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

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MAR 27 1984

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP#2F2623. Cypermethrin in/on cottonseed, meat and milk. Risk Assessment.

Tox. Chem. No. 271DD

TO: Tim Gardner, PM#17
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Budd 3/27/84

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W L Burnam 3-27-84

ICI Americas Inc. has proposed that tolerances be established for residues of the insecticide cypermethrin (parent only) as follows:

0.5 ppm in or on cottonseed

0.05 ppm in the meat, fat and meat byproducts of cattle, goats, hogs, horses and sheep

0.05 ppm in milk

Toxicity data submitted in support of this tolerance proposal has been reviewed by Toxicology Branch and on the basis of this and all other available toxicological data, it has been determined that there is sufficient evidence to conclude that, at a dosage level of 1600 ppm in the diet for a lifetime, cypermethrin exhibits a low oncogenic potential in female mice. See the attached document titled "Cypermethrin: Assessment of Chronic and Oncogenic Effects, A Summary" by John Doherty, Ph.D., dated March 1, 1984, for a discussion of the evidence and rationale which led to this conclusion. Accordingly, a risk assessment for the proposed use of cypermethrin on cotton was performed by Bertram Litt, Toxicology Branch statistician. This risk assessment is summarized below.

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Estimated Human Exposures to Cypermethrin

1. Dietary Exposure to General Population

Residue Chemistry Branch (see attached memorandum by John Onley, Ph.D., dated January 26, 1984) has stated that maximum residues of cypermethrin (parent plus metabolite) reported or calculated in or on the concerned raw agricultural commodities are as follows:

Commodity	Maximum Residue, ppm*	Proposed Tolerance, ppm
Cottonseed	0.45	0.5
Milk	0.002	0.05
Meat	0.007	0.05
Fat	0.049	0.05
Meat by-products	0.01	0.05

*Note that these are "actual residues", not the proposed tolerance levels.

Starting with these maximum residues, the contribution of residue in each commodity to the average daily dietary intake (for humans) was calculated by Toxicology Branch. For this purpose, the residues in meat, fat and meat byproducts were combined into a single commodity, red meat. The "representative maximum residue" for this commodity was chosen to be 0.01 ppm.

Commodity	Maximum Residue, ppm	x 1.5(1)	Average Daily Dietary Intake of Residue, mg/day(2)
Cottonseed	0.45	0.675	0.001013
Milk	0.002	0.003	0.000859
Red meat	0.01	0.015	0.001622
		Total	0.003494

(1) Correction factor for average total daily dietary intake of 1.5 kg for all foods.

(2) Calculated by multiplying by the "food factor" (average daily dietary intake of commodity, in percent; 0.15% for cottonseed (oil), 28.62% for milk (and dairy products), 10.81% for red meat).

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By dividing the average daily dietary intake of residue (0.003494 mg/day) by the average human body weight (60 kg), the average dietary exposure to residues, in units of mg/kg/day, is obtained.

$$\frac{0.003494 \text{ mg/day}}{60 \text{ kg}} = 0.000058 \text{ mg/kg/day "actual residues"}$$

In addition, starting with the proposed tolerance levels, the contribution of residue in each commodity to the average daily dietary intake (for humans) was also calculated in a similar manner.

Commodity	Proposed Tolerance, ppm	X 1.5	Average Daily Dietary Intake of Residue, mg/day
Cottonseed	0.5	0.75	0.001125
Milk	0.05	0.075	0.021465
Red meat	0.05	0.075	0.008108
		TOTAL	0.030698

and

$$\frac{0.030698 \text{ mg/day}}{60 \text{ kg}} = 0.000512 \text{ mg/kg/day "tolerance residues"}$$

2. Occupational Exposure to Cotton Field Workers -

Exposure Assessment Branch (see attached memorandum by Robert Hitch, dated March 2, 1984) has calculated annual exposure estimates to cypermethrin for cotton field workers as follows:

	Annual Exposures (mg/yr)			
	Typical Case		Range	
	Dermal	Inhalation	Dermal	Inhalation
For Aerial Application				
Mixers/Loaders(1)	960	negligible	20-4800	negligible
Pilots(2)	1.5	0.1	1-2	negligible - C
For Ground Application				
Mixers/Loaders(3)	420	negligible	8.3-2000	negligible
Applicators(4)	0.9	negligible	0.2-1.8	negligible - C
Total Ground(5)	420.9	negligible	8.5-2001.8	negligible - C

(1) Mixing cypermethrin with water for aerial application and loading it into the airplane.

(2) Pilot applying cypermethrin in water.

(3) Mixing/loading cypermethrin with water for ground application.

(4) Ground application of cypermethrin in water by tractor.

(5) It is assumed that applicators working from tractors do their own mixing and loading.

The following quotation is from the Exposure Assessment Branch memorandum referred to above (p. 6).

