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

OCT 22 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: **PP#1F03985.** Lambda-cyhalothrin. Tolerance Petition for Residues In or On Head Lettuce. Evaluation of Residue Data. MRID #'s 418639-00, -01, -02. DEB # 7998. DP Barcode D164464. HED # 1-1276.

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THROUGH: Robert S. Quick, Acting Chief
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TO: G. LaRocca/A. Heyward, PM 15
Insecticide-Rodenticide Branch
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and
Toxicology Branch I
Health Effects Division (H7505C)

ICI Agricultural Products is requesting the establishment of tolerances for Lambda-cyhalothrin in Head Lettuce, at 2.0 ppm with wrapper leaves and 0.3 ppm without wrapper leaves. Tolerances are established for parent Lambda-cyhalothrin [1alpha-(S), 3alpha(Z)]-(+)-cyano-(3-phenoxyphenyl)methyl-3-(2-dimethylcyclopropanecarboxylate) on corn, cottonseed, wheat grain, soybeans and sunflower seeds at levels ranging from 0.01 to 0.05 ppm (40 CFR 180.438). Tolerances with an expiration date of August 30, 1991, are also established for the fat and meat of cattle, goats, hogs, horses and sheep at 0.01 ppm and for milk at 0.01 ppm in 40 CFR 180.438.

CONCLUSIONS

1. The manufacturing process for technical grade of lambda-cyhalothrin has been adequately described. However, the WG formulation has not been registered by RD. Confirmation from the Chemical Abstract Service that the proposed CAS name given to lambda-cyhalothrin, is the correct one, is needed.

2. The residue data do not adequately reflect the proposed use. Because there are no residue data for aerial application submitted, the petitioner must either revise the use label restricting use to ground application only or submit additional residue data for aerial application.

3a. The nature of the residue in lettuce is adequately defined. However, a conclusion on the residue(s) of concern, is deferred pending consultation with TOX Branch as to the toxicological significance of the identified residues.

3b. Since lettuce is not a significant livestock feed item, there is no concern for livestock metabolism and feeding studies in this petition.

4. ICI method 81 for lambda-cyhalothrin in plant matrices has undergone successful EPA Method Validation. However, CBTS will withhold its conclusions concerning the adequacy of the analytical methodology until the nature of the residue in plants is adequately defined.

   Additional metabolite methods may need independent laboratory validation and EPA Method Validation if it's determined that CPA and 3-PBAcid or other metabolites should appear in the tolerance expression.

5. We can draw no conclusion concerning the adequacy of the proposed tolerance on head lettuce until the residue of concern is defined. The petitioner should note that the commodity definition for head lettuce is lettuce with wrapper leaves. Residue data for lettuce without wrapper leaves should be used in calculations of anticipated residues. A revised section F is needed reflecting a tolerance proposal for the rac only.

6a. Residues of lambda-cyhalothrin are stable in various plant matrices under frozen storage for up to 26 months at <-18°C. The ratio of Lambda-cyhalothrin and its epimer is stable when stored for 16 months at <-18°C. Parent and its epimer analyses were conducted in a period of 13 to 24 months after harvest. Therefore, additional storage stability data for the ratio of parent and its epimer should be submitted for longer periods of time to support the subject petition.

6b. Available storage stability data indicate that CPA, 3-PBAcid and 3-PBAlcohol are stable in various racs for 3 months under frozen storage. This period of time is inadequate to support the subject petition. Additional storage stability data are needed reflecting storage time and conditions used for the field residue samples in this submission.

7. An International Residue Limit Status sheet is attached to this review. There are no Codex, Canadian or Mexican tolerances established for lambda-cyhalothrin in head lettuce. Therefore, we anticipate no compatibility problems.

RECOMMENDATION

CBTS recommends against the proposed tolerances for reasons given in Conclusions 1 (CAS name), 2 (revised section B), 3a (nature of the residue in plants), 4 (analytical methodology), 5 (revised section F) and 6a and 6b (storage stability data).

