



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

MAR 15 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#7F3488 (RCB No. 3208) - Karate on Soybeans -
Amendment Dated December 16, 1987 - MRID Nos.
404461-01, 404461-02, and 404461-03

FROM: Nancy Dodd, Chemist *Nancy Dodd*
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THRU: Charles L. Trichilo, Ph.D., Chief *h. O. Schmitt*
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and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

The petitioner, ICI Americas, submits an amendment to PP#7F3488 concerning the proposed permanent tolerances for residues of (+)-alpha-cyano-(3-phenoxyphenyl)methyl(+)-cis-3-(Z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate (PP321/Karate®) at 0.01 ppm in or on soybeans and poultry meat, fat, and meat by-products.

The request for a 0.01 ppm tolerance on cottonseed, milk, and meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep is in reject status (PP#6F3318, S. Willett, January 22, 1988).

Summary of Deficiencies that Need Resolution

- ° Product Chemistry data requirements are outstanding pending review by RCB (relates to Deficiency No. 1).

- ° The Section B/label should be revised to specify application in 3.0 to 15.0 gal spray/A for aerial applications (relates to Deficiency No. 2).
- ° The Section F should be revised to include soybeans, eggs, and the other animal commodities as follows (relates to Deficiency No. 7):

<u>Commodity</u>	<u>ppm</u>
Soybeans	0.01
Meat of cattle, goats, hogs, horses, poultry, and sheep	0.01
Fat of cattle, goats, hogs, horses, poultry, and sheep	0.01
Meat by-products of cattle, goats, hogs, horses, poultry, and sheep	0.01
Milk	0.01
Eggs	0.01

Recommendations

RCB continues to recommend against the establishment of the proposed Karate tolerances of 0.01 ppm in/on soybeans and poultry meat, fat, and meat by-products for the reasons given above (under "Summary of Deficiencies that Need Resolution").

Conclusions

- ① Product Chemistry data are under review by RCB in conjunction with another petition review (PP#6F3318). (Deficiency No. 1 of RCB's August 13, 1987 review is not resolved at this time.)
2. The Section B/label should be revised to specify application in 3.0 to 15.0 gal spray/A for aerial applications since that spray volume for aerial applications is supported by residue data. (Deficiency No. 2 is not resolved.)
- ③ The nature of the residue in animals is adequately understood for this use on soybeans only. Parent per se is the residue of concern in animals for this use on soybeans only.

4. For this proposed use on soybeans which involves residues below the limit of detection, the available poultry metabolism study is adequate. For other uses, further poultry metabolism work may be needed.
5. A satisfactory method trial has been conducted for Method No. 81 on soybeans at 0.01 and 0.02 ppm, and for Method No. 86 on liver and milk at 0.01 and 0.02 ppm.
6. The petitioner has submitted recoveries of PP321 for Protocols I, II, III, and IV on cabbage and for Protocols I and IV on soybeans in MRID No. 404461-02. This submission will be forwarded to the Food and Drug Administration (FDA).
7. Adequate storage stability data are available on poultry.
8. Standard operating procedures indicate that samples are stored frozen between sampling and analysis.
9. Adequate control data have been supplied since data for 16 studies are available.
10. Both Methods Nos. 70 and 81 can detect both PP321 and its enantiomer R157836.
11. A soybean processing study is not needed since no detectable residues were found on soybeans resulting from a 5X maximum treatment.
12. A revised Section F should be submitted which proposes tolerances for soybeans, eggs, and the other animal commodities as follows:

<u>Commodity</u>	<u>ppm</u>
Soybeans	0.01
Meat of cattle, goats, hogs, horses, poultry, and sheep	0.01
Fat of cattle, goats, hogs, horses, poultry, and sheep	0.01
Meat by-products of cattle, goats, hogs, horses, poultry, and sheep	0.01
Milk	0.01
Eggs	0.01

(Deficiency No. 7 has not been resolved.)

13. An International Residue Limit Status sheet is attached to RCB's review of PP#7F3488 dated August 13, 1987. No Codex, Canadian, or Mexican tolerances or limits have been established for Karate on soybeans and poultry. Therefore, there are no compatibility problems with respect to Codex.

DETAILED CONSIDERATIONS

The deficiencies which were listed in the August 13, 1987 review are outlined below, followed by the petitioner's responses and RCB's discussions/conclusions.

RCB's Deficiency No. 1

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

Petitioner's Response to Deficiency No. 1

ICI believes that information to satisfy all of the product chemistry data requirements has been provided.

RCB's Discussion/Conclusion No. 1

Product Chemistry data are under review by RCB at this time in conjunction with the review of PP#6F3318.

