Shaughnessy No: 109702

Due Date: 9-9-85

Init:

AUG 26 1985

To: A. Heyward
Product Manager # 17
Registration Division (TS-767)

From: Joseph C. Reinert, Ph.D., Chief
Special Review Section
Exposure Assessment Branch
Hazard Evaluation Division (TS-769C)

Attached please find the EAB review of:

Reg./File No.: 10182-64

Chemical: Cypermethrin

Type Product: Insecticide

Product Name: Cymbush 3E

Company Name: ICI Americas

Submission Purpose: Review of letter submitted by ICI Americas.

Date In: 7-17-85

Date Completed: 7-22-85

ACTION CODE: 300

EAB # 5760

TAIS (level II)	Days
62	2

Deferrals To:

____ Ecological Effects Branch

____ Residue Chemistry Branch

_X_ Toxicology Branch

1.0 INTRODUCTION:

ICI Americas Inc. has requested an expedited reassessment of exposure during application of Cymbush to pecans. Three issues are involved. These are:

1. EAB's calculation of mixer/loader exposure based on surrogate data available in the literature rather than on an applicator exposure study (1) done by the registrant in support of the registration of the subject product on cotton.

2. ICI's proposal to modify the EAB linear regression line for exposure during air blast application (2) to fit the low application rates used for cypermethrin.

3. EAB's lack of determination of a yearly exposure because of lack of data from BUD (3).

EAB believes that although the original calculations for mixer/loader exposure were based on a valid surrogate, a more representative data base is now available. A study performed by the British Agrochemicals Association Ltd. (BAAL) (4), for the calculation of mixer/loader exposure for the other crops in our May 16 assessment can be applied to mixer/ loaders for cypermethrin and is more appropriate because it evaluates exposure in terms of mg/kg/lb handled rather than mg/kg/hour worked. Further, since it is true that the mixing and loading operation in the above ICI study is essentially the same as that used for application to pecans, we have reevaluated the potential exposure both using the BAAL study (4) and comparing it with the data from the ICI study (1).

With regard to the linear regression line, EAB does not agree with the manipulation of the data proposed, even though it is true that confidence limits at low application rates are less than desirable, and at zero application rate, obviously an applicator is not receiving any exposure from spraying. An examination of the data that were used in the data base indicates a level of exposure to hands that is higher than would be expected for applicators operating airblast equipment, and that this exposure may be independent of the application rate of the pesticide. Although the data do not reveal the source of this contamination, it is evident that the operation of the equipment involves handling spray nozzles and touching the sides of the tractor which is likely to hold a certain level of the chemical. Thus, even when the pesticide is not being applied, there is a potential for exposure to the applicator, and this is reflected in the linear regression line when it crosses the Y axis at 16.

Finally, the acquisition of new data from BUD (5) has allowed us to calculate the yearly exposure.

1.1 Chemical Formulation:

Cymbush 3E is ICI Americas' trade name for their 22.86% EC formulation of cypermethrin, a synthetic pyrethrin pesticide. Cypermethrin is + cyano(3-phenoxyphenyl)-methyl(+)cis/trans-3-2, 2-dichloroethenyl-2,2-dimethylcyclopropane carboxylate.

1.2 Application:

ICI is applying for use of Cymbush on pecans, as a supplemental label.

2.0 Issue 1: Mixer-Loader Exposure

EAB did not use the ICI study submitted November 13, 1984, for the May 16, 1985 determination of mixer/loader (M/L) exposure because the study in question was conducted to determine exposure for aerial application of a ULV oil formulation to cotton. Our general policy is that for a study to be applied to a specific registration, it must be designed to evaluate the use in question. Airblast application to pecans is a different use than ULV oil applied aerially, and since the study includes proprietary information, it was not readily available for other exposure assessments.

Our concern at the time an exposure assessment was requested was to match the application method with an appropriate data base. As referenced in the May 16 report, we have various surrogate studies for mixer/ loaders, one of which was used in the earlier assessment.

However, the ICI study monitors the same formulation for pecans as for cotton, and the mixing operation is similar in this usage, except for the diluant (water rather than oil) and the amount mixed. Since there is a question on the surrogate used in the May 16 assessment, we have re-examined the exposure values reported in the ICI study and compared them with values obtained by using a different data base (4) as surrogate.