DETAILED CONSIDERATIONS

PRODUCT CHEMISTRY

The detailed manufacturing process for lambda-cyhalothrin was submitted in support of PP#6F3318 (MRID # 401820-01) and discussed in S. Willett's memo of 9/29/87. There are no toxicological concerns for any of lambda-cyhalothrin impurities. Discussion about isomers and the chemical name of lambda-cyhalothrin appears in M. Flood's memo of 9/19/91 (PP#7F3560/7H5543). There should be written confirmation from the Chemical Abstract Service that the proposed CAS name given for lambda-cyhalothrin, is the correct Chemical Abstract name.

There were two formulations proposed for use: "EC" (best known as KARATE Insecticide EPA Registration No. 10182-96) and "WG". ICI plans to market the EC formulation as TROPHY insecticide. TROPHY has 13.1% of the active compound or 1 pound of active ingredient per gallon. The WG formulation is a 12% wettable granule, that like EC, is mixed with water prior application. There is no information concerning the chemical nature of WG submitted to CBTS.

CBTS concludes that the manufacturing process of technical grade lambda-cyhalothrin has been adequately described. We note that the WG formulation has not been registered by RD.

PROPOSED USE

For control of alfalfa looper, cabbage looper, cabbage worm, cutworms, saltmarsh caterpillar and green cloverworm; the label specifies application as required, by scouting, at a rate of 1.92 to 3.2 fl. oz./acre (0.015 to 0.025 lb ai/acre/application). For armyworm, flea beetle, grasshoppers, leafhoppers, etc.; the label specifies application of 2.56 to 5.12 fl. oz./acre (0.020 to 0.04 lb ai/acre/application). Intervals of 5 or more days are specified for both treatments. The product should not be applied within 1 day of harvest. There is a specified maximum year application of 0.3 lb ai/acre. The pesticide can be applied with ground or air equipment using sufficient water to obtain full coverage of foliage.

The residue data do not adequately reflect the proposed use (see discussion under residue data). No residue data were submitted reflecting aerial application. These data are needed. Alternatively, the petitioner may submit a revised Section B, restricting application to ground equipment only.

NATURE OF THE RESIDUE

Plants

Plant metabolism of lambda-cyhalothrin has been discussed in F. Boyd's memo of 2/3/88. Plant metabolism studies on cotton plants and cotton seed, soybean plants and cabbage have been conducted, using ^{14}C-cyclopropane labeled and ^{14}C-benzyl labeled compounds. Studies on lambda-cyhalothrin metabolism show that it follows that of other pyrethroids. The ester linkage is cleaved to form cyclopropane carboxylic acids and the corresponding phenoxybenzyl alcohol. In cotton and soybean studies the parent compound was the principal constituent of the residue. Cabbage plant studies have shown that the cis and trans cyclopropane carboxylic acids were the major constituents. In the most recently conducted study on wheat, the parent was the principal constituent of the residue in both wheat grain and straw at PHI's up to 30 days. After 85 days of treatment, there is lower level of parent, the cyclopropane carboxylic acids being the major constituents of the residue. In the grain, less than half of the residue could be identified. Data on wheat straw have not been submitted. Therefore, the nature of the residue in wheat is not understood (M. Flood's memo of 4/16/91).

According to the petitioner, on a meeting in September 27, 1988; it was concluded that the submitted metabolism studies in cotton, soybean and cabbage, would support uses on cotton, soybean, cole crops and lettuce. We have not found any memo on that meeting in our files.

The nature of the residue in lettuce is understood, however, there are unresolved questions concerning the residues of toxicological concern in plants. Wheat straw metabolism studies must be submitted in order for CBTS and TOX to draw an overall conclusion as to the plant residues of concern. Residue data for lettuce will be considered when CBTS and TOX meet to determine what residues are of concern (M. Flood's memo of 7/30/91).

Animals

Since lettuce is not fed to livestock, there is no concern for animal metabolism and transfer studies in the proposed tolerance on lettuce.