Deficiency No. 1 remains outstanding at this time.

RCB's Deficiency No. 2

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

Petitioner's Response to Deficiency No. 2

The petitioner has submitted a revised Section B/label. The revised label includes the following statements:

"Usually 1-15 gal/acre are recommended for aerial application and 5-30 gal/acre are recommended for ground application."

"Apply as required with air or ground equipment."

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RCB's Discussion/Conclusion No. 2

Residue data are available for ground applications in a volume of 5.5 to 39.2 gal spray/A for ground applications and in a volume of 3.0 to 10.0 gal/A for aerial applications.

RCB concludes that the Section B/label should be revised to specify application in 3.0 to 15.0 gal spray/A for aerial applications since that spray volume for aerial applications is supported by residue data.

Deficiency No. 2 is not resolved.

RCB's Deficiency No. 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.

Petitioner's Response to Deficiency No. 3b

ICI refers to its responses to EPA's Conclusions Nos. 3c, 4a, 4b, 5, 6a, 6b, and 6c.

RCB's Discussion/Conclusion No. 3b

RCB made the following conclusions in its review of PP#7F3488 dated August 13, 1987 (S. Brooks):

"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 ¹⁴C-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,

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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."

RCB indicated in a meeting with ICI on September 3, 1987 that further identification of residues comprising 10 to 12 percent of the radioactivity in poultry is not needed for this use on soybeans since the proposed tolerance on soybeans is only 0.01 ppm.

RCB concludes, for this use on soybeans only, that the nature of the residues in animals is adequately understood. Parent per se is the residue of concern in animals for this use on soybeans only.

Deficiency No. 3b is resolved.

RCB's Deficiency No. 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).

Petitioner's Response to Deficiency No. 3c

In the reviewed poultry metabolism study, the dose level was 1000 times the proposed tolerance of 0.01 ppm. The petitioner expects real residues in poultry and eggs resulting from the proposed use to be below the limit of detection.

RCB's Discussion/Conclusion No. 3c

For the proposed use on soybeans which involves residues below the limit of detection, the available poultry metabolism study is adequate. For other uses, further poultry metabolism work may be needed.

Deficiency No. 3c is resolved.

RCB's Deficiency No. 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.

Petitioner's Response to Deficiency No. 4a

ICI understands that a successful MTO has been completed.

RCB's Discussion/Conclusion No. 4a

A satisfactory MTO has been conducted for Method No. 81 on soybeans at 0.01 and 0.02 ppm, and for Method No. 86 on liver and milk at 0.01 and 0.02 ppm (PP#6F3318, S. Brooks, October 30, 1987).

Deficiency No. 4a is resolved.

RCB's Deficiency No. 4b

The petitioner should supply results from the analysis of control samples and 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.

Petitioner's Response to Deficiency No. 4b

The petitioner indicates that the requested information is available in the following reports:

1. "PP321: Residues in Soybeans," ICI Report No. TMU 1490/B (MRID No. 400279-08).
2. "PP321 Residues from Aerial/Ground Applications to Soybeans - 1984 and 1985 USA Field Trials," ICI Report No. TMU 1991/B (MRID No. 400279-09).

These reports use Analytical Method No. 70 rather than No. 81. However, the petitioner indicates that these methods are similar except in choice of adsorbants in the adsorption column cleanup step. ICI Method No. 70 uses either Florisil or Fractosil; ICI Method No. 81 uses either Florisil or Silica (BOND-ELUT). In the two studies above, Florisil was the adsorbant.

RCB's Discussion/Conclusion No. 4b

A comparison of Method No. 70 (submitted in PP#6F3318 on October 24, 1985, Accession No. 073982, Reference 4D) and Method No. 81 (submitted in PP#7F3488 on December 23, 1986, MRID No. 400547-01) indicates that these methods are similar.

In MRID No. 400279-08, recoveries of PP321 at fortification levels of 0.007 to 0.14 ppm ranged from 81.4 to 116.3 percent. Recoveries of its enantiomer R157836 at fortification levels of 0.010 to 0.19 ppm were 85.8 to 117.0 percent. Controls for PP321 and R157836 were all < 0.01 ppm.

In MRID No. 400279-09, recoveries of PP321 at fortification levels of 0.009 to 0.047 ppm were 68.1 to 97.1 percent. Recoveries of its enantiomer R157836 at fortification levels of 0.012 to 0.061 ppm were 71.0 to 97.5 percent. Controls for PP321 and R157836 were all < 0.01 ppm.

A satisfactory MTO has been conducted for Method No. 81 on soybeans (at 0.01 and 0.02 ppm), and for Method No. 86 on liver and milk (PP#6F3318, S. Brooks, October 30, 1987).

