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

AUG 13 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#7F3488 - Karate® Insecticide (PP321) on Soybeans - Evaluation of Residue Data and Analytical Methods - RCB No. 1880 - MRID Nos. 400279-02 through -15 and 400547-01

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and

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THRU: Charles L. Trichilo, Ph.D., Chief
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ICI Americas proposes that a tolerance be established for residues of (±)-alpha-cyano-(3-phenoxyphenyl)methyl(±)-cis-3-(Z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethyl-cyclopropanecarboxylate (PP321/Karate®) at 0.01 ppm in or on soybeans and poultry meat, fat, and byproducts.

The first permanent request for a 0.01 ppm tolerance on cottonseed; milk; and meat, fat, and meat byproducts of cattle, goats, hogs, horses, and sheep is currently in reject status pending resolution of several deficiencies (see M. Firestone memorandum, January 22, 1986).

Conclusions

1. The product chemistry data and information, recently received as an amendment to PP#6F3318, will be reviewed at a later date.

2. The petitioner should modify Section B to specify application volumes using both air and ground equipment, and a minimum interval between treatments.

3a. RCB concludes that the major residue on soybeans is the parent compound and its isomers for the present proposed use only. Additional metabolism work for characterization of the residues in soybeans may be required in the event of changes in use rates or removal of restrictions against use of forage, hay, and straw treated with PP321. The preceding could cause the need for including the major metabolites in the tolerance expression.

3b. In conjunction with the proposed use of Karate on soybeans, RCB will not reach any final conclusion regarding which residues to include in the animal commodity tolerance expression until issues involving the proposed methodology and residue data have been adequately resolved.

3c. RCB will reserve its conclusion on the acceptance of the results from the ^{14}C-cyclopropane labeled poultry metabolism study until the petitioner has fully discussed the 10 percent unknown spot on the chromatogram of egg yolk (Figure 3, Vol. 6, page 21) and the 12 percent unknown spot on the chromatogram of liver (Figure 4, Vol. 6, page 23).

3d. With regard to the results obtained from the ^{14}C-phenoxy-labeled cypermethrin poultry metabolism study, RCB concludes that these results are applicable to Karate.

4a. A method tryout (MTO) for Karate on cottonseed, milk, and beef muscle has been requested. RCB awaits the results of the MTO before deciding upon the adequacy of the proposed analytical methodology.

4b. The petitioner should supply results from the analysis of controls sample and some recovery data on soybeans fortified at the proposed tolerance level of 0.01 ppm using the proposed method of enforcement, ICI Method 81.

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4c. The petitioner will need to test for residues of Karate using the FDA multiresidue method protocols described in the FEDERAL REGISTER, Vol. 51, No. 187, September 26, 1986.

5. The adequacy of the storage stability data cannot be determined at this time. The petitioner will need to submit information concerning the length of storage for samples of the poultry residue study.

6. RCB cannot determine the adequacy of the proposed 0.01 ppm tolerance on soybeans at this time for the following reasons:

   a. The petitioner will need to describe the processing methods referred to as GRAM-4 and SOP/R/017.

   b. The petitioner will need to supply data on the analyses of control samples from all field trials.

   c. The petitioner will need to show that the proposed enforcement method for soybeans, ICI Method No. 81, is capable of detecting PP321 and its enantiomer R157836, since isomeric conversions are known to occur during plant metabolism of Karate.

   d. RCB will reserve its conclusion as to whether a processing study is needed until all questions pertaining to the analytical methodology, including the MTO, and residue data have been resolved.

7. RCB is unable to reach any final conclusions regarding the adequacy of the proposed Karate tolerances for meat, milk, poultry, and eggs until issues concerning the analytical methodology and residue data have been resolved.

8. An International Residue Limit Status sheet is included with this review. Since Codex, Canada and Mexico have not established any tolerances for Karate residues on poultry, there are no compatibility problems.

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Recommendations

RCB recommends against the establishment of the proposed tolerances on soybeans and poultry meat, fat, and byproducts for reasons given in Conclusion Nos. 1, 2, 3b, 3c, 4a, 4b, 4c, 5, 6 (a through d), and 7.