ANALYTICAL METHODOLOGY

The analytical methodology used to determine the residues of lambda-cyhalothrin and its epimer was first described in MRID # 400540-01. Samples are extracted with organic solvents. These are washed with water and the aqueous phase is discarded. The organic phase is subjected to liquid partition chromatography. The eluted compounds are purified on a florisil column and the final determination is made by capillary GC with a Ni^{63} electron capture detector. This method has undergone EPA Method Validation for soybeans (PP#6F3318/PP#7F3488, E. Greer memo of 9/30/87).

The analytical method for metabolites was submitted in FAP#0H5599:

"Method for Analysis of Lambda-cyhalothrin metabolites in Hops" D.M. Clarke and A. Sapieto, 6/1990, Laboratory Project ID 54114B. (MRID# 416146-03)

This method provides the co-analysis of cis and trans CPA (PP890). Lambda-cyhalothrin includes the cis isomer only. The trans configuration is in lower amounts, and it is believed to result from photoisomerization of the metabolite on the plant surface. The analysis of 3-phenoxybenzoic acid (3-PB acid) and 3-phenoxybenzyl alcohol (3-PB alcohol) can be carried out by this methodology. 3-PB alcohol is oxidized to 3-PB acid and the 3-PB acid residue is quantified. Data are reported as the combination of 3-PB acid and 3-PB alcohol.

Samples are extracted, filtered and subjected to a C_{18} solid phase extraction. The extract is rotoevaporated, concentrated with HCl and refluxed for 2 hours. After cooling, the extract is partitioned with organic solvent and the aqueous phase is discarded. Jones reagent (23 mL of concentrated sulfuric acid, 77 mL of water and 24g of chromium (VI) oxide) is added to the organic phase and after the reaction is carried out, the extract is diluted with water and partitioned with organic solvent. The organic layer extract is acid washed and then partitioned with tetraborate buffer (pH 9.0). The aqueous layer is retained, acidified, and partitioned with dichloromethane. The extract is evaporated to dryness and derivatized with trifluoroacetic anhydride and trifluoroethanol at 100°C for 5 minutes. This derivatized extract is analyzed by capillary GC using a mass selective detector.

CBTS will withhold conclusions concerning the adequacy of the analytical methodology until a determination on the regulation of the metabolites is made. Additional methods may need EPA Method Validation if it is determined that CPA and 3-PBAcid or other metabolites should appear in the tolerance expression. Note that any additional methodology must be validated by an independent laboratory prior to submitting it to EPA (see PR Notice 88-5).

MULTIRESIDUE TESTING

The petitioner has determined recoveries of cyhalothrin under FDA's multiresidue protocols (S. Willett's memo of 3/15/88). Additionally, PP890 AND 3-PB acid have been quantified using the analytical methods in FDA Manual Volume 1. These data were forwarded to FDA for review (M. Flood's memo of 9/19/91).

RESIDUE DATA

Data from fourteen field trials were submitted in support of the tolerance proposal on lettuce. Trials were conducted in California (4), Arizona (1), Florida (2), New Mexico (1), New York (1), Colorado (1), Texas (1), New Jersey (1) and Michigan (1). These trials were conducted during the 1988 growing season. According to Agricultural Statistics,1985, these states accounted for at least 99% of the lettuce grown in the United States. Furrow and conventional irrigation methods were used. Although two formulations were used, EC and WG, the proposed formulation for use in lettuce is EC. Head lettuce plots received a total of 10 applications of lambda-cyhalothrin at rates of 0.03 lb ai/acre/application and a total of 0.30 lb ai/acre/season. Applications were made in 5-day to 14-day intervals, using either mounted sprayers or backpack sprayers with the sprays directed to the plants. Mature lettuce heads were harvested one and three days after the last treatment.

Samples were frozen within a few hours of sampling and shipped directly to either the Eastern Research Center, Goldsboro, NC or to the Western Research Center, Richmond, CA. Frozen head lettuce samples were ground with dry ice, subsampled and stored at -20°C ± 10°C prior to analysis.