RCB concludes that Deficiency No. 4b is resolved.

RCB's Deficiency No. 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.

Petitioner's Response to Deficiency No. 4c

ICI has tested for Karate using the FDA multiresidue method protocols. The results are submitted in ICI Report No. TMU3399/B, ICI Volume No. 40 (MRID No. 404461-02). Recoveries of PP321 (cis B isomers of cyhalothrin) and the cis A isomers of cyhalothrin were determined using a cyhalothrin analytical standard. Recoveries from cabbage were determined using Protocols I, II, III, and IV. Recoveries from soybeans were determined using Protocols I and IV. Recoveries for PP321 from cabbage are shown below:

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Percent Recovery of PP321 (Cis B Isomers of Cyhalothrin) from Cabbage

<u>Sample Type and Fortification Level</u>	<u>Protocol 1A</u>	<u>Protocol 1B</u>	<u>Protocol 2</u>	<u>Protocol 3</u>	<u>Protocol 4</u>
Reagent Blank	< 0.01	< 0.01	--	< 0.01	< 0.01
Control Sample	< 0.01	< 0.01	--	< 0.01	< 0.01
0.011 ppm	--	--	--	--	61.6, 59.3
0.022 ppm	135, 26.2	73.2, 98.7	--	4.9, 2.4	--
0.043 ppm	--	--	0	15.8, 16.1	--
0.056 ppm	--	--	--	--	50.3, 52.6
0.022 ppm	109, 155	71.7, 89.4	--	--	--

Protocol 1A: 6.0% diethyl ether/petroleum ether eluate used in Florisil column cleanup procedure (1).

Protocol 1B: 20% methylene chloride/hexane eluate used in Florisil column cleanup procedure (4).

Protocol 2: Detector provides inadequate sensitivity for quantitation.

Protocol 4: Interference observed for cis A isomer recoveries reported without control correction.

Recoveries of PP321 from soybeans are shown below:

Percent Recovery of PP321 (Cis B Isomers of Cyhalothrin)
from Soybeans

<u>Sample Type and Fortification Level</u>	<u>Protocol 1A</u>	<u>Protocol 1B</u>	<u>Protocol 4</u>
Reagent Blank	< 0.01	< 0.01	< 0.01
Control Sample	< 0.01	< 0.01	< 0.01
0.022 ppm	--	0, 60.8	51.8, 54.1
0.043 ppm	44.1, 20.7	--	--
0.11 ppm	--	--	31.6, 56.3
0.22 ppm	--	0, 0	--
0.43 ppm	60.9, 73.9	--	--

Protocol 1A: 6.0% diethyl ether/petroleum ether eluate used in Florisil column cleanup procedure (1).

Protocol 1B: 20% dichloromethane/hexane eluate used in Florisil column cleanup procedure (4).

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RCB's Discussion/Conclusion No. 4c

The petitioner has submitted recoveries of PP321 for Protocols I, II, III, and IV on cabbage and for Protocols I and IV on soybeans.

Deficiency No. 4c is resolved.

RCB's Deficiency No. 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.

Petitioner's Response to Deficiency No. 5

After storage for 2 years at -18 °C, residues in poultry tissues and eggs were reanalyzed. No significant change in residues was found. See ICI Report No. M4608B, ICI Volume No. 41 (MRID No. 404461-03).

RCB's Discussion/Conclusion No. 5

Storage stability data for poultry for a 3-month period were previously submitted. No significant decline in residues over a 3-month period was observed when samples were spiked and stored frozen for that period.

ICI indicated (PP#7F3488, MRID No. 400279-15, Vol. 16, pp. 8 to 9) that samples from a poultry feeding study which was conducted in May 1985 were kept at the lab for 3 months between receipt and analysis. According to the residue transfer study in laying hens (PP#7F3488, MRID No. 400279-14), the experimental period began in April 1985 and ended in May 1985. The report is dated January 1986.

In the poultry storage stability study now submitted ("PP321: Storage Stability in Frozen Poultry Tissues and Eggs," PP#7F3488, MRID No. 404461-03), samples from the feeding study which was conducted in April and May 1985 were reanalyzed 2 years after the original analyses. No significant change was observed in residues in eggs and poultry tissues stored at -18 °C for 2 years.

Deficiency No. 5 is resolved. Adequate storage stability data are available on poultry.

RCB's Deficiency No. 6a

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

Petitioner's Response to Deficiency No. 6a

The documents (1) SOP/R/028, (2) SOP/R/017, and (3) GRAM-4 were submitted in connection with PP#6F3318 (Reference 5D, Accession No. 073092, dated October 24, 1985). GRAM-4 was replaced by SOP/R/017.