Detailed Considerations

Manufacture

Karate comprises two of the four enantiomers (i.e., one of the two diastereomers) of cyhalothrin. Its structure is such that it contains three asymmetric carbon atoms as well as a center for geometrical isomerism about the double bond within the 2-chloro-3,3,3-trifluoroprop-1-enyl group (i.e., either an E or Z configuration). Thus, 16 isomers (enantiomeric pairs) are possible of which 8 isomers have a cis configuration about the 1,3 bond of the cyclopropane ring, and the other 8 isomers have a trans configuration. Cyhalothrin consists of the four cis isomers containing the Z configuration as follows of which Karate consists only of the enantiomeric pair B:

A - Z (1R) cis (R) alpha-CN and Z (1S) cis (S) alpha-CN;
B - Z (1R) cis (S) alpha-CN and Z (1S) cis (R) alpha-CN.

PP321 is prepared by fractionation of cyhalothrin.

The petitioner was requested to submit additional product chemistry information and data concerning the manufacturing process, formation of impurities, preliminary analyses of technical grade Karate, methodology used to generate the preliminary analytical data, as well as certified limits for the active ingredient and all impurities present at > 0.1 percent in technical Karate, in connection with the review of Karate on cottonseed (PP#6F3318). The requested information has been submitted and recently received by RCB. This information will be reviewed at a later date.

Formulation

The formulation proposed for use on soybeans is Karate 1E Insecticide, an emulsifiable concentrate containing 13.1 percent ai or 1.0 lb ai/gal. The petitioner submitted a Confidential Statement of Formula (CSF) for the product with PP#6F3318, Karate on cottonseed. All inerts in Karate are cleared for use under 40 CFR 180.1001(c) or (d).

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Proposed Use on Soybeans

For the control of several pest insects, Karate is to be applied at rates from 0.015 to 0.03 lb ai/A. The product is to be applied using sufficient water to obtain full coverage of foliage. The maximum seasonal application specified is 0.05 lb ai/A with a PHI of 45 days. The grazing of livestock and harvesting of foliage for forage or hay is prohibited.

The petitioner should specify application volumes using both air and ground equipment and a minimum interval between treatments.

Nature of Residue (MRID Nos. 4000279-03 through -05)

Plants

Previous plant metabolism studies were conducted with Karate on cotton (PP#6F3318). The adequacy and implications of these studies are questionable at this time. A two part soybean metabolism study, submitted with this petition, is discussed below.

In the first report soybean plants were sprayed at first pod set with ^{14}C-benzyl-labeled PP321 or ^{14}C-cyclopropane-labeled PP321 at a rate of 20 g/ha (about 0.02 lb/A). The applications were repeated after 18 days, the plants were grown to maturity, and the soybeans harvested 51 days after the second application for a total application rate of 0.4 lb ai/A. The plants were stored at -15 °C + 5 °C until analyzed. The radioactivity of residues was measured using combustion and LSC. Radioactive residues in the soybeans were quantified and the following results were obtained:

^{14}C-cyclopropane-labeled PP321: 0.007 to 0.01 ug/g
^{14}C-benzyl-labeled PP321: 0.003 to 0.005 ug/g

The radioactive residues were not characterized because of the low levels present.

In the second report, soybean plants were sprayed at first pod set with ^{14}C-benzyl-labeled PP321 or ^{14}C-cyclopropane-labeled PP321 at a rate of 20 g/ha (0.02 lb/A). A second treatment was administered 18 days later. The plants were grown to maturity and the leaves were harvested 39 days after the second application. The results are summarized in the tables that follow.

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Table I. Soya Leaves from Plants Treated with ^{14}C-Cyclopropane-Labeled PP321

Total Radioactive Residues (TRR) - 1.48* - 1.87 mg/kg^{-1}	
Proportion of $CH_3C{\equiv}N$ extractable residue	85.8%
Proportion of $CH_3C{\equiv}N/H_2O$ extractable residue	8.1%
Proportion of unextractable residue	3.4%
	97.3%

Characterization of residue extracted with acetonitrile and acetonitrile/water:

		ppm Equivalents
PP321 (free and conjugated):	51.7-52.0%	0.77
Compound Ia (conjugated):	25.0-25.3%	0.37
Compound Ib (conjugated):	1.4-2.0%	0.03
Compound XI (conjugated):	2.0-2.4%	0.04
Unknowns (at least 5 compounds):	5.8%	0.09
Water-soluble material after hydrolysis:	2.3%	0.03
Polar material after acid hydrolysis:	2.3%	0.03
Remainder*:	4.5-6.1%	0.09
Residue not extracted with acetonitrile/acetonitrile water:	3.4%	0.05

* Plant used in characterization.

