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

APR 16 1991

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#7F3560 /7H5543. KARATE® Insecticide (Lambdacyhalothrin or PP321 in/on Wheat, Sweet Corn & Sunflowers. Amendment of 12/13/90. Response to DEB Review of 8/15/90.

MRID #'s 417262-01, -02. DEB # 7510.

FROM: Michael T. Flood, Ph.D., Chemist
Tolerance Petition Section II
Chemistry Branch I -- Tolerance Support
Health Effects Division (H7509C)

Mike Flood

THROUGH: Richard D. Schmitt, Ph.D., Chief
Chemistry Branch I -- Tolerance Support
Health Effects Division (H7509C)

R. Loranger for

TO: G. LaRocca/A. Heyward, PM 15
Herbicide-Insecticide Branch
Registration Division (H7505C)

and

Toxicology Branch I
Health Effects Division (H7509C)

This submission is a response to the CBTS (formerly DEB) 12/13/90 review of ICI's wheat metabolism study.

ICI is proposing tolerances for residues of lambdacyhalothrin [(±)-alpha-cyano-(3-phenoxyphenyl)-methyl (±)-cis-3-(Z-2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate] in or on the following commodities:

Wheat Grain	0.01 ppm
Sweet Corn	0.01
Sunflower Seeds	0.03
Poultry Meat, Fat and Meat Byproducts	0.01
Sunflower Hulls	0.07
Sunflower Oil	0.05

1

Summary of Deficiencies Remaining to Be Resolved

Metabolism data on wheat straw incomplete.

Conclusions

1a. The nature of the residue in wheat straw is not adequately understood. Data from Plot B, reflecting two applications at 0.2 lb ai/A and harvest 85 days after the last application have not been submitted. Since the Plot B application scheme most nearly approximates the proposed application scheme, such data are necessary.

1b. The data on wheat foliage that have been submitted show that lambdacyhalothrin + isomers is the principal constituent of the residue.

Recommendation

CBTS does not recommend that the proposed tolerances for residues of lambdacyhalothrin on wheat, sweet corn and sunflowers be established for the reason given in Conclusion 1a.

Detailed Considerations

Deficiencies in our 8/15/90 memo will be given along with ICI Americas' responses and CBTS's comments.

CBTS Deficiency #1 (Conclusion #1 from our 8/15/90 memo).

DEB is unable to conclude the adequacy of the submitted wheat metabolism study at this time.....

This deficiency has six subsections. These will be individually listed with our comments.

1a. The term "ear emergence" needs to be refined.

ICI Response

This and the other ICI responses appear in the following report:

"ICI Response to the August 15, 1990 DEB Review of the Lambda-Cyhalothrin Metabolism Study in Wheat Grain," J.P. Leahey and C.A. Smith, 12/90. (MRID # 417262-01)

Ear emergence is the emergence from the leaf sheath of the part of the plant which eventually forms the seed head. The spraying was timed to avoid any direct spray into the seed head

so that this part of the experiment would measure the levels of translocated radioactive residue into the grain.

CBTS Comment

Deficiency 1a has been satisfied.

1b. The total recovered radioactivity on wheat grain was obtained by summing the counts in the solvent extracts and combustion analysis on the residue after extraction. In order to demonstrate that activity was not lost during the extraction process, combustion data on the harvested wheat grain samples prior to any fractionation manipulation must be provided.

ICI Response

The total radioactive residue in grain samples was measured by extracting a subsample with hexane and then acetonitrile, or with acetonitrile and then acetonitrile/water, at ambient temperature. The liquid extracts were then separated from the solid by centrifugation and the radioactivity in the extracts was measured prior to any concentration or other "work-up" procedure on the extracts. ICI believes that radioactivity cannot be lost during such a procedure. The radioactivity in the solid was then measured by combustion. Work-up procedures in which radioactivity might be lost were carried out subsequent to this total radioactivity measurement.

CBTS Comment

As ICI correctly notes, our "Overview of Residue Chemistry Guidelines", dated 10/10/89, addresses this issue for those samples where the residue is not evenly distributed or which have a high water content and concludes that a procedure such as ICI's is acceptable. We agree with ICI that its procedure would not result in significant losses of radioactivity. This deficiency is resolved.

1c. Wheat plants in plot A and plot B were twice sprayed with acid label PP321 or alcohol label PP321, both on the same days and at the same growth stages. The total amounts applied were virtually the same (0.373 or 0.383 lb ai/A to plot A versus 0.373 lb ai/A to plot B). Wheat grains from plot B were allowed to mature and were harvested 85 days after the second application whereas wheat grains from plot A were not allowed to mature and were harvested 14 days later. Thus, a higher level of radioactivity would be expected in the immature grains harvested soon after treatment (14 days PHI) from plot A. Yet the results indicate that there is an increase in the acid label experiment (0.002 ppm

3

vs 0.018 ppm).