Analysis of lettuce for parent and its epimer occurred 13 to 24 months after harvest. Metabolite analysis were completed within 13 to 26 months after harvest. Parent and metabolite analysis were conducted using the methodology previously described.

Recovery data were obtained from untreated samples fortified with cyhalothrin at levels ranging from 0.013 to 4.2 mg/kg and these were analyzed with the treated samples. Recoveries of 86% and 84% were obtained for lambda-cyhalothrin and the epimer R157836 respectively. The recovery data for the metabolites PP890, 3-PB acid and 3-PB alcohol, with samples fortified in a range from 0.02 to 0.1 mg/kg, were 93% for PP890, 104% for 3-PB acid and 99% for 3-PB alcohol. Submitted chromatograms show well resolved peaks in support of this data.

Residues of lambda-cyhalothrin were shown to be stable when stored at <-18°C for up to twenty-six months in commodities like peach, sugarbeet root, cottonseed, apple, cabbage and potatoes. Lambda-cyhalothrin and its epimer R157836, have no change in isomer ratio after storage for sixteen months at <-18°C. Metabolites residues have shown to be stable for up to three months at -20°C ± 10°C in a variety of raw agricultural commodities like cabbage, lettuce, tomatoes, apples, cottonseed and tobacco. Data to support stability of metabolites for longer periods is being developed.

CBTS concludes that available storage stability data are not adequate. Additional storage stability data for metabolites are needed reflecting the length of time and storage conditions used for the subject field residue samples, i.e., up to 26 months. Additional storage stability data for the ratio of parent and its epimer should be submitted for longer periods of time to support the subject petition.

Tables I and II summarize the quantity of residues found in head lettuce with or without wrapper leaves. Based on results from 1-day PHI and 3-day PHI, ICI selected the 1-day PHI use pattern. As can be seen from both tables, there is a significant reduction in residues when wrapper leaves are removed from lettuce. Also, residue levels resulting from treatment with the EC formulation are essentially identical to those resulting from treatment with the WG formulation.

The proposed tolerance of 2.0 ppm of lambda-cyhalothrin in/on lettuce is tentatively appropriate, pending a conclusion on the residue(s) of concern. However, in the absence of data reflecting aerial application, the registrant must either revise the use label or submit additional data. The rac is lettuce with all but decomposed/wilted wrapper leaves. Therefore, a tolerance for lettuce without wrapper leaves should not be proposed. A revised section F is needed.

Table I. Residues (ppm) of Lambda-cyhalothrin and metabolites in Head Lettuce with wrapper leaves.[1]

Study Location	Formulation	IC1A0321[2]	R157836[3]	PP890[4]	3-PB Acid[5]
CA	WG	0.11	0.03	0.05	0.02
CA	WG	0.93	0.21		
	EC	1.10	0.14		
CA	WG	0.11	0.04	0.08	0.03
	EC	0.18	0.02	0.02	<0.01
CA	WG	0.05	<0.01		
	EC	0.05	<0.01	0.03	<0.01
AZ	WG	0.32	0.03	0.05	0.03
	EC	0.19	0.03	0.06	0.06
AZ	WG	0.33	0.04	0.11	0.07
	EC	0.68	0.09	0.25	0.07
FL	WG	0.17	0.03		
	EC	0.36	0.04	0.07	0.02
FL	WG	0.38	0.06	0.10	0.08
	EC	0.24	0.03	0.09	0.06
TX	WG	0.27	0.02	<0.01	<0.01
	EC	0.16	<0.01	0.02	<0.01
NY	WG	0.29	0.08		
CO	WG	0.43	0.11	0.06	0.02
	EC	0.51	0.07	0.14	0.08
NJ	WG	0.95	0.04		
	EC	1.10	0.10	0.19	0.09
MI	WG	0.48	0.06	0.06	0.04
	EC	0.66	0.09	0.18	0.09
NM	WG	0.21	0.06	0.05	0.03