Table II. Soya Leaves from Plants Treated with ^{14}C-Benzyl-Labeled PP321

TRR - 1.20*-1.45 mg/kg^{-1}	
CH_3CN extractable residue	75.8%
CH_3CN/H_2O extractable residue	20.0%
Unextractable residue	4.2%
	100.0%

Characterization of residue extracted with acetonitrile and acetonitrile/water:

		ppm Equivalents
PP321:	42.9-47.3%	0.57
Compound III (conjugated):	2.2-3.4%	0.04
Compound V (conjugated):	4.5-6.7%	0.08
Compound VI (conjugated):	3.9-5.5%	0.07
Compound XIII (conjugated):	4.6-7.0%	0.08
Unknown 1:	4.0-5.0%	0.06
Unknown 2:	3.5%	0.04
Unknown 3:	1.0-1.2%	0.01
Unknown 4:	3.0-3.2%	0.04
Other unknowns (at least 3 compounds):	6.1%	0.07
Polar material:	3.9-5.7%	0.07
Water-soluble material after acid hydrolysis:	4.3%	0.05
Remainder**:	0-16.1%	0-.19

Metabolites from ^{14}C-benzyl-labeled PP321 are already extensively studied since they are common to many other pyrethroid insecticides, including fenvalerate, permethrin, and cyhalothrin.

*Plant used in characterization.

**Mainly due to radioactivity detected, by the very sensitive scanning system used, at just above background level in the regions between distinct radioactive bands on the chromatograms. This "radioactivity" probably represents a mixture of machine noise and low levels of radioactivity uniformly streaked over the length of the chromatogram.

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RCB's Comments Re: Soybean Metabolism Study

The proposed label specifies a seasonal maximum of 0.05 lb ai/A and a PHI of 45 days. The soybean metabolism study reflects seasonal uses of 0.04 lb ai/A and PHI's of 51 (soybean analysis - Report No. RJ0438B) and 39 days (leaf analysis - Report No. RJ0507B). In the field studies no residue of parent PP321 (Karate) was detected at or above 0.01 ppm in any sample of soybeans treated at either 1.2 or 5X reflecting PHI's ranging from 27 to 63 days. The metabolism study indicates that Karate equivalent residues ranged from 0.003 to 0.01 ppm in or on soybeans.

RCB concludes that from this metabolism study the major residue on soybeans is the parent compound and its isomers for the present proposed use only. Additional metabolism work to characterize the residues in soybeans may be required in the event of changes in use rates or removal of restrictions against use of forage, hay, and straw treated with PP321. The preceding could cause the need for including the major metabolites in the tolerance expression.

Animal Metabolism

A goat metabolism study was submitted in support of use of Karate on cotton (PP#6F3318, MRID No. 073982). It was concluded that the primary terminal residues in ruminants consisted of Karate (parent compound) and its metabolites CTFPA (3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethyl-cyclopropanecarboxylic acid), OHMe-CTFPA (3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2-hydroxymethyl-2-methyl cyclopropane-carboxylic acid), 3-PBAcid (3-phenoxybenzoic acid), and 4-OH-3PBAcid (4-hydroxy-3-phenoxybenzoic acid). These findings resulted from the feeding of both ^{14}C-benzyl and ^{14}C-cyclo-propyl-labeled materials.

A poultry metabolism study (MRID No. 400279-16) was submitted with this petition. This PP321 metabolism study was conducted only with acid-labeled material and gave information on the metabolic fate of the PP321 ester and the cyclopropanecarboxylic acid moiety.

Two laying hens were dosed with ^{14}C-cyclopropane-labeled PP321 at a rate equivalent to 10.8 mg/kg in their total diet. The dose was administered daily for 14 days and the hens sacrificed 24 hours after the final dose. Eggs and excreta were collected throughout the dosing period and

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samples of meat, fat, and liver were taken at sacrifice. The results (PP321 equivalents) of the analyses were as follows:

Analyte	Activity, mg/kg^{-1} PP321 Equivalents	
	Minimum	Maximum
Egg albumin	< 0.01	0.01
Egg yolk	< 0.01	0.32
Breast muscle	< 0.01	0.01
Leg muscle	< 0.01	0.01
Liver	0.36	0.60
Fat	0.17	0.46

98 to 100% of the radiochemical dose was excreted.

