001323

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

OFFICE OF TOXIC SUBSTANCES

MEMORANDUM

DATE: August 1, 1980

SUBJECT: Pirimicarb (4,5-Dimethyl-2-Dimethylamino-6-pyrimidinyl dimethylcarbamate) and all Registrations Petitions Related to its use. (PP#9F2235/9H5232; 9G2257/9H5238; 7F1915/9H5224; 9F2175; EPA Reg. Nos. 10182-7 and 10182-EUP-2) CASWELL #359 C

FROM: Robert B. Jaeger, Acting Section Head
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TO: Marilyn Mautz, PM #16
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Reference Toxicology Branch previous correspondence on this subject, review dated 2/22/80, R.B. Jaeger. Many of the questions and issues raised in that review were addressed and resolved in a meeting with ICI representatives on 6/30/80, (see report of meeting, 6/30/80, attached).

The important items extracted from that memo are as follow:

A. Rhesus Monkey - ICI will attempt to gather data which correlates a positive direct Coomb's Test with a viral infection in Rhesus monkeys. If this attempt fails, ICI agreed that it would have to repeat the 17 week Rhesus study.

B. Foxhound Study - ICI conceded that the same hemolytic effects occurred in Foxhounds as in Beagles. They will histopath the remaining spleen to clearly assess a finding of no adverse effects at 1.8 mg/kg/day.

C. Beagle Dog - EPA agreed with ICI that reassessment of the data relative to a reclassification of megaloblasts to proerythroblasts supports the finding of no adverse effects at 1.8 mg/kg/day.

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D. Plant Metabolite Studies in Rats - EPA stated the studies remain "Supplementary" but agreed with ICI that hypochromic anemia was not demonstrated.

E. Hydroxypyrimidine metabolites - ICI submitted a copy of the 2 year dog feeding study on ethirimol (PP#7F1941 report No. HO/IH/P/54, August 1972). Subject report resolves the toxicity questions relative to a similar hydroxypyrimidine structure (metab. VI) with a demonstrated NEL = 30 mg/kg. Therefore, Toxicology Branch does not consider the hydroxypyrimidine metabolites referred to by RCB, to be toxicologically significant.

Recommendations

Based on the above considerations Toxicology Branch recommends in favor of Conditional Registration in order for ICI to resolve the questions discussed and submitt the necessary data indicated in 1. and 2. above.

Review

1. Data Considered in Support of Pirimor 50W

Acute Oral LD50 (Rat) (Core-Minimum)	male - 200 mg/kg female - 173 mg/kg
Acute Dermal LD50 (Rabbit) (Core-Minimum)	greater then 1000 mg/kg
Primary Dermal Irritation (Rabbit) (Core-Minimum)	slight to mild edema and erythema
Primary Eye Irritation (Rabbit) (Core-Minimum)	mild (no corneal involvement)
Delayed Neurotoxicity (Hen) (Supplementary)	negative at highest dose of 25 mg/kg
Teratology (Rabbit) (Core-Minimum)	negative at 5 mg/kg
3-Generation Reproduction (Rat) (Core-Minimum)	no adverse effects on reproduction at 750 ppm (high dose) LEL is 250 ppm (growth depression in adult)

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Oncogenicity (Mouse) (Core-Minimum)	negative at highest dose of 1500 ppm
Mutagenicity-Dominant Lethal (Mouse) (Core-Minimum)	negative at the high dose (20 mg/kg/day)
2-Year Rat Feeding (Core-Minimum)	NEL 175 ppm (based on additional data submitted)
	LEL 250 ppm (growht depression); Not carcinogenic at 750 ppm (high dose)
2-Year Dog Feeding (Core-Minimum)	NEL 1.8 mg/kg;
	LEL 4.0 mg/kg based on hemolytic anemia and erythyropoiesis effects (substantiated by Foxhound study)
90/180-Day Dog Oral Dosing (Core-Minimum)	NEL 1.8 mg/kg (0.4 and 1.8 mg/kg for 90 days; 4.0 mg/kg for 180 days)
	LEL 4.0 mg/kg based on hemolytic anemia and erythropoiesis effects.