ICI's Response

The experiment was designed so that Plot A and Plot B grain would contain only translocated residues in that the ear (seed head) had not emerged at the time of spraying. Therefore, the grain samples harvested 85 days after treatment would have had more time for translocated residues to have moved to the grain. Thus if residues do translocate, a higher residue would be expected after 85 days compared with 14 days.

CBTS Comment

ICI's response is plausible. In any event the levels found were very low. This deficiency is resolved.

1d. The total amounts of PP321 applied to wheat plants in plot C were higher than those in plot B (1.43x acid label and 1.58x alcohol label). While higher levels of radioactivity would be expected from wheat plants in plot C because of a shorter PHI (30 days vs 85 days), the difference in the two levels seems excessive (7x in the acid label and 22x in the alcohol label).

ICI Response

Plot B grain did not come in direct contact with the test material because the immature grain was covered by the plant sheath. Plot C grain, however, did come in direct contact with ^{14}C-PP321. Therefore, higher residues would be detected in the Plot C grain.

CBTS Comment

ICI's response is plausible and related to responses in 1a and 1c. This deficiency is resolved.

1e. Wheat plants in plot B received 2 applications of P321, one prior to ear emergence and the second one at ear emergence. Data from plot B experiment showed substantial degradation of PP321 to cis acid Ia, trans acid Ib and hydroxylated acid XI when mature grains were harvested 85 days after the second treatment. Wheat plants in plot C received a third application in addition to the 2 treatments made on the same 2 days when PP321 was applied to plot B plants. Yet, residue analysis of plot C wheat grains showed only undegraded PP321 and cis acid Ia; the trans acid Ib and the hydroxylated compound XI were not detected.

4

ICI Response

Plot B was sprayed prior to seed head emergence. As noted above, the resulting residue represents metabolites which had translocated to the grain. Analysis of Plot B cyclopropane labeled grain showed extremely low levels of Metabolite Ib (0.00027 ppm) and Metabolite XI (0.00045 ppm). These residues were generated in the organosoluble fraction, 65% of which was generated by acid hydrolysis. The residues therefore resulted primarily from conjugates.

Characterization of these low levels was difficult and could be achieved only after applying low levels of radioactivity onto a TLC plate (to minimize interferences with co-extractives) and exposing X-ray film for 3 months. When grain from plot C was analyzed, the residue was dominated by parent. The organosoluble fraction resulting from acid hydrolysis represented only 2.8% (0.004 ppm) of the total radioactive residue. This fraction was dirty, and because of the low level, no further characterization was attempted. Hence the fraction that would have contained metabolites Ib and XI was not analyzed.

CBTS Comment

As stated in our "Overview of Residue Chemistry Guidelines", such low levels as found in the study do not require extensive characterization. This deficiency is resolved.

1f. Data thus far indicate that PP321 degrades extensively 85 days after application (Plot B experiment). In the acid label experiment, the only analyzed fraction (Fraction U) represents ca 18% of the TRR in wheat grain. Other terminal fractions include: a dichloromethane fraction containing 2.2% TRR, acid fraction (56.6%) and solid residue fraction (10.6% ....) and TLC analysis data were not provided for these 3 fractions. Since activity in the "acid fraction" accounts for more than 50% of the TRR in grain, the registrant should provide TLC analysis on this fraction. Attempts should also be made to identify or characterize the component(s) in this fraction.

ICI Response

Data from the plot B experiment do not show that PP321 degrades extensively during 85 days. It shows that only low residues of cyclopropane labeled metabolites can translocate into the grain.

Although the activity in the acid fraction accounts for more than 50% of the TRR, this fraction represents a residue of 0.01 ppm, so according to the EPA guidance document further analysis

is not required. ICI emphasizes that the fraction has been partially characterized -- it is water soluble and cannot be rendered organosoluble by acid hydrolysis. The hydrolysis product was so "dirty" that the resulting sample was virtually impossible to analyze by TLC.

CBTS Comment

It would be more accurate to say that the activity found in wheat grain represents metabolized lambdacyhalothrin, but because translocation is minimal only a small fraction of the applied lambdacyhalothrin is metabolized.

We agree that for the low levels of total residue encountered, additional characterization is not required. This deficiency is resolved. It should be noted that the total applications in the metabolite study were 0.37-0.39 lb ai/A. The proposed maximum use level for winter wheat is 0.02 lb ai/A/season.

1g. Wheat straw may be fed to livestock and is a major feed item. Metabolism data on wheat straw need to be provided.

ICI Response

ICI has submitted the following study:

"Lambda-Cyhalothrin: Quantification and Characterisation of Radioactive Residues in Foliage from Wheat Treated with ^{14}C-Lambda-Cyhalothrin," J.P.Leahey and S.J. Grout, 11/29/90, Laboratory Project ID 88JH144. The study was carried out at ICI Agrochemicals' laboratory in Bracknell, Berkshire, UK. (MRID # 417262-02)

^{14}C-cyclopropane-labeled and ^{14}C-phenyl-labeled lambda-cyhalothrin were applied to separate plots of winter wheat. Three different application schemes were used:

Plot A: Two spray applications were made at a rate of 0.2 lb ai/A. The first at crop emergence; the second just prior to ear emergence 6 1/2 months later. The wheat was harvested immature 14 days after the second application.