The petitioner's characterization of tissue with sufficient amounts of radioactivity yielded the following results:

"a. Egg Yolk

Residue in composite sample analysed = 0.23 mg kg^{-1}

Residue characterised as:

PP321,	61% (0.14 mg kg^{-1})
Unknown (Rf 0.17, solvent system 2),	6% (0.014 mg kg^{-1})
Unknown (origin, solvent system 2),	1% (0.002 mg kg^{-1})
Lost during concentration of the acetonitrile extract,	7% (0.016 mg kg^{-1})
Hexane soluble extract (too "dirty to analyse"),	9% (0.021 mg kg^{-1})
Unextracted,	13% (0.03 mg kg^{-1})

b. Liver

Residue in composite sample analysed = 0.43 mg kg^{-1}

Residue characterised as follows:

Compound Ia,	50-51% (0.22 mg kg^{-1})
Compound XI,	10-13% (0.043-0.056 mg kg^{-1})
Unknown (Rf 0.4, solvent system 4),	1% (0.009 mg kg^{-1})
Unknown (Rf 0.07, solvent system 4),	9% (0.043 mg kg^{-1})
Unknown (origin, solvent system 4),	9% (0.034 mg kg^{-1})
Unextracted with acetonitrile*	20% (0.086 mg kg^{-1})

c. Fat

Residue in composite sample analysed = 0.28 mg kg^{-1}

Residue characterised as:

PP321,	77-82%	(0.22-0.23 mg kg^{-1})
Unknown (Rf 0.22, solvent system 2),	8-9%	(0.022-0.025 mg kg^{-1})
Unknown (origin, solvent system 2),	3%	(0.008 mg kg^{-1})
Lost during concentration of the acetonitrile extract,	6%	(0.017 mg kg^{-1})"

Compound Ia

(1RS)-cis-3-(ZE-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid (CTFPA).

Compound XI

3-(Z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2-hydroxymethyl-2-methylcyclopropanecarboxylic acid (OHMe-CTFPA).

The poultry metabolism study discussed above involves Karate radiolabeled in the cyclopropane ring only. The results show that CTFPA and OHMe-CTFPA are major residues of concern. However, the petitioner should discuss further the residues that are reflected by the following spots on the submitted figures (autoradiogram and radioscan of the chromatograms):

Figure 3. (Vol. 6, pg. 21) - 10% spot;
Figure 4. (Vol. 6, pg. 23) - 12% spot below Compound XI (OHMe-CTFPA).

The petitioner has also given an ICI Reference No. D0601 with regard to a ^{14}C-phenoxy-labeled cypermethrin poultry metabolism study (Accession No. 071764 - PP#3F2936). The phenoxy portion of PP321 (Karate) is identical to that of cypermethrin.

The petitioner points out that ^{14}C-phenoxy-labeled cypermethrin was administered to laying hens for 14 days at 10 ppm in the diet. Eggs were collected during the dosing period and the hens sacrificed 4 hours after the last dose. Residues were < 0.01 ppm in egg albumin and 0.15 ppm in the yolk. A third of the residue in the yolk was parent compound, with 2 percent as 3-phenoxybenzoic acid and 1 to 4 percent as other metabolites, including 4'-hydroxy-3-phenoxy-benzoic acid. Residues in muscle were 0.01 to 0.02 ppm, in fat 0.08

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ppm, and in liver 0.37 ppm cypermethrin equivalents. Sixteen percent of the residue in the liver was parent compound and 3 percent was 3-phenoxybenzoic acid and 4'-hydroxy-3-phenoxybenzoic acid. Most of the residue in fat (0.05 ppm) was parent compound.

RCB concludes that the primary terminal residues of concern in ruminants are Karate (parent compound) and its metabolites CTFPA (3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid), OHMe-CTFPA (3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2-hydroxymethyl-2-methyl cyclopropanecarboxylic acid), 3-PBAcid(3-phenoxybenzoic acid), and 4-OH-3PBAcid(4-hydroxy-3-phenoxybenzoic acid).

In conjunction with the proposed use of Karate on soybeans, RCB will not reach any final conclusion regarding which residues to include in the animal commodity tolerance expression until issues involving the proposed methodology and residue data have been resolved.