SOP/R/014 calls for freezing samples immediately after harvest. If samples cannot be frozen within 2 hours of harvest, they must be chilled with ice until they can be frozen.

All 1983 soybean samples reported in ICI Report No. TMU1490/B (MRID No. 400279-08) were frozen when received at ICI's Biological Research Center (BRC), except for trial No. 45AL83-072 which was cold but not frozen. All 1984 and 1985 soybean samples reported in ICI Report No. TMU 1991/B (MRID No. 400279-09) were received frozen at BRC.

RCB's Discussion/Conclusion No. 6a

According to SOP/R/017, samples are checked upon arrival to see that they are frozen. Samples are stored at -10 °F before and after processing (i.e., grinding, mixing, etc.). Samples are packed in dry ice for shipping.

GRAM-4 instructs that samples which are received are to be ground, mixed, put in bags, and stored at -10 °F. Samples to be shipped are packed in dry ice.

Deficiency No. 6a is resolved.

RCB's Deficiency No. 6b

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

Petitioner's Response to Deficiency No. 6b

ICI Report No. TMU 1490/B (MRID No. 400279-08) and ICI Report No. TMU 1991/B (MRID No. 400279-09) report the analyses of controls.

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RCB's Discussion/Conclusion No. 6b

MRID Nos. 400279-08 and 400279-09 contain control values for the eight soybean residue studies conducted in 1983 and the eight soybean studies conducted in 1984, respectively. All control values are < 0.01 ppm for each of PP321 and its enantiomer R157836. No control data have been submitted for the seven studies conducted in 1985.

RCB concludes that adequate control data have been supplied since data for 16 studies are available.

Deficiency No. 6b is resolved.

RCB's Deficiency No. 6c

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.

Petitioner's Response to Deficiency No. 6c

For the residue trials of Karate on soybeans (MRID Nos. 400279-08 and 400279-09), ICI Methods No. 70 and 81 were the same. Both methods can detect PP321 and its enantiomer R157836.

RCB's Discussion/Conclusion No. 6c

As discussed under Conclusion No. 4b, recoveries from soybeans of the enantiomer R157836 using Method No. 70 are satisfactory. Method Nos. 70 and 81 are similar.

A satisfactory MTO for PP321 on soybeans has been conducted.

Deficiency No. 6c is resolved.

RCB's Deficiency No. 6d

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.

Petitioner's Response to Deficiency No. 6d

The petitioner refers to his responses to EPA Conclusions 3c, 4a, 4b, 5, 6a, 6b, and 6c.

RCB's Discussion/Conclusion No. 6d

No residues of PP321 or its diastereomer were detected (< 0.01 ppm) in any sample of soybeans treated at 1.2X or 5X (PP#7F3488, S. Brooks, August 13, 1987).

RCB concludes that no processing study is needed since no detectable residues were found at the 5X treatment rate.

Deficiency No. 6d is resolved.

RCB's Deficiency No. 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.

Petitioner's Response to Deficiency No. 7

The petitioner refers to his responses to EPA's Conclusions 3c, 4a, 5, 6a, 6b, and 6c.

RCB's Discussion/Conclusion No. 7

RCB concludes that the tolerances proposed in PP#7F3488 and PP#6F3318 of 0.01 ppm for parent per se in meat, fat, and meat by-products of cattle, goats, hogs, horses, poultry, and sheep, and milk are adequate to cover the proposed use on soybeans.

However, a revised Section F should be submitted which lists soybeans and all of the above proposed tolerances and also a 0.01 ppm tolerance on eggs.

Deficiency No. 7 is not resolved. A revised Section F should be submitted which proposes tolerances for soybeans, eggs, and the other animal commodities as follows:

<u>Commodity</u>	<u>ppm</u>
Soybeans	0.01
Meat of cattle, goats, hogs, horses, poultry, and sheep	0.01
Fat of cattle, goats, hogs, horses, poultry, and sheep	0.01
Meat by-products of cattle, goats, hogs, horses, poultry, and sheep	0.01
Milk	0.01
Eggs	0.01

Other Considerations

An International Residue Limit Status sheet is attached to RCB's review of PP#7F3488 dated August 13, 1987. No Codex, Canadian, or Mexican tolerances or limits have been established for Karate on soybeans and poultry. Therefore, there are no compatibility problems with respect to Codex.

cc: RF, SF, PP#7F3488, FDA, Circu, Reviewer-N. Dodd, TOX,
PM #15, PMSD/ISB-Eldredge
RDI: JHOnley:03/03/88:RDSchmitt:03/03/88
TS-769:RCB:CM#2:RM810:X1681:N.Dodd:Kendrick & Co.:03/08/88

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