241414
RECORD NO.

128897
SHAUGHNESSEY NO.

REVIEW NO.

EEB REVIEW

DATE: IN 3-13-89 OUT 3/3/89

FILE OR REG. NO 10182-96

PETITION OR EXP. NO.

DATE OF SUBMISSION 2-28-89

DATE RECEIVED BY EFED 3-9-89

RD REQUESTED COMPLETION DATE 4-17-89

EEB ESTIMATED COMPLETION DATE 4-17-89

RD ACTION CODE/TYPE OF REVIEW 570

TYPE PRODUCT(S) : I, D, H, F, N, R, S Synthetic Pyrethroid

DATA ACCESSION NO(S). 410161-1

PRODUCT MANAGER NO. G. LaRocca(15)

PRODUCT NAME(S) Karate 1E

COMPANY NAME ICI Agricultural Products Inc.

SUBMISSION PURPOSE Submission of further data concerning fish life cycle study

SHAUGHNESSEY NO.	CHEMICAL, & FORMULATION	% A.I.
	Lambdacyhalothrin	

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

MAR 3 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Review of Second Interim Report of Fish Life-Cycle Study on Lamdacyhalothrin (Karate-PP321)

FROM: James W. Akerman, Chief
Ecological Effects Branch
Environmental Fate and Effects Division (H-7507C)

TO: George LaRocca, Product Manager 15
Insecticide and Rodenticide Branch
Registration Division (H-7505C)

The Ecological Effects Branch (EEB) received the second interim report on the fish life-cycle study on March 9, 1989, and has had personal communications with Dr. John Tapp, author of this study on March 15, 1989. EEB has completed the review, and is recommending that the final report include the following:

1- Since the juveniles had started spawning more than 8 weeks before the adults were divided into pairs, the study authors should clearly indicate at what point, specifically day of study, the eggs used for the second generation embryo-larvae study were taken for each replicate.

2- The number of normal larvae at hatching for each incubation cup should be reported.

3- The growth and deformities of fish at end of 4 and 8 week exposure periods in each replicate growth chamber should be reported.

4- Survival and deformities of fish at the time of selection for paired spawning; growth and sex of discarded fish not selected for spawning; survival growth and deformities of male and female fish at end of spawning test period in each duplicate spawning tank should be reported.

5- In addition to the number of eggs per spawn, the total number of eggs by each pair of adults in individual spawning chambers along with the mean number of eggs per female for the two replicates should be reported. It should be noted that the number of eggs reported should be from the time the pairs were put into their separate breeding compartments until test

2

termination, since before that point the numbers of eggs per female would be unattainable with all the fish grouped in the adult spawning chambers.

Also, the number of fish per growth chamber from week 12 until separation into breeding compartments should be reported on a daily basis, per chamber, even though the study authors were not capable of sexing the fish at that point.

6- The hatchability per batch should be reported per individual test chamber.

The data (raw and summary) should be reported for individual incubation cups, growth chambers, spawning chambers, and individual breeding compartments, for statistical analysis purposes.

In addition, EEB was questioning why the fathead minnow started spawning so early, since it is typical that these fish do not spawn until week 20-24 after hatch(personal communications, Al Jarvinin, EPA Laboratory, Duluth, MN 3/13/89). The data indicate that spawning initiated week 12 of the study. This masks the delay in spawning that is evident in Figure 1 of the second interim report. We have since learned that the study authors have maintained the study at a constant day-length of 16 hours light and 8 hours dark. Dr. Tapp indicated that the day-length period was causing the early spawning.

EEB is recommending that future fish life cycle studies use the photoperiod which replicates Evansville, Indiana, which allows for a 5 month pre-spawning period. Please refer to the following protocol:

Benoit, Duane. 1982. User's Guide for Conducting Life-Cycle Chronic Toxicity with Fathead Minnows (Pimephales promelas). Environmental Research Laboratory Duluth, MN, EPA-600/8-81-011.