RCB will reserve its conclusion on the acceptance of the results from the ^{14}C-cyclopropane-labeled poultry metabolism study until the petitioner has fully discussed the 10 percent unknown spot on the chromatogram of egg yolk (Figure 3, Vol. 6, pg. 21) and the 12 percent unknown spot on the chromatogram of liver (Figure 4, Vol. 6, pg. 23). This information is very important since this poultry metabolism study will probably serve not only to support soybean tolerances but also to support possible future tolerances involving other poultry feed items. The petitioner may want to use GLC/mass spectrometry or other techniques for characterizing these residues. Could one of these spots (residues) be the amide of Karate?

With regard to the results obtained from the ^{14}C-phenoxy-labeled cypermethrin poultry metabolism study, RCB concludes that these results are applicable to Karate.

Analytical Methodology

The petitioner has submitted methods for the determination of PP321 parent compound in crops and products of animal origin, MRID Nos. 400547-01 and 400279-07, respectively. Both methods use internal standards to quantify results, but also contain recovery data to support the use of an external standard. The same methods were reviewed in support of previous submissions (PP#6F3318 and PP#0G3458).

The methods for both crops and animal commodities are summarized as follows.

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Crops

The method involves extraction with a 1:1 solvent mixture of acetone:hexane. The organic extracts are then washed with water to remove acetone.

Coextracted lipids are remove by acetonitrile liquid-liquid column cleanup when necessary. All samples are subjected to adsorption chromatography to remove interferences. Final determination is performed by packed or capillary column gas-liquid chromatography, using a ^{63}Ni electron capture detector. The limit of detection is reportedly 0.01 ppm. This method detects residues of parent compound only.

External standard recovery data were reported as follows:

Crop	Fortification Level 0.05	0.1	0.2
Root vegetables	--	84-117% (n = 8)	106
Leafy vegetables	114	75-104 (n = 6)	--
Legume vegetables	--	74-108 (n = 3)	--
Fruiting vegetables	117	--	104
Pome fruits	--	88-111 (n = 8)	84-96 (n = 3)
Stone fruits	--	85,99 (n = 2)	
Small fruits and berries	--	97-105 (n = 3)	101
Cereal grains	--	94-103 (n = 3)	105
Fodder and straws	--	87-109 (n = 10)	77-113 (n = 3)
Oilseed	80-109 (n = 3)	76-93 (n = 7)	
Tropical seed	91	82	

No data for controls were provided.
n = number of data points.

Animals

The methodology is similar to that described in the method for determination of PP321 in crops.

Karate residues are extracted from milk by homogenization with 50 percent acetone:hexane and from tissues by maceration with the same solvent. The aqueous fraction is removed using a separatory funnel and the organic layer is dried using anhydrous sodium sulfate. The organic fraction is cleaned up by Florisil column chromatography prior to determination by packed column gas chromatography using a ^{63}Ni electron capture detector. An alternate capillary column chromatography quantitation step was

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also given. The limit of determination was reported as 0.01 mg/kg for tissue samples and 0.002 mg/kg^{-1} for milk samples.

The following fortification/recovery data are reported

Sample	Fortification (ppm Karate)	Percent Recovery Range/(Average)
Milk	0.005-0.50	66-129 / 93 (n = 22)
Muscle	0.05-1.0	60-132 / 92 (n = 12)
Kidney	0.10-0.3	69-101 / 89 (n = 5)
Liver	0.05-1.0	65-118 / 92 (n = 9)
Fat	0.20-5.0	62-102 / 83 (n = 4)

The above recoveries were calculated using an external standard procedure after analysis by an internally standardized method.

RCB cannot determine the adequacy of the analytical methodology for the following reasons:

- A method trial for analysis of Karate/PP321 from beef muscle and milk has been requested (see memorandum of L. Cheng, February 1987, PP#6G3458) the results of which will be applicable to soybeans, poultry, and its commodities. RCB will need to review the results of the method trial before determining whether adequate methodology is available for enforcement of the proposed tolerances for soybeans; meat, fat, and meat byproducts; and poultry.

- The petitioner should supply results from the analysis of control samples and also some recovery data on soybeans fortified at the proposed tolerance level of 0.01 ppm using the proposed method of enforcement, ICI Method No. 81.

- The petitioner will also need to test for residues of Karate/PP321 using the FDA multiresidue method protocols described in the FEDERAL REGISTER, Vol. 51, No. 187, September 26, 1986.

Residue Data

Storage Stability (MRID Nos. 400279-10 through -13 and 400279-15)

Storage stability data on fruits, vegetables, poultry, eggs, animal tissue, milk, and soil were submitted by the registrant in support of this petition.