2.1 Comparison of Application Rates and Quantities Handled

Formulation: 22.86% EC, 3# a.i./gal concentrate

Proposed application to pecans (BUD, 3):

Application rate: 0.06-0.1 lb. a.i./A (ave = 0.08)

Pounds Handled per Mixing Operation:

5 A/tank x 0.1 lb/A (worst case) = 0.5 lb/tank, 6 tanks/day

Reported application to cotton (ICI, 1):

Application rate: 0.06 lb/A

Pounds Handled per mixing operation:

200 A/tank x 0.06 lb/A = 12 lb/tank, 12 tanks per day

(exposure values given for one mixing operation)

2.2 Comparision of Protective Clothing

Pecan Label: "Protective clothing" plus impermeable gloves, full face shield, rubber apron, rubber boots for mixer/loaders when handling or mixing. (Note: the label supplied to EAB at the time of our May 16 review specified nothing other than "protective clothing, face shield or goggles and impermeable gloves" for mixer/loaders).

Cotton Study: Tyvek coveralls including hood and gauntlets, plus nylon socks were used for sampling material, under "protective equipment" consisting of rubber apron, arm length rubber gauntlets, rubber boots, face shield. "Actual" vs. "potential" dermal exposure was determined by calculating the amount of pesticide impinging on the area of sampling material corresponding to a particular exposed area. "Potential" referred to all the sampling material, whether under protective equipment or not, while "actual" measured the area of hands alone or hands and forearms, under the rubber gauntlets.

Surrogate Study (4): Strentex 'Corovin' disposable overalls, Strentex 'Tyvek'gauntlets and white nylon socks were selected as dermal sampling media. Footwear consisted of either rubber boots or leather shoes, with the trouser legs worn outside the footwear. Thus the sampling media measured whatever pesticide impinged on the sampled area without protective equipment. It was assumed in our calculations that use of impermeable gloves reduced exposure 90%.

2.3 Discussion of Cotton Study Results

Variations in levels measured for both mixer/loaders and applicators are discussed at length in the study. Most are less than ten fold. In EPA's database, studies of mixing and loading a variety of pesticides show more variability than this, which seems to depend on the care taken by the worker to avoid spills. Further, the exposure levels measured are quite low for the amount of pesticide handled, and this would be expected considering the protective equipment used.

It should be noted that in the cotton study, protective equipment used included arm length rubber gauntlets, but the label for use of Cymbush 3E on pecans does not specify the length of the gloves. If a monitoring study is to be used, the protective clothing must correspond to the label specifications.

2.4 Re-evaluation of Exposure

In response to ICI's points, the following are the results for mixer/loader exposure reported in ICI's study and mixer/loader exposure calculated using the BAAL study (4) as surrogate.

In the BAAL study mixer/loader exposure was determined for 6 replicate operations for each of 3 operators, while ICI's study is based on 2 mixer/loaders each doing 3 replicate operations. The sampling materials measured the exposure with rubber gloves in the ICI study, and without gloves in the surrogate, and a 90% protection correction factor was applied for the surrogate calculations.

A. Surrogate Study (4):

Three different tank sizes were used in the study. One of the tanks required two fillings per replicate, while the others took one filling per replicate. The highest values were found for the tank that was filled twice during the sampling period, and these higher values are attributed to filling the tank twice.

The exposure to the mixer/loader in each was determined, in terms of mg/kg body weight per pound handled, and the mean and range of all 18 replicates were determined.

Mean Exposure to 2,4 D: 0.0085 mg/kg/lb handled

(Range: 0.0070-0.24 mg/kg/lb.)

B. Mixer/loader Exposure to Cypermethrin, from Surrogate Data:

Quantity Handled: 0.5 lb a.i./tank

0.0085 mg/kg/lb x 0.5 lb x 0.1 = 0.43 ug/kg/lb

(Range: 0.35 - 12 ug/kg/lb)

C. Mixer/loader Exposure According to ICI Study (1):

"Potential dermal" exposure: 0.12 $\pm$0.08 mg/kg cypermethrin

Converting: $\frac{0.12 \text{ mg/kg}}{2.2 \text{ lb/kg} \times 70 \text{ kg body weight}}$ = 0.79 ug/kg/lb

(Range = 0.19-1.7 ug/kg/lb)

"Actual dermal" exposure: 0.028 mg/kg cypermethrin

Converting: $\frac{0.028 \text{ mg/kg}}{2.2 \text{ lb/kg} \times 70 \text{ kg}}$ = 0.19 ug/kg/lb

(Range = 0.18-0.4 ug/kg/lb

3.0 Issue 2: Modification of the Linear Regression Line for Applicator Exposure During Airblast Application

EAB examined a number of studies to determine a correlation of applicator exposure during airblast application. The studies showed a definite correlation between exposure and application rate, and a linear regression line was derived that intersects the Y axis at 16

mg/hr for zero application rate. Modification of the linear regression line to intersect the dermal exposure axis at zero may be intuitively correct, but is not statistically correct. The points on the linear regression line have a known coefficient of variation associated with them and are meaningful. In particular, as discussed in the introduction, there is a real exposure value for applicators during performance of tasks other than the actual spraying, and this could account for the intersection of the line at 16 mg/hr.