2. New toxicity data submitted is indicated in E. above (previously submitted in PP#7F1941, Ethirimol).

3. Tolerances established under 40 CFR 180.365.

4. Acceptable Daily Intake Data

2-Year Dog Feeding - NEL = 1.8 mg/kg/ (72 ppm)
S.F. = 100
ADI = 0.018 mg/kg/day
MPI = 1.08 mg/day/60 Kg

5. Published Tolerances (PP#5F1608)

Potatoes	-	0.1 ppm
food factor	-	5.43
TMRC	=	0.00814 mg/day/1.5 kg
% ADI	=	0.75%

Proposed Tolerances (PP#9G2199)

Pecans	-	0.05 ppm
food factor		0.03
TMRC	=	0.00002 mg/day/1.5 kg
% ADI	=	.0019%

Proposed Tolerances (9F2235/9H5232)

1.0 ppm - apples
0.05 ppm - cottonseed
2.0 ppm - apple pomace
2.0 ppm - apple pulp
0.2 ppm - cottonseed oil

Proposed Tolerances (9G2257/9H5238) EPA Reg. #10182-EUP-2

1.0 ppm - apples
0.05 ppm - cottonseed
0.5 ppm - cabbage
1.0 ppm - head lettuce
0.5 ppm - bell peppers
0.05 ppm - milk
0.05 ppm - meat, fat, meat by-products of cattle, goats, hogs, horses and sheep
0.05 ppm - poultry, eggs

2.0 ppm - apple pomace
2.0 ppm - apple pulp
0.2 ppm - cottonseed oil
2.0 ppm - cabbage wrapper leaves
2.0 ppm - lettuce wrapper leaves

Proposed Tolerances (7F1915/FAP 9H5224)

1.0 ppm - broccoli
0.5 ppm - brusel sprouts
0.5 ppm - cabbage
0.5 ppm - cauliflower
1.0 ppm - lettuce
2.0 ppm - peppers (chili)
0.5 ppm - peppers (bell)

20 ppm - brocoli trimmings
20 ppm - brussels sprouts trimmings
20 ppm - cabbage wrapper leaves
20 ppm - cauliflower trimmings
20 ppm - lettuce wrapper leaves

Proposed Tolerances (9F2175) EPA Reg. #10182-7

Alfalfa - 10 ppm fresh alfalfa; 50 ppm alfalfa hay
0.05 ppm - Pecans

All proposed tolerances could contribute 0.1122 mg/day/1.5 kg and utilize 10.39% of the MPI.

6. No regulatory actions are pending against the pesticide.

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ACCEPTABLE DAILY INTAKE DATA

Dog NOEL mg/kg	NOEL ppm	S.F.	ADI mg/kg/day	MPI mg/day/60kg
1.800	72.00	100	0.0180	1.0800

Publisned Tolerances

CROP	Tolerance	Food Factor	mg/day/1.5kg
Potatoes(127)	0.100	5.43	0.00814

MPI	TMRC	% ADI
1.0800 mg/day/60kg	0.0081 mg/day/1.5kg	0.75

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Current Action 9G2199,9F2235/9H5232,9G2257/9H5238,7F1915/9H5224,9F2175

CROP	Tolerance	Food Factor	mg/day/1.5kg	F FG PP's
Pecans(118)	0.050	0.03	0.00002	"
Apples(2)	1.000	2.53	0.03795	"
Cottonseed(41)	0.050	0.15	0.00011	"
bbage,sauerkraut(22)	0.500	0.74	0.00552	"
Lettuce(84)	1.000	1.31	0.01962	"
Bell Peppers(120)	0.500	0.12	0.00092	"
k&Dairy Products(93)	0.050	28.62	0.02146	G
Eggs(54)	0.050	2.77	0.00208	G
Meat,inc poultry(89)	0.050	13.85	0.01039	G
Broccoli(19)	1.000	0.10	0.00153	F
Brussel Sprouts(20)	0.500	0.03	0.00023	F
Cauliflower(27)	0.500	0.07	0.00054	F
Chil Peppers(120)	2.000	0.12	0.00368	F

MPI	TMRC	% ADI
1.0800 mg/day/60kg	0.1122 mg/day/1.5kg	10.39

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