UNITED ST ES ENVIRONMENTAL PROTECTION ENCY

001802

DATE: January, 1978

SUBJECT: Request for tolerance for pesticide methazole and its metabolites in or on potatoes at 0.1 ppm. Pesticide Petition 7G 1950, Caswell No. 549AA.

FROM: John Doherty, Chemist (Biochemist) John Doherty
Toxicology Branch, Registration Division (WH-567) E 2/28/78

TO: Product Manager SRS

Petitioner: Velsicol Chemical Company
341 East Ohio Street
Chicago, Illinois 60611

Recommendations:

1. Toxicology Branch has no objections to granting an experimental use permit (EUP) for a tolerance for methazole at 0.1 ppm in or on potatoes.

2. This level of exposure will result in at most 6.4% of the PADI (see review, section F) when previously granted tolerance on onions and cottonseed oil are taken into consideration.

Remarks:

A. The following studies were performed by Industrial Biotest.

(1) A7163 (April 25, 1969) - Acute Oral LD_{50}.

(2) B7369 (November 10, 1969) - 90 day subacute oral rat.

(3) C7370 (November 19, 1969) - 90 day subacute oral dogs.

(4) 8533-08240 (~~November~~ oct. 14, 1976) - 3 generation reproduction, rat

(5) 8580-08238 (December 17, 1976) - Oncogenicity mice.

(6) 632-03373 (July 25, 1973) - Mutagencity.

(7) A7678 (September 23, 1969) - Acute Oral LD_{50}.

(8) A8037 (January 16, 1970) - Acute Dermal LD_{50}.

(9) A8037 (January 16, 1976) - Eye Irritation.

(10) A8037 (January 16, 1976) - Skin Irritation.

(11) A8037 (January 16, 1976) - Aerosol Toxicity.

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iii. No changes considered to be compound related were seen in any of the parameters measured except that spleen weights of female rats at the 300 and 450 ppm levels and kidney weights of female rats at 450 ppm dietary level had statistically significant increases over control values.

iv. CORE minimal. NEL 150 ppm.

5. Ninety-day Oral Subacute Toxicity Study in Dogs with 1-(3,4-dichlorophenyl)-urea.

i. IRDC, 163-157, 1/26/73.

ii. Four male and four female beagle dogs were fed 0, 25, 75, 150 and 300 ppm of 1-(3,4-dichlorophenyl)-urea for 90 days.

iii. Only one possible compound related effect of this metabolite was observed. Microscopically, the occurance of brown pigment in hepatic Kupffer cells in 1 of 8 dogs from the 300 ppm dietary level. All other parameters, biochemical, urinalysis, or necropsy were within normal limits.

iv. [illegible] minimal, NEL 150 ppm.

6. Teratology with Metabolites of Metazole.

i. ✓ 1 [illegible].4-dichlorophenyl)-3-methyl urea; IRDC, 163-158 1/29/73.

[illegible]-(3,4-dichlorophenyl)-3-methyl urea; IRDC, 163-159, 3/2/73.

✓ 1-(3,4-dichlorophenyl)-urea; IRDC, 163-160, 12/29/72. DCPMU

ii. Four rabbits per groups were treated with 0, 5, 10, 20 30 and 50 mg/kg/day of DCPM. Four rabbits per group were treated with 0, 10, 20, 30, 50, 80 mg/kg/day DCPMU. In 163-159, 20-22 rabbits were used at each dose level of 0, 10, 50 or 100 mg/kg/day of DCPMU. All rabbits received the test material

on days 6th through 18th of gestation. Rabbit pups were delivered in the 28th day of gestation by Cesarian section. Thalidomide, 150 mg/kg/day was utilized as a postive control.

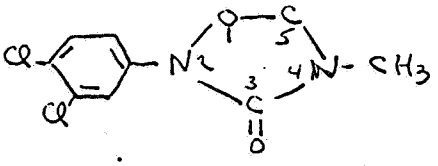
iii. DCPM gave no compound related effects with regard to reproductive performance, teratology or embroyolethality.

DCPMU in the initial study (163-158) gave no compound related effect. However, the number of dead fetuses for the 80 mg/kg/day treated rabbits were noticably above those of the control. In a follow-up study (163-159), a moderate increase in embroyo-lethality was observed at 100 mg/kg/day (i.e. 12 of the 82 implantations vs. 2 of 111 for control). The results indicate that DCPMU is not a teratogenic substance.

iv. CORE Minimal.

Section E - Absorption, Excretion and Metabolism of Methazole 14_C isomers.

Methazole was synthetized with 14_C labelled in the phenylring, the 3 position or the 5 position as indicated:



Methazole labelled in the 3 position was studied E9890 by IBT (E 8841), in the ring position IBT (E 9889), and in the 5 position IBT (E 1532 and E 1534).

The results of determining the excretion and disposition of each of these isomers as shown in the following table.