The samples were homogenized, weighed into plastic bags or jars, and fortified with Karate/PP321 or cyhalothrin (58:48 R157836 and PP321 isomers). The results are summarized below.

Commodity	Fortification Level (ppm)	Storage Interval (mos) Mean Recoveries (%) 0	1	2	3	6	9	12
Peach	0.5	100			90	93	96	
Pea		100			93	94	95	
Rapeseed oil		100			93	95	90	
Wheat grain		100			79	87	76	
Sugar beet roots		99			95	94	96	
Cottonseed		100			93	101	--	
Apple*	1.0	105			98	94	112	
Cabbage*		103			98	98	111	
Poultry muscle	0.2	105	100		95			
Liver		103	93		93			
Subcutaneous fat and skin		103	95		93			
Abdominal fat		100	98		90			
Egg		105	108		95			
Milk	0.2	100	100	100	105			

*Fortified with cyhalothrin.

Additionally, samples of animal tissues from a cow residue transfer study were reanalyzed in duplicate 9 weeks after the original analysis. The samples were analyzed initially after a maximum of 7 weeks storage then were stored for a further 9 weeks under the same conditions. The results were as follows:

Tissue	Average Residue 1st Analysis (ppm)	Average Residue 2nd Analysis (ppm)
Adductor muscle	0.14	0.13
Pectoral muscle	0.39	0.44
Kidney	0.45	0.56
Liver	0.08	0.10
Subcutaneous fat	4.3	4.5
Peritoneal fat	7.2	6.4
Fortification levels	0.1-5.0 mg/kg^{-1}	

All analyses of soybean field study samples were reportedly completed within 6 months, for which adequate storage stability data have been supplied. The timeframe of the poultry residue study was not given. Storage stability data were supplied for a 3-month period. The petitioner will need to submit information

concerning the length of storage for all treated samples from the poultry residue study.

Soybeans (MRID No. 400279-08 and -09)

Samples of soybeans from eight field trials conducted in Alabama, Arkansas, Delaware, Georgia, Illinois, Louisiana, Missouri, and Mississippi during the 1983 growing season were analyzed for residues of PP321 and its enantiomer formed by epimerization, R157836. Each trial site received two applications of 0.03 lb of PP321 per acre (1.2X). All of the field trials were sprayed with ground equipment in spray volumes of 5.5 to 39.2 gallons per acre. PHI's ranged from 27 to 64 days.

Field trials during 1984 were conducted in Arkansas, Illinois, Indiana, Iowa, Louisiana, Maryland, North Carolina, and South Dakota. All sites received the same application rate--12 applications of 0.03 lb ai/A (1.2X). Six of the trials were sprayed with ground equipment in spray volumes of 5.5 to 37.8 gal/A. Two trials (Arkansas, Louisiana) were sprayed aerially in volumes of 3.0 to 5.0 gal/A. Samples of mature soybeans and controls from each trial were collected at PHI's from 28 to 62 days.

Seven field trials in 1985 were conducted in Alabama, Iowa, Illinois, Georgia, Minnesota, and Mississippi (2). Four of these trials had been sprayed with ground equipment. In two of the ground trials, two applications of PP321 were applied separately to single plots at 0.03 lb ai/A (1.2X) or at 0.15 lb ai/A (5X). The remaining ground trials received two applications of 0.03 lb ai/A. The PHI's ranged from 28 to 65 days.

The 1983 field trial samples were processed according to ICI Americas, Inc., GRAM-4. The 1984 and 1985 field trial samples were shipped frozen to ICI Americas, Inc., in Goldboro, North Carolina, and stored in a freezer at -20 °C. These samples were processed according to the ICI Americas, Inc. method SOP/R/017.

The residue analyses were done using ICI Method No. 70, The Determination of Residues of Cyhalothrin in Crops. The limit of determination was reportedly 0.01 ppm for both PP321 and its enantiomer R157836. All samples were analyzed within 6 months of their receipt. A summary of the residue data follows.

Trial Sites	Year	Application Rate (lb ai/A)	Method of Application	PHI's (Days)	Total Residues (ppm)
MS, LA, AL, GA, AR, MO, DE, IL	1983	0.03	Ground	27-64	< 0.01
IN, IA, SD, IL, MD, NC	1984	0.03	Ground	28-61	< 0.01
AR, LA, MN	1984	0.15	Aerial	28-62	< 0.01
AL, IL, MS	1985	0.03	Ground	35-65	< 0.01
MS	1985	0.15	Ground	65	< 0.01
MS, GA, IA	1985	0.03	Aerial	44-46	< 0.01

Number of applications (all sites) = 2.