If the company does not believe that the surrogate data are applicable in the range of their proposed use, they will need to perform a study on this use pattern, as we currently have no other data base on which to evaluate low level application rates. A detailed protocol for such a study must be approved by the agency prior to initiation of the study.

4.0 Issue 3: Yearly Exposure Rate

EAB has obtained further information from BUD on the yearly exposure (5).

4.1 Applicators:

At a rate of 5.2 acres per tank load, 28.6 minutes to spray one tank, and 6 hours per day spraying time, an applicator would be exposed to 0.8 mg/kg/day. Assuming 9 hours to treat a 98 acre orchard once and 5 treatments per year, probable rate according to ICI, the yearly exposure is 72 x 0.14 mg/kg/hr or 5.6 mg/kg per year. BUD estimates one treatment per year but performed their calculation of hours from the maximum of eight times per year permitted on the label, so the range is 1.3 - 10 mg/kg/year.

4.2 Mixer/Loaders:

A. Surrogate Calculation

At an annual application of 0.1 lb/acre and 98 x 8 acre-treatments per year, 78 pounds would be applied per year. These values agree with data in a memo from ICI (6). Using our surrogate value of 0.00043 mg/kg/lb applied , the exposure is 0.034 mg/kg body weight per year. This is the value recommended to Toxicology Branch for use in their risk assessment.

B. ICI Calculation

Using the ICI study the yearly dermal exposure rate is:

"Potential" = 0.00079 mg/kg/lb x 78.6 lb/year = 0.062 mg/kg/year

"Actual":

Hands and forearms = 000036 mg/kg/lb x 78.6 lb/year = 0.028 mg/kg/year

Hands alone = 0.00018 mg/kg/lb x 78.6 lb/year = 0.014 mg/kg/year

6

5.0 Conclusions:

1. The mixer/loader exposures found in the ICI study and corrected for the application rate for pecans are within the range calculated using the data in our newly available data base.

2. The exposure for applicators will not be revised by modifying the linear regression line resulting from the data in EAB's files.

3. The yearly application rate will be calculated for five applications per year with a range for 1-8 applications.

Therefore our estimate of exposure in Table 1 of the May 16 report can be revised as follows:

TABLE I

Exposure to Cypermethrin

MIXER/LOADER:	Unit Exposure ug/kg/lb	Annual Applic'n lbs/year	Yearly Exposure mg/kg/year
	0.43 (0.35 - 12)*	78	0.034 (0.027 - 0.94)

APPLICATOR:	mg/kg/hr	hrs/yr	mg/kg/year
	0.14	45 (9-72)	6.3 (1.3-10)

*Figures in parentheses denote range

NOTE: If the same person performs both tasks, these yearly exposures are of course additive. It is not clear, however, from the memo supplied by BUD (3) that this is the case.

Anne R. Keller

Anne R. Keller, Chemist
Special Review Section 2
Exposure Assessment Branch
Hazard Evaluation Division

REFERENCES:

1. Chester, G., and Hart, T.B., 1984. Cypermethrin - Dermal Exposure and Absorption in Workers During Ultra Low Volume Aerial Application of CYMBUSH 3E Formulation in Oil to Cotton. Submission to EPA in Support of Registration.

2. Reinert, J.C., and Severn, D.J., 1985. Dermal Exposure to Pesticides: The Environmental Protection Agency's Viewpoint. ACS Symposium Series.

3. Gross, William L., 1985. Memorandum to Anne Keller, EAB. Projected Parameters for Applicator Exposure for Applying Cypermethrin to Cabbage, Field Corn, and Sweet Corn, and Projected Parameters for Applicator Exposure for Applying Cypermethrin to Pecans.

4. British Agrochemicals Association Limited. 1983. Alembic House, 93 Albert Embankment, London, SE1 7TU

5. Gross, William L., 1985. Memorandum to Anne Keller, EAB. Review of ICI Americas Submission on Cypermethrin.

6. Kaminski, Barbara J. 1984. Letter to Timothy A. Gardner, RD. Cypermethrin: Applicator Exposure in Pecan Orchards.