All the raw data must be submitted along with the final report. In addition to expedite the review, we recommend sending the data on 5 1/4 " floppy disks, formatted for IBM and compatible PCs, using the Lotus 1-2-3 software.

With regards to the second set of ICI responses that were submitted along with the second interim report, EEB is awaiting the final report before determining if the deviations from the protocol significantly detract from the study's scientific soundness.

If you have any questions, please feel free contact Candy Brassard (703) 557-0019.

Agricultural Products

Hand Delivered

February 28, 1989

ICI Agricultural Products Group
Wilmington
Delaware 19897
Telephone (302) 479-8000
Telex 4945649
Fax (302) 479-8553

Mr. George T. LaRocca
Product Manager 15
Insecticide-Rodenticide Branch
Registration Division (TS-767C)
U.S. Environmental Protection Agency
Crystal Mall 2, Room 204
1921 Jefferson Davis Highway
Arlington, VA 22202

Dear Mr. LaRocca:

Re: Karate 1E Insecticide (EPA Reg. No. 10182-96)
PP321 Fish Life-Cycle Study

The submission of a PP321 fish life-cycle study is a condition of registration for Karate 1E Insecticide. The in-life portion of this study is now complete, and a copy of the second progress report is enclosed. The final report is due to the Agency by August 1990.

Enclosed is the EEB review of April 29, 1988 regarding the PP321 fish life-cycle study. On July 21, 1988, ICI submitted a response to the reviewer's comments as well as the first interim report. Enclosed is a second response to the reviewer's comments and the second interim report for the above referenced study. Please note that the second interim report includes significantly more data and better addresses the concerns mentioned in the April 1988 EEB review.

As indicated in the enclosed response, ICI believes that it has satisfactorily addressed all the reviewer's comments with the exception of one. The remaining concern, i.e. analysis of fish tissues, is in progress and will be fully addressed in the final report.

If after review of the above EEB has remaining concerns, ICI wishes to meet with the Agency to discuss and resolve the concerns. ICI wishes to tentatively schedule a meeting from 10:30 to noon on Friday, March 17. Mr. Adam Heyward has

4

indicated that the this time will be convenient for him. If it is not convenient for other members of the Agency, perhaps another time during the day would be convenient.

Individuals from ICI who will attend are Dr. John Tapp, the U.K. study director for the referenced study, Dr. Zim Punja, the U.K. Registration Manager for the Americas Region, Mr. Jim Wagner, the Wilmington EPA Registration Manager for PP321, and myself.

If after reviewing the enclosed documents there are no remaining EEB concerns, then a meeting will not be necessary.

I will call you by Tuesday, March 14 to discuss whether or not EEB has remaining concerns. This will allow time for the ICI meeting participants who will be returning to the U.K. to change their travel plans if necessary.

Thank you.

Sincerely,

Cynthia Ann Smith

Cynthia Ann Smith
Pesticide Regulatory Specialist

Enclosures

cc: C. Brassard
A. Heyward

SECOND ICI RESPONSE TO CONCERNS RAISED IN THE
EEB REVIEW OF APRIL 29, 1988
REGARDING THE PP321 FISH LIFE-CYCLE STUDY

Introduction:

ICI has received the attached EEB review of April 29, 1988 regarding the PP321 fish life-cycle study. On July 21, 1988, ICI submitted a response to the reviewer's comments and the first interim report for the PP321 fish life-cycle study. The in-life portion of the study is now complete and is reported in the attached second interim report. Please note that the second interim report includes significantly more data than the first interim report and better addresses the concerns mentioned in the April 1988 EEB review.

Concerns Expressed in the 4/88 Review and ICI Responses:

1. EEB Concern:

"ICI Americas Inc. proposes to use dechlorinated water as the dilution medium.