No residue of PP321 or its diastereomer was detected at or above 0.01 ppm in any sample of soybeans treated at either 1.2X or 5X, according to these results. The petitioner thus concluded there was no need for a processing study.

RCB cannot determine whether the proposed 0.01 ppm tolerance for PP321 is adequate for the following reasons:

1. Details concerning the handling of the field trial samples are unclear. It appears that the 1983 samples were not frozen immediately. The petitioner will need to describe their processing methods referred to as GRAM-4 and SOP/R/017, and give details of storage conditions prior to analysis.

2. The method of analysis used to determine residues in the field studies was for the determination of cyhalothrin, ICI Method No. 70. The petitioner will need to show that the proposed enforcement methodology, ICI Method No. 81, is capable of detecting both PP321 and its enantiomer R157836, since interconversion of isomers is said to occur when Karate is metabolized by plants.

3. No data on the analyses of control samples were provided. The petitioner will need to supply such data for controls from all field trials.

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4. RCB will reserve its conclusion as to whether a processing study is needed until all questions pertaining to the analytical methodology, including the MTO and residue data have been resolved.

Meat, Milk, Poultry, and Eggs

Soybean and its fractions comprise a significant percentage of livestock diet. The maximum percentage is in the diet of laying hens, in which 50 percent of the diet can be soybean seeds.

The registrant has supplied a feeding study in which 7 groups of 10 laying hens were fed diets containing 1.0, 5.0, and 25 mg/kg^{-1} of PP321 for up to 28 consecutive days. At the end of the treatment period, the birds from the 1.0 and 5.0 ppm dose rate groups and one of the 25 ppm rate group were slaughtered. The remaining two groups that had received 25 ppm of Karate daily were fed untreated diets for 7 and 14 days, respectively, and then slaughtered. Eggs were collected throughout the trial, including the pretreatment acclimatization and posttreatment recovery periods. The samples were stored at -20 $\pm$ 5 °C until analyzed. The samples were analyzed using PPRM No. 86. The limit of detection for eggs was 0.005 ppm, .002 ppm in muscle, and .005 ppm fat and liver (MRID No. 400279-14).

According to the study data, PP321 residues did not accumulate and declined when feeding of the treated diet ceased. The mean plateau residues in whole eggs were < 0.005 ppm, 0.01 ppm, and 0.05 ppm for the 1.0, 5.0, and 25 ppm dose rates, respectively. PP321 residues in tissues were generally in the order of abdominal fat and skin plus subcutaneous fat >> muscle > liver. Tissue samples from birds fed at the 1.0 and 5.0 ppm rate contained less than 0.005 ppm. The exception was fat, which contained up to 0.09 ppm.

Tissues from birds fed at 25 ppm contained residues which ranged from < 0.005 to 0.006 ppm in liver, 0.005 to 0.02 ppm in muscle, and up to 0.82 ppm in fat. The results from the feeding study are consistent with those obtained from the metabolism study.

A ruminant feeding study was conducted in conjunction with the use of PP321 on cottonseed (PP#6F3318, MRID No. 073982). In this study, cows were fed for 30 days on diets containing 1.0, 5.0, and 25 ppm of PP321. In milk, the residues did not accumulate but declined when feeding was stopped, and reached a maximum during the dosing of 0.02 ppm. In fat, the mean

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residue was 0.17 ppm. Mean residues in the meat, liver, and kidney were all below 0.01 ppm.

At this time RCB is unable to reach any final conclusions regarding the adequacy of the proposed Karate tolerances for meat, milk, poultry, and eggs until issues concerning the analytical methodology and residue data have been resolved.

Other Considerations

An International Residue Limit Status sheet is included with this review as Attachment 1. Since Codex, Canada, and Mexico have not established any tolerances for Karate residues on soybeans or poultry commodities, there are no compatibility problems.

Attachment 1: International Residue Limit Status Sheet
TS-769:RCB:SHB:Kendrick&Co-8/10/87:CM#2RM804:X1669
cc: R.F., Circu., Brooks, TOX, PP#7F3488, PM#15, PMSD/ISB
RDI: J. Onley, 7/31/87; R. Schmitt, 7/31/87