3-11-81

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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg.#352-371; 352-372; PP#1F2448; Oxamyl in or on pears at 2 ppm. CASWELL#625A; Accession#099754

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

TO: Jay Ellenberger (12)
Registration Division (TS-767)
and
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

Recommendations:

1) The requested tolerance can be toxicologically supported.

2) The following study is required to be submitted within a reasonable period of time:

a) oncogenicity - 2nd species

Section F: Proposed Residue Tolerance

It is proposed that a residue tolerance be established for residues of oxamyl, methyl N'N'-dimethyl-N-(methylcarbamoyl)oxy-1-thiooamimidate in or on pears at 2 ppm.

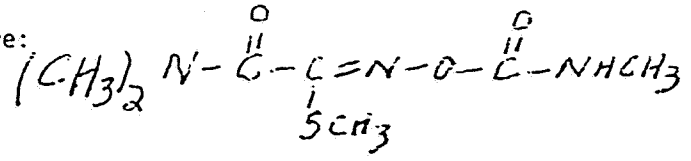
A. Substance Identification

1. Chemical Name: methyl N',N'-dimethyl-N-[(methylcarbamoyl)oxy] -1-thiooxamimidate

2. Synonyms: Vydate, oxamyl, DPX1410

3. Purity of technical: 95%

4. Structure:



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B. Formulations (CONFIDENTIAL)

1. Vydate L Oxamyl Insecticide

Ingredients	Percent Weight
oxamyl, technical (95%)	10.8
[redacted]	
	100.0

*Inerts cleared under 180.1001(c) & (d).

2. Vydate G Oxamyl Insecticide

Ingredients	Percent Weight
oxamyl, technical (95%)	10.8
[redacted]	
	100.0

*Inerts cleared under 180.1001(c) & (d).

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Review:

1) Tolerances are established under 40 CFR 180.303.

2) Previously submitted toxicity data:

°Acute Oral LD_{50} in Rats = 37 mg/kg (26% formulation)
°Acute Delayed Neurotoxicity: negative aaaaat 40 mg/kg
°Rat Teratology: negative at 300 ppm
°3-Generation Rat Reproduction: NOEL = 50 ppm
°Mutagenicity Studies: Ames Assay, Recessive Assay, Host-Mediated All negative
°2-Year Rat Feeding Study: Oncogenic potential: negative; NOEL = 50 ppm
°2-Year Dog Feeding Study: NOEL = 100 ppm
°Salmonella/microsome assay of formamide, 1-cyano-N',N'-dimethyl: negative

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3) Toxicity Data submitted with this petition.

a. Teratology Study in Rabbits with Oxamyl (Hazelton Project#201-405; October, 1980)

This study was designed to evaluate the embryotoxic and teratogenic effects of oxamyl when administered orally to pregnant rabbits (17/group) from days 6 through 19 of gestation at dosage levels of 1, 2 and 4 mg/kg/day. An additional group of seventeen rabbits served as the control group and received only distilled water. On day 29 of gestation, all surviving females were sacrificed and fetuses taken by cesarean section.

Maternal survival, clinical observations, body weights, food consumption, ovarian and uterine weights, gross pathology, number of corpora lutea and implantations, implantation efficiency and fetal data were evaluated for compound effect.

Results:

No statistically significant effects were noted with respect to maternal survival, food consumption, pregnancy rate, implantation efficiency, gross pathology, ovarian and uterine weights; fetal viability, weight and length, and visceral and skeletal variants and anomalies.

Significantly lower mean weight changes were noted during the treatment period (days 6-19) in the mid and high-dose groups. A slightly higher incidence of resorption was noted in the high-dose group, but this was not statistically significant.

Conclusion:

Oxamyl was not teratogenic at dosages up to 4 mg/kg/day during gestation. The NOEL for fetotoxicity is considered to be 2 mg/kg/day. Core minimum

b. Oral LD_{50} Test in Rats (Haskell Lab Report#781-80; 8/20/80)

Oxamyl, as an aqueous solution, was administered by intragastric intubation in single doses to groups of 10 young adult ChR-CD male rats at dosages of 3.0, 4.0, 4.5, 5.0, 6.0, 8.0 and 10.0 mg/kg. The surviving rats were weighed and observed during a 14-day recovery period and then sacrificed.

Results: LD_{50} = 6.7 mg/kg (males)

Toxic Signs: All deaths occurred within 1 day after dosing; the most commonly observed clinical signs were tremors, fasiculations, salivation, lacrimation, chromodacryorrhea,

stained and wet perineal area, and stained face.

Body Weight: Weight loss in survivors.

Necropsy: Not reported.

Toxicity Category I: DANGER

Classificaiton: Core-Minimum Data

(a) Females not tested.

C. Oral LD_{50} Test in Rats - EPA Proposed Guidelines (Haskell Lab Report#775-80; 7/24/80)

Oxamyl, as an aqueous solution, was administered by intragastric intubation in single doses to groups of 10 fasted young adult males (4 groups; 2.0, 3.0, 4.0 and 5.0 mg/kg) and fasted young adult females (6 groups; 1.0, 2.0, 2.1, 2.4, 2.5, 3.0 mg/kg). The surviving rats were weighed and observed during a 14-day recovery period and then sacrificed.

Results: LD_{50} = 3.1 mg/kg (males)
LD_{50} = 2.5 mg/kg (females)

Toxic Signs: All deaths occurred within 2 days after dosing. Clinical signs observed at most dose levels included: tremors, fasiculations, exophthalmos, salivation, chromodacryorrhea, stained face and stained and wet perineal area, piloerection.

Body Weight: Weight loss

Necropsy: Gross pathologic changes were observed in the lungs, liver, and thymus at most dose levels.

Toxicity Category I: DANGER

Classification: Core-Guidelines

4. The ADI is based on the NOEL of 50 ppm (2.5 mg/kg/day) in the two-year rat feeding study. A 100 fold safety factor was used to calculate the ADI.

$$\text{ADI} = 2.5 \text{ mg/kg/day} \times \frac{1}{100} = .025 \text{ mg/kg/day}$$

The MPI for a 60 kg person is 1.5 mg/day

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5. Published tolerances utilize 23.94% of the ADI. Unpublished, TOX approved tolerances utilize the ADI to 37.24%. The current action utilizes the ADI to 37.75%. Therefore the current action utilizes 0.51% of the ADI. (Computer printout attached).

6. No RPAR criteria have been exceeded and no regulatory actions are pending against the pesticide.

Conclusions and Recommendations

The requested tolerance can be toxicologically supported. The following study is required to be submitted within a reasonable period of time:

a) oncogenicity - 2nd species

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