The levels of residual chlorine were reported to range from >4.0 ug/l to 9.0 ug/l. ASTM, 1980, recommends that the residual chlorine not exceed 3 ug/l. After reviewing Brungs, 1976, it appears that the reported level of residual chlorine is within the acceptable limits for the species being tested. Brungs, 1976, reported that the highest mean total residual chlorine (TRC) having no measurable effect was 0.014 mg/l (14 ug/l) for the fathead minnow. The study author should be aware the literature indicates that there is a narrow threshold by which adverse effects were noted and no adverse effects were seen, and indeed the TRC should be monitored. If adverse effects are noted in the control and/or solvent control, then the study may not fulfill data requirements."

ICI Response:

The total residual chlorine was monitored, and the results of the analyses are reported in section 3.2.1 of the enclosed second interim report. Also, please note that the data reported in the second interim report clearly

C

indicate that there were no adverse effects recorded for any of the various monitored parameters for either the dilution water control or the solvent control.

ICI concludes that EEB's concern is addressed by the second interim report.

2. EEB Concern:

"ICI proposes to reduce the number of eggs required to start from 200 to 80, so that there are only 20 instead of 50 embryos in each of the four initial replicates. The submitted study design does not coincide with EEB's recommended study design ...[as described in the SEP]. The proposal to reduce the number of embryos from 200 to 80 viable embryos at test initiation may effect the statistical sensitivity of the study. If the study results indicate a poor performance in the controls, then the study would not be acceptable and therefore, would not fulfill data requirements."

ICI Response:

ICI accepts that, in theory, increasing the number of replicates and the size of the sample tested may increase the statistical sensitivity of the study. However, ICI believes that the PP321 fish life-cycle study is scientifically sound and will provide sufficient data to be statistically valid.

Please note that the 8-week (56 days post-hatch) survival of the F0 larvae is summarized in section 3.7 and detailed in Table 3 of the second interim report. Please also note that the inter-replicate variability regarding the above survival rate was quite low.

The second interim report demonstrates that the survival of the F1 generation larvae is a more sensitive indicator of PP321 toxicity than is the survival of the F0 generation larvae. During the F1 generation phase of the study, the level of replication that is recommended in the SEP is followed, i.e. there were 2 test groups per replicate and 4 replicates per concentration.

The data reported in the attached second interim report clearly indicate that there was a good performance in the controls.

Again, ICI believes that the PP321 fish life-cycle study is scientifically sound and will provide sufficient data to be statistically valid.

3. EEB Concern:

"The study author should note that selection of viable embryos is only permitted at test initiation; from then on only random selection (including lethargic and deformed) should be used when the numbers of test organisms are reduced (when transferring into larval tanks, selected from breeding pairs)."

ICI Response:

Subsequent to the selection of embryos for the study, only random selection of test individuals was used in the study. Please note that section 2.1, paragraph 3 reads,

> "Sets of five eggs were randomly selected, microscopically examined for viability and placed in incubating cups by a stratified random assignment. This process was repeated until each of the 28 cups contained 20 randomly selected eggs."

Please also note that section 2.3, paragraph 2 reads,

> "25 larvae were selected at random from the two batches in each replicate were then released into the progeny tanks."

Please further note that section 2.3, paragraph 7, reads,

> "On 18 August 1988 (exposure day 149) perforated stainless dividers were placed in the adult tanks. These divided each tank into four equal sized breeding compartments. The fish were individually examined and where sexual characteristics could be discerned the fish were randomly paired (one male and one female per breeding chamber)."

Other than the initial selection of embryos, no additional selection of individuals were made within the course of the study. Other than the initial selection of embryos, each of the selections of individuals were random selections.

ICI concludes that EEB's concern has been addressed in the second interim report.

4. EEB Concern:

"Another disadvantage of the ICI test method design is that the test organisms are randomly selected at an earlier stage than the SEP recommends. With this test design, there are only two instead of four recommended larval tanks, therefore reducing the number of replicates by one-half."

ICI Response:

Please see the ICI response to item 2.