1. Head lettuce received a total of 10 applications of lambda-cyhalothrin at rates of 0.03 lb ai/acre/application and a total of 0.30 lb ai/acre/season. Applications were made in 5 day to 14 day intervals with PHI of 1 day.
2. Lambda-cyhalothrin
3. epimer of lambda-cyhalothrin
4. 3-(2-chloro-3,3,3-trifluoropro-1-enyl)-2,2-dimethylcyclopropane carboxylic acid
5. 3-phenoxybenzoic acid

Table II. Residues (ppm) of Lambda-cyhalothrin without wrapper leaves.[1]

Study Location	Formulation	IC1A0321[2]	R157836[3]	PP890[4]	3-PB Acid[5]
CA	WG	0.04	<0.01	0.02	<0.01
CA	WG	0.12	0.04		
	EC	0.20	0.02		
CA	WG	<0.01	<0.01	<0.01	<0.01
	EC	0.08	<0.01	0.02	<0.01
CA	WG	<0.01	<0.01		
	EC	<0.01	<0.01	<0.01	<0.01
AZ	WG	0.03	<0.01	<0.01	<0.01
	EC	0.05	<0.01	0.01	<0.01
AZ	WG	0.05	<0.01	0.02	<0.01
	EC	0.10	<0.01	0.03	<0.01
FL	WG	0.02	<0.01	<0.01	<0.01
	EC	0.05	<0.01		
FL	WG	0.06	<0.01	0.01	<0.01
	EC	0.07	<0.01	0.02	0.01
TX	WG	0.04	<0.01	0.04	<0.01
	EC	0.03	<0.01	<0.01	<0.01
NY	WG	0.02	<0.01		
CO	WG	<0.01	<0.01	<0.01	<0.01
	EC	<0.01	<0.01	<0.01	<0.01
NJ	WG	0.06	<0.01		
MI	WG	0.07	<0.01	0.02	0.01
	EC	0.03	<0.01	<0.01	<0.01
NM	WG	0.02	0.01	<0.01	<0.01

1. Head lettuce received a total of 10 applications of lambda-cyhalothrin at rates of 0.03 lb ai/acre/ application and a total of 0.3 lb ai/acre/season. Applications were made in 5 day to 14 day intervals with PHI of 1 day.
2. Lambda-cyhalothrin
3. epimer of lambda-cyhalothrin
4. 3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropane carboxylic acid
5. 3-phenoxybenzoic acid

OTHER CONSIDERATIONS

An International Residue Limit (IRL) Status sheet is appended to this review. There are no Codex, Canadian or Mexican limits established for lambda-cyhalothrin on head lettuce. Therefore, no compatibility problems exist.

Since the rac is lettuce with wrapper leaves, a tolerance for lettuce with wrapper leaves removed should not be proposed. This residue data would be useful for calculations of anticipated residues.

Attachment: International Residue Limit status sheet.

cc: SF, RF, Circu., C. Furlow (PIB/FOD), José J.Morales, E. Haeberer, PP#1F03985.

H7509C: Reviewer (JJM): CM#2: Rm 812-c: 557-2990: typist (JJM): 9/30/91.

RDI: E. Haeberer (10/21/91): R. Loranger (10/21/91)

Attachment: Page 1 of 1

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Cyhalothrin

CODEX NO. 146

CODEX STATUS:

[✓] No Codex Proposal Step 6 or Above (on head lettuce)

Residue (if Step 8): _____

Crop(s)	Limit (mg/kg)

PROPOSED U.S. TOLERANCES:

Petition No. 1F03985

DEB Reviewer 812-C (MORALES)

Residue: Lambda-cyhalothrin

Crop(s)	Limit (mg/kg)
Head Lettuce	2.0 ppm

CANADIAN LIMITS:

[✓] No Canadian Limit

Residue: _____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

[✓] No Mexican Limit

Residue: _____

Crop(s)	Limit (mg/kg)

NOTES

Form Revised 1989