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

DEC 15 1981

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: December 10, 1981

SUBJECT: PP#2F2595; Ronilan in/on Lettuce at 5.0 ppm
CASWELL#323C Accession#070455

FROM: William Dykstra, Toxicologist
Toxicology Branch/HED (TS-769)

WHD FDC 12/14/81
HFA OEP

TO: Henry Jacoby (21)
Registration Division (TS-767)

Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

Recommendations:

1) The requested tolerance can be toxicologically supported.

2) The following studies are currently lacking and are required to be submitted within a reasonable period of time:

a) 6-month (or longer) dog feeding study

Review:

1) Section F - Proposed Tolerance

This petition requests that a tolerance be established for residues of the fungicide 3-(3,5-dichlorophenyl)-5-ethenyl-5-methyl-2,4-oxazolidinedione and its 3,5-dichloroaniline - containing metabolites in or on the raw agricultural commodities as follows:

5 ppm ---------- lettuce

2) No new toxicity data submitted.

3) Previously reviewed toxicity data.

a. Memo of 4/17/78 from R. Gessert in PP#8G2068.

°Studies conducted with Formulation: Ronilan

°Rat Acute Oral LD_{50} > 16,000 mg/kg (both sexes)
°Rabbit Acute Dermal LD_{50} > 2000 mg/kg (both sexes)
°Rat Acute Inhalation LC_{50} > 1.7 mg/L for 4 hours

°Studies conducted with Technical

°Rat Acute Oral LD_{50} > 10,000 mg/kg (both sexes)
°Rat Acute Dermal LD_{50} > 2500 mg/kg (both sexes)
°90-Day Rat Feeding: NOEL = 450 ppm
°90-Day Dog Feeding: NOEL = 300 ppm
°Mouse Teratology: Negative at 600 ppm
°3-Generation Rat Reproduction: NOEL = 1458 ppm
°Dominant Lethal Assay in Mice: Negative at 2000 mg/kg for five days.
°Chronic Feeding/Oncogenicity in Rats for 103 Weeks: oncogenic potential: negative; NOEL = 486 ppm
°Chronic Feeding/Oncogenicity in Mice for 26 Months: oncogenic potential: negative; NOEL = 1458 ppm
°Metabolism: Repeated oral dosing in rats

4) Tolerances established under 40 CFR 180.380.

5) Evaluation of the provisional ADI (PADI).

An examination of the feeding studies conducted with the technical material shows that dog to be the most sensitive species for which feeding toxicity data are available.

Study	NOEL (ppm)	mg/kg/day
90-Day Dog	300	7.5
90-Day Rat	450	45.0
Chronic Rat	486	24.3
Chronic Mouse	1458	218.7

Therefore, a provisional ADI, using a 2000 fold safety factor, has been used.

$$PADI = NOEL \times \frac{1}{2000}$$

$$PADI = 7.5 \text{ mg/kg/day} \times \frac{1}{2000} = 0.0038 \text{ mg/kg/day}$$

The provisional MPI (PADI) is 0.2250 mg/day for a 60 kg person

6) Published tolerance utilize 14.26% of the PADI. Unpublished, Tox approved tolerances utilize the PADI to 32.25%. The current action utilizes 43.6% of the PADI. All tolerances utilize 75.85% of the PADI (computer printout attached).

Conclusions and Recommendations:

The oncogenic potential of the pesticide in two species (mouse and rat) is negative. The adverse reproduction potential is negative in the rat up to 1458 ppm and the teratogenic potential in one species (mouse) is negative at 600 ppm. The petitioner is currently undertaking the 6-month dog study which will be the basis for an ADI.

The 90-day dog study was conducted at 100, 300, 1000 and 2000 ppm.

At 1000 ppm (the LEL), an increase in thrombocytes occurred in the hematograms of female dogs. Differential blood counts showed Jolly Bodies. Histological investigations disclosed hepatic cholestasis.

The 6-month dog study will utilize a 1000 fold safety factor to calculate the ADI.

Given these considerations, the proposed tolerance can be toxicologically supported.

TS-769:th:TOX/HED:WDykstra:12-10-81:card 2

CFR 180.380 Ronilan 12/10/81

File last updated 12/10/81

ACCEPTABLE DAILY INTAKE DATA

Dog mg/kg	NOEL ppm	S.F.	PADI mg/kg/day	MPI mg/day(60kg)
7.500	300.00	2000	0.0038	0.2250

Published Tolerances

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Kiwi Fruit(204)	10.000	0.03	0.00450
Strawberries(152)	10.000	0.18	0.02759

MPI	TMRC	% ADI
0.2250 mg/day(60kg)	0.0321 mg/day(1.5kg)	14.26

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Unpublished,Tox Approved PP# 1E2457

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Grapes, not raisins(67)	6.000	0.45	0.04047

MPI	TMRC	% ADI
0.2250 mg/day(60kg)	0.0726 mg/day(1.5kg)	32.25

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Current Action PP# 2F2595

CROP	Tolerance	Food Factor	mg/day(1.5kg)
Lettuce(84)	5.000	1.31	0.09811

MPI	TMRC	% ADI
0.2250 mg/day(60kg)	0.1707 mg/day(1.5kg)	75.85

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