5. EEB Concern:

"...if the embryos are indeed less than 24 hours old, as recommended in the protocols, then it would be difficult to determine if the embryos are viable."

ICI Response:

The data presented in Table 2 of the second interim report document the reliability of the viability assessment. The lowest observed viability for all groups was 63 of 80, i.e. 79%. The viability of the controls was 68 of 80 (85%) and 70 of 80 (88%).

ICI concludes that the data adequately address this concern.

6. EEB Concern:

"Since the SEP Guideline clearly requires 200 embryos at initiation, EEB cannot concur on the proposed modifications in the study design."

ICI Response:

As the reviewer noted, the SEP is a guideline. Guidelines by their very nature provide guidance but do not set rigid rules. Deviations from the SEP therefore need to be

evaluated on a case-by-case basis. A deviation which can be supported on the basis of good science should not be cause for the rejection of a study.

The reviewer's comment can be better stated, "The SEP clearly recommends 200 embryos at initiation." ICI's comments above support the selection of 80 embryos rather than 200 embryos.

7. EEB Concern:

"The proposed study design must also include the evaluation of the second generation embryos and larval-juvenile exposure."

ICI Response:

Section 2.3, paragraphs 9-11 of the second interim report addresses the evaluation and exposure of the second generation larvae/juveniles. The report reads,

> "A total of 81 hatchability and 23 embryo-larval trials were completed (Tables 7 and 8).
>
> The embryo-larval tests terminated on post-hatch day 56 and measurements of individual fish larvae weight and length were recorded. No fish larvae were fed within 24 hours of weighing. The fish larvae from all the embryo-larval studies from each replicate tank were frozen after measurement and stored for subsequent residue analysis.
>
> ...The last of the embryo-larval studies terminated on day 312 (27 January 1989)."

Please also note that sections 3.12 through 3.15 of the second interim report summarize the data pertinent to the second generation individuals.

ICI concludes that this concern has been addressed in the second interim report.

8. EEB Concern:

"Again, as noted in EEB's review dated August 19, 1987,

residue analyses are recommended and considered important information. If the chemical is not measured (detected) below the effect concentration then the study will be rejected. Residue analyses are required to determine a correlation between body burdens and effect responses for each stage of growth of the fish. Without these data, it is impossible to determine when the fish accumulated the residue, and which life stage and/or tissue appears to be most critical. The mesocosm data submitted by ICI Americas Inc. does not include residue analyses of the fish."

ICI Response:

Tissue analyses were recently initiated and results will be included in the final report. Preliminary results made available subsequent to the writing of the second interim report indicate that the bioconcentration factor in adult fish is on the order of 1000-3000X. These preliminary data are consistent with expectations based upon earlier work.

ICI anticipates that this concern will be fully addressed in the final report.

9. EEB Concern:

"The proposed study must include as part of the reported results a no-observable-effect level and a low-observable-effect level."

ICI Response:

Please note that section 3.19 reports both the no-observable-effect level (NOEL) and the low-observable-effect level (LOEL). The NOEL was determined to be 0.06 ug/l nominal (0.029 corrected mean measured). The LOEL was determined to be 0.12 nominal (0.059 ug/l corrected mean measured).

ICI concludes that the second interim report addresses this concern.

Conclusion:

The concerns regarding the PP321 fish life-cycle study expressed in the EEB review of April 29, 1988 are addresses in the attached second interim report. The one remaining

concern, i.e. residues found in the fish tissues, will be addressed in the final report.

CAS
2/89

RECEIVED

JUN 7 1988

REGISTRATION & REGULATORY AFFAIRS DEPARTMENT

214356
RECORD NO.

122897
SHAUGHNESSEY NO.

REVIEW NO.

EEB REVIEW

1988

DATE: IN 2-12-88 OUT 4-27-88 APR 29

FILE OR REG. NO 10182-OA

PETITION OR EXP. NO.

