitted, the petitioner must either revised the use label or submit additional residue data from aerial application.

ICI Response

The requested revised Section F has been submitted. The comment regarding aerial application is identical to those above.

CBTS Comment

This deficiency is resolved pending change of the use label. The tolerance expression must be revised to include epimer. (This will not change the value of the tolerance.)

CBTS Deficiency #7d

CB and TOX will decide whether or not metabolites and/or the epimer should be included in the tolerance expression. A separate memo will be forthcoming.

ICI Response

No response

CBTS Comment

As noted above, metabolites need not appear in the tolerance expression. (The question of HO-CPA remains unresolved at this time.) In a meeting dated 10/31/91, CBTS and TB1 agreed that the epimer be included in the tolerance expression.

9

CBTS Deficiency #9

A processing study on tomatoes indicates concentration in wet and dry pomace. Based on the concentration factors and a tolerance of 0.1 ppm for tomatoes, the registrant should submit a revised Section F in which a feed additive tolerance of 6.0 ppm is proposed for residues of lambda-cyhalothrin in/on tomato pomace, wet or dry. As noted above, metabolites may have to be included in the tolerance expression.

ICI Response

ICI proposes to establish a tolerance of 4 ppm rather than 6 ppm for dried tomato pomace. Even though the tolerance is 0.1 ppm, ICI's analytical method can clearly distinguish between 0.1 ppm and 0.06 ppm [see earlier comment]. Application of the concentration factor of 54 to 0.06 ppm would lead to a tolerance of 4 ppm.

CBTS Comment

For tolerance setting purposes our policy is to apply concentration factors to the tolerance. Therefore, the appropriate tolerance is 6 ppm. We note that for anticipated residue calculations, current practice is to apply the average concentration factor to the average residue to determine the anticipated residue for the processed product.

A revised Section F of 6.0 ppm for residues of lambda-cyhalothrin and its epimer in/on tomato pomace should be submitted. This deficiency remains.

CBTS Deficiency #10a

Based on results from ruminant and poultry feeding studies, ICI should submit a revised Section F in which the following tolerances for lambda-cyhalothrin are proposed:

Milk, meat and mbyp of cattle, goats, hogs, horses and sheep	0.2 ppm
Fat of cattle, goats, hogs, horses and sheep	4.0 ppm
Meat, fat, mbyp and eggs of poultry	0.01 ppm

CBTS Deficiency #10b

Because lambda-cyhalothrin -- as other pyrethroids --

concentrates in fat, data are necessary to show concentration of residues in the fat of milk.... Based on the concentration factor, an appropriate tolerance for lambda-cyhalothrin in milk fat should be proposed.

ICI Response and CBTS Comment

These deficiencies with ICI's response were addressed in our 3/92 memo for FAP#0H5599.

ICI has submitted a revised Section F in which the following tolerances are proposed:

Milk, fat (reflecting 0.1 ppm in whole milk)	3	ppm
Meat and mbyp of cattle, goats, hogs, horses and sheep	0.2	ppm
Fat of cattle, goats, hogs, horses and sheep	3	ppm
Meat, fat, mbyp and eggs of poultry	0.01	ppm

As noted in our 3/92 memo, ICI's proposed tolerances were calculated by using maximum measured residue values instead of tolerance values for proposed worst case diets. The tolerance of 3 ppm for milkfat was determined assuming that 3% of whole milk is fat and all the pesticide concentrates in the fat. In our memo we discussed the notion of tolerances versus anticipated residues. Tolerances for animal commodities are obtained from a diet in which commodities have pesticide residues at their tolerances. The assumption that all lambda-cyhalothrin concentrates in the fat of milk is valid, however CBTS routinely assumes that 4% of whole milk is fat. Therefore, appropriate tolerances are the following:

Meat and mbyp of cattle, goats, hogs, horses and sheep	0.2	ppm
Fat of cattle, goats, hogs, horses and sheep	4.0	ppm
Meat, fat, mbyp and eggs of poultry	0.01	ppm
Milkfat (reflecting 0.2 ppm in whole milk)	5.0	ppm

As noted in our 3/92 memo, the tolerances for meat products of cattle include a contribution from dermal use of lambda-cyhalothrin. If fat of cattle were separated from fat of the other animals, a tolerance of 3.0 ppm could be proposed for residues in goats, hogs, horses and sheep. For simplicity we recommend that one tolerance of 4.0 ppm be established for fat; however, a tolerance of 4.0 ppm for the fat of cattle and 3.0 ppm

for the fat of the other animals would be acceptable. (In calculations of anticipated residues this separation would be taken into account.)

The petitioner should submit a revised Section F in which the above tolerances are proposed.

Other Considerations

The nomenclature for lambda-cyhalothrin has been discussed in detail in our concurrent memo for FAP#0H5599. We concluded that the CAS name is now known to be correct but that the IUPAC name for lambda-cyhalothrin appear in the regulation. The IUPAC name for lambda-cyhalothrin is --

A 1:1 mixture of

(S)-α-cyano-3-phenoxybenzyl-(Z)-(1R,3R)-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate

and

(R)-α-cyano-3-phenoxybenzyl-(Z)-(1S,3S)-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate

The IUPAC name for the epimer of lambda-cyhalothrin is a 1:1 mixture of the (S,S,S) and (R,R,R) isomers.

Both lambda-cyhalothrin, per se, and its epimer should appear in the tolerance expression.

cc: SF, RF, Circu., C.Furlow(PIB/FOD), Mike Flood, E.Haeberer, PP#7F3560/7H5543, PP#1F3952/1H5607, FAP#0H5599.

H7509C:CBTS:Reviewer(MTF):CM#2:Rm800A:305-6362:typist(mtf):4/8/92.
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