Plot B: Radiochemicals were applied using the same spray regime as for Plot A. The wheat was left to mature and harvested 85 days after the second application.

Plot C: Radiochemicals were applied three times at a rate of 0.2 lb ai/A. The first two applications were

at the same dates as Plots A and B; the third application was made 30 days before maturity. The wheat was harvested 30 days after the last application.

Characterization

Plot A.

^{14}C-Phenyl Label. Representative subsamples of foliage were extracted with acetonitrile, then acetonitrile:water (1:1, v/v), and extracts were combined. By summing the radioactivity in the extracts and the solid residual, the total radioactive residue was determined to be 1.81 mg/kg (as lambda-cyhalothrin). (The fractionation scheme appears as Figure 2 of the report.)

The combined extracts were acidified and partitioned with dichloromethane. 92.7% of the total radioactive residue (TRR) appeared in the dichloromethane fraction. Two dimensional TLC showed that almost all of the radioactivity (96.7%, 89.6% of TRR) was due to lambda-cyhalothrin + isomers. The solid fraction was combined with the aqueous fraction from the dichloromethane partition and refluxed for 2 hours in 2 M HCl. After filtering, the remaining solution was partitioned with dichloromethane (1.6% of TRR). Two dimensional TLC of this fraction showed two polar unknowns comprising 40.3% and 38.5% of the fraction. 3-Phenoxybenzoic acid and 3-phenoxybenzyl alcohol were present at 4.5% and 4.8%, respectively.

^{14}C-Cyclopropane Label. The fractionation scheme (Figure 5 of the report) was slightly different from that for the ^{14}C-phenyl-labeled residue. Total radioactive residue in the foliage was found to be 0.451 mg/kg.

Just as for the ^{14}C-phenyl-labeled residue, lambda-cyhalothrin + isomers was the major constituent, comprising 91.0% of TRR. Refluxing in acid to release conjugates was not carried out.

Plot B.

Plot B data are not present in this report. Since the proposed label in PP#7F3488 specified a PHI of 12 weeks for lambda-cyhalothrin when used on winter wheat and the PHI used in the Plot B studies was 85 days, this study is the most relevant of the three. Metabolism data should be submitted. (We would expect that percent parent in TRR would be significantly lower.)

Plot C.

^{14}C-Phenyl Label. The fractionation scheme is given in Figure 7 of the report. The total radioactive residue amounted

7

to 7.95 mg/kg. Samples of straw were first extracted with hexane, then with acetonitrile. Lambda-cyhalothrin + isomers from both extracts comprised 78.5% of TRR. Solid residue remaining was successively extracted with acetonitrile:1M HCl (1:1,v/v), 2M HCl (reflux 2 hrs.) and 6M HCl (reflux 4 hrs.). Extracts were partitioned with dichloromethane. (The resulting aqueous phases were combined with the remaining solids and extracted with the next stronger acid.) An additional 1.5% of parent was released giving a total parent concentration of 80.0% of TRR. An additional 2.6% of TRR consisted of 3-phenoxybenzoic acid and 4-hydroxy-3-phenoxybenzyl alcohol.

^{14}C-Phenyl Label. The fractionation scheme was identical to that for the ^{14}C-phenyl label. The total radioactive residue amounted to 10.00 mg/kg. (Table 22, page 55 refers to a total radioactive residue in grain. This is an error.) As in the ^{14}C-phenyl-labeled residue, lambda-cyhalothrin + isomers was the principal residue, constituting 83.8% of TRR. A total of 1.9% of TRR was comprised of (1RS)-cis-3-(ZE)-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid, which results when the ester linkage in parent is cleaved; its trans isomer; and cis-3-(2-chloro-3,3,3-trifluoroprop-1-enyl_2-hydroxymethyl-2-methylcyclopropanecarboxylic acid, related to the first ester cleavage product but with one of the methyls attached to the cyclopropane ring replaced with a hydroxyl group.

We conclude that the residue from Plots A and C has been satisfactorily characterized. The principal component of the residue is parent. However, we cannot say that the nature of the residue in wheat straw has been adequately understood until data from Plot B have been submitted. This deficiency remains.

cc: Circu., RF, SF, PP#7F3560/7H5543, MikeFlood, E.Haeberer, PIB/FOD.
H7509C:CBTS:Reviewer(MTF):CM#2:Rm800A:557-4362:typist(mtf):4/10/91
RDI:SectionHead:ETHaeberer:4/10/91:BranchSeniorScientist:RALoranger: 4/10/91.

8