DATE OF SUBMISSION 2/8/88

DATE RECEIVED BY HED 2-12-88

RD REQUESTED COMPLETION DATE 3-14-88

EEB ESTIMATED COMPLETION DATE

RD ACTION CODE/TYPE OF REVIEW 117

TYPE PRODUCT(S) : I, D, H, F, N, R, S Insecticide

DATA ACCESSION NO(S).

PRODUCT MANAGER NO. G. Larocca(15)

PRODUCT NAME(S) Karate (PP321)

COMPANY NAME ICI Americas, Inc.

SUBMISSION PURPOSE Fish Full Life Cycle Protocol review

SHAUGHNESSEY NO.	CHEMICAL, & FORMULATION	% A.I.
	Karate/PP321	

13

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

APR 29 1988

MEMORANDUM

SUBJECT: Review of Fish Life Cycle Protocol Modifications for Karate (PP321)

FROM: Candy Brassard
Ecological Effects Branch
Hazard Evaluation Divsion (TS-769-C) Candy Brassard 4-28-88

THRU: Douglas J. Urban, Head-Section
Ecological Effects Branch
Hazard Evaluation Division (TS-769-C) 4/29/88

THRU: James W. Akerman, Chief
Ecological Effects Branch
Hazard Evaluation Division (TS-769-C) 4/29/88

TO: George LaRocca, Product Manager-Team 15
Insecticide and Rodenticide Branch
Registration Division (TS-767-C)

On February 12, 1988, the Ecological Effects Branch (EEB) received the recommended modifications for a fish full life cycle study that is to be conducted on PP321 (also referred to as Karate or lamda cyhalothrin).

There are two recommendations that ICI Americas, Inc. requests be waived. They are as follows:

1) ICI Americas, Inc. proposes to use dechlorinated water as the dilution medium.

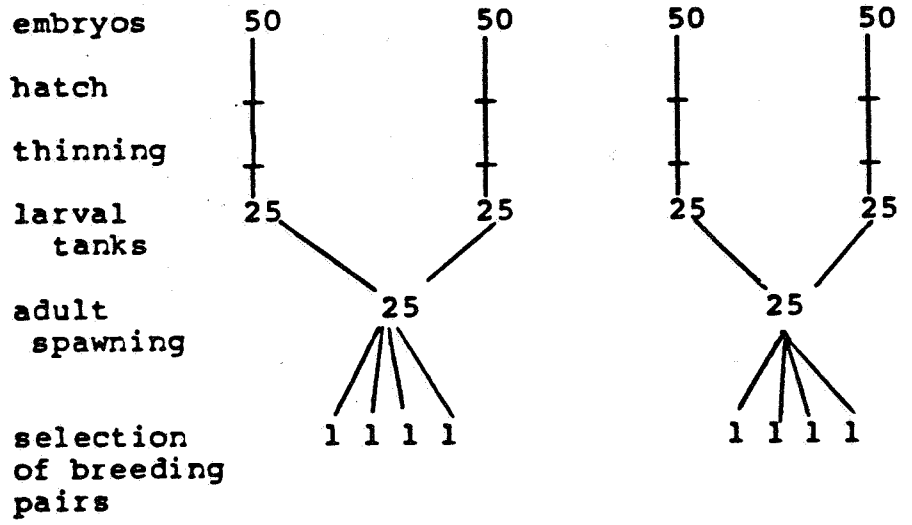
The levels of residual chlorine were reported to range from >4.0 ug/l to 9.0 ug/l. ASTM, 1980, recommends that the residual chlorine not exceed 3 ug/l. After reviewing Brungs, 1976, it appears that the reported level of residual chlorine is within the acceptable limits for the species

being tested. Brungs, 1976, reported that the highest mean total residual chlorine (TRC) concentrations having no measurable effect was 0.014 mg/l (14 ug/l) for the fathead minnow. The study author should be aware the literature indicates that there is a narrow threshold by which adverse effects were noted and no adverse effects were seen, and indeed the TRC should be monitored. If adverse effects are noted in the control and /or solvent control, then the study may not fulfill data requirements.