> "The Exposure Assessment Branch has no surrogate data for pesticides which have been aerially applied in oil. It is recommended that a field study be submitted to the Agency prior to further consideration of registration applications involving Ultra Low Volume (ULV) application of cypermethrin in oil. Of particular concern is the possibility that exposures to humans due to this use may differ substantially from the exposures expected for aqueous spray mixes."

Starting with the reported annual exposures (in mg/yr), average daily lifetime exposures were calculated by Toxicology Branch by dividing by 2 (adjustment for occupational exposure of one-half a lifetime), then by 365 days (to give mg/day) and then by 70 kg, average body weight of worker (to give mg/kg/day). When exposures were presented for both dermal and inhalation exposure, they were combined.

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	Annual Exposure, mg/yr	Average Daily Lifetime Exposure, mg/kg/day
For Aerial Application		
Mixers/Loaders		
typical case	960	1.9×10^{-2}
minimum	20	3.9×10^{-4}
maximum	4800	9.4×10^{-2}
Pilots		
typical case	1.6	3.1×10^{-5}
minimum	1.0	2.0×10^{-5}
maximum	2.17	4.2×10^{-5}
For Ground Application		
Mixers/Loaders		
typical case	420	8.2×10^{-3}
minimum	8.3	1.6×10^{-4}
maximum	2000	3.9×10^{-2}
Applicators		
typical case	0.9	1.8×10^{-5}
minimum	0.2	3.9×10^{-6}
maximum	1.9	3.7×10^{-5}
Total Ground(1)		
typical case	420.9	8.2×10^{-3}
minimum	8.5	1.7×10^{-4}
maximum	2001.9	3.9×10^{-2}

(1) Assuming applicators working from tractors do their own mixing and loading.

Calculation of Q_1^* (Multi-stage and One-Hit Models)

Q_1^* values were calculated utilizing the multi-stage and one-hit models, based on incidence data for lung tumors from the ICI-1982 mouse oncogenic study on cypermethrin. The dietary dosage levels in this study in ppm were adjusted to dosage levels in mg/kg/day by dividing by 7 and then to human equivalents by use of a surface area adjustment based on a 60 kg human weight and a 50 gm mouse weight. The Q_1^* for the multi-stage model (low-dose only) was 0.019. The Q_1^* for the one-hit model (all doses) was 0.018.

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Risks of Oncogenicity for Humans

The following table presents the calculated risks of oncogenicity for humans resulting from the application of cypermethrin to cotton. These risks were calculated by multiplying the average daily lifetime exposure for each group at risk by the Q_1^* value for the multi-stage model and separately for the one-hit model.

Estimated Human Exposures to Cypermethrin and Related Risks of Oncogenicity Calculated by Application of the Multi-Stage and One-Hit Models to Mouse Lung Tumor Data

Group at Risk	Average Daily Lifetime Exposure (mg/kg/day)	Multi-Stage Q_1^* = 0.019 (low dose only)	One-Hit Q_1^* = 0.018 (all doses)
General Population			
Dietary exposure			
"actual residues"	5.8×10^{-5}	1.1×10^{-6}	1.0×10^{-6}
"tolerance residues"	5.1×10^{-4}	9.7×10^{-6}	9.2×10^{-6}
Cotton Field Workers			
Aerial Application			
Mixers/Loaders			
typical case	1.9×10^{-2}	3.6×10^{-4}	3.4×10^{-4}
minimum	3.9×10^{-4}	7.4×10^{-6}	7.0×10^{-6}
maximum	9.4×10^{-2}	1.8×10^{-3}	1.7×10^{-3}
Pilots			
typical case	3.1×10^{-5}	5.9×10^{-7}	5.6×10^{-7}
minimum	2.0×10^{-5}	3.8×10^{-7}	3.6×10^{-7}
maximum	4.2×10^{-5}	8.0×10^{-7}	7.6×10^{-7}
Ground Application			
Mixers/Loaders			
typical case	8.2×10^{-3}	1.6×10^{-4}	1.5×10^{-4}
minimum	1.6×10^{-4}	3.0×10^{-6}	2.9×10^{-6}
maximum	3.9×10^{-2}	7.4×10^{-4}	7.0×10^{-4}
Applicators			
typical case	1.8×10^{-5}	3.4×10^{-7}	3.2×10^{-7}
minimum	3.9×10^{-6}	7.4×10^{-8}	7.0×10^{-8}
maximum	3.7×10^{-5}	7.0×10^{-7}	6.7×10^{-7}
Total Ground			
typical case	8.2×10^{-3}	1.6×10^{-4}	1.5×10^{-4}
minimum	1.7×10^{-4}	3.2×10^{-6}	3.1×10^{-6}
maximum	3.9×10^{-2}	7.4×10^{-4}	7.0×10^{-4}

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