2) ICI proposes to reduce the number of eggs required to start from 200 to 80, so that there are only 20 instead of 50 embryos in each of the four initial replicates.

The submitted study design does not coincide with EEB's recommended study design. The following study design is recommended:

<u>According to SEP</u>



The proposal to reduce the number of embryos from 200 to 80 viable embryos at test initiation may affect the statistical sensitivity of the study. If the study results indicate a poor performance in the controls, then the study would not be acceptable and therefore, would not fulfill data requirements. The study author should note that selection of viable embryos is only permitted at test initiation, from then on only random selection (including lethargic and deformed) should be used when the numbers of test organisms are reduced (when transferring into larval tanks, selection for breeding pairs).

Another disadvantage to the ICI test method design, is that the test organisms are randomly selected at an earlier stage than the SEP recommends. With this study design, there are only two instead of the four recommended larval tanks, therefore reducing the number of replicates by one-half.

ICI Americas, Inc. states that one of the reasons for reducing the number of embryos from 50 to 20 is to reduce the chances for fungal infection. If this is the concern, we suggest that the number of replicates be increased so that you are not reducing the number of embryos per test concentration. Al Jarvinin (personal communications, Environmental Research Laboratory, ORD, Duluth, MN, 4/11/88) reported that 200 embryos are typically used in the full life cycle studies at the Duluth Lab. Another note, if the embryos are indeed less than 24 hours old, as recommended in the protocols, than it would be difficult to determine if the embryos are viable.

ICI did not completely quote the citation by Benoit, D.A., 1981. First, Benoit stated that another option was to reduce the number of embryos to 25 not 20, as stated by ICI. Secondly, the remainder of the sentence should have been quoted. The sentence reads as follows: "Another option to the above method would be to impartially reduce the embryos to 25 before hatching and release all larvae into the growth chamber after hatching." ICI is proposing to reduce the number into the larval tanks, not include all larvae into the growth chamber, as Benoit recommended.

Since the SEP Guideline clearly requires 200 embryos at test initiation, EEB cannot concur on the proposed modifications in the study design.

The proposed study design must also include the evaluation of the second generation embryos and larval-juvenile exposure.

Again, as noted in EEBs review, dated August 19, 1987, residue analyses are recommended and considered important information. If the chemical is not measured (detected) below the effect concentration then the study may be rejected. Residue analyses are required to determine a correlation between body burdens and effect responses for each stage of growth of the fish. Without these data, it is impossible to determine when the fish accumulated the residue, and which life stage and/or tissue appears to be most critical. The mesocosm data submitted by ICI Americas, Inc. does not include residue analyses of the fish.

The proposed study must include as part of the reported results, a no-observable-effect level and a low-observable-effect level. The study must not significantly deviate from the recommended guidance (SEP Guidelines and the recommended protocols) or the study may not fulfill guideline data requirements.

If there are any further questions, please feel free to contact EEB at any time.

CITATIONS

ASTM Standard E 729-80, Practice for Conducting Acute Toxicity Tests with Fishes, Macroinvertebrates, and Amphibians. American Society for Testing and Materials, 1916 Race Street, Philadelphia, PA 19103.

Benoit, D.A. (1981) User's Guide for Conducting Life Cycle Chronic Toxicity Tests with Fathead Minnows (Pimephales promelas). Environ. Res. Lab.-Duluth, Duluth, MN EPA- 600/8-81-011.

Brungs, W.A. (1976) Effects of Wastewater and Cooling Water Chlorination on Aquatic Life. Environ,. Res. Lab.-Duluth, Duluth, MN EPA-600/3-76-098.

Rexrode, M. and T.M. Armitage (1986) Fish Life Cycle Toxicity Tests. Hazard Evaluation Division, Standard Evaluation Procedure, U.S. E.P.A., Office of Pesticide Programs, Washington, D.C. 20460. EPA 540/9-86-137.