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

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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Oxamyl: Waiver request for low-dose metabolism studies in rats

Caswell No. 561A MRID No. None

TO: Brigid Lowery/L. Schnaubelt, PM Team 72
Special Review and Registration Division (7508C)

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The registrant, du Pont Agricultural Products, is seeking a data waiver for a low-dose and a repeated low-dose metabolism studies on oxamyl in rats. The relevant information concerning this request has been reviewed. Based on the following reasons the Tox. Branch II recommends the request be granted.

a. In a recently submitted high-dose rat metabolism study (MRID No. 415208-01), the results showed that oxamyl was readily absorbed and quickly metabolized with oral administration (1 mg/kg). Greater than 80% of the administered radioactivity was eliminated in the urine during the first 24 hours after dosing. Approximately 2% and 5% of the dose was found in the feces and carcass, respectively. Oxamyl was not sequestered in any tissues examined in any significant amount. The major metabolite was shown to be a glucuronide of the oxime. The parent compound was also found in the urine, and it accounted for 7-11% of the administered dose. No sex difference in absorption, elimination, distribution, and metabolism of oxamyl in rats was found. Based upon the results of this

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study, a low-dose and a repeated low-dose metabolism studies in rats would unlikely to yield additional information which might better elucidate the toxicity of this compound.

b. Oxamyl has been shown to be acutely toxic by inhibiting cholinesterase activity. The oral LD_{50} was approximately 3 mg/kg for rats. The results of a chronic feeding/ oncogenicity study showed that rats which received oxamyl at dietary concentrations of 25 to 150 ppm did not produce any tumor incidence or significant chronic toxicity other than cholinesterase inhibition in rats of the two highest dose groups. The cholinesterase inhibition did not result in any deaths (MRID No. 419631-01).

One of important objectives of a metabolism study is to provide a certain understanding of the mechanism of the chronic toxicity of a chemical. In the absence of any significant chronic toxicity, waiving the requirements for a low-dose and a repeated low-dose metabolism studies would not limit the understanding of the toxicity of oxamyl.

U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDES/HED/SACB
TOX ONELINERS

TOXCHEM NO. 561A (Oxamyl)

FILE LAST PRINTED: ~~2/10/92~~

CITATION	MATERIAL	ACCESSION/ MRID. NO.	RESULTS	TOX CAT	CORE GRADE/ DOCUMENT #
Data Waiver: Low dose in metabolism study (585-1)	^{14}C-Oxamyl (99.2% purity)	415208-01	The requirements for a low-dose and a repeated low-dose metabolism studies on oxamyl in rats were recommended to be waived for the following reasons: a. In a recently submitted high-dose rat metabolism study (MRID No. 415208-01), the results showed that oxamyl was readily absorbed and quickly metabolized with oral administration (1 mg/kg). Greater than 80% of the administered radioactivity was eliminated in the urine during the first 24 hours after dosing. Approximately 2% and 5% of the dose was found in the feces and carcass, respectively. Oxamyl was not sequestered in any tissues examined in any significant amount. The major metabolite was shown to be a glucuronide of the oxime. The parent compound was also found in the urine, and it accounted for 7-11% of the administered dose. No sex difference in absorption, elimination, distribution, and metabolism of oxamyl in rats was found. Based upon the results of this study, a low-dose and a repeated low-dose metabolism studies in rats would unlikely to yield additional information which might better elucidate the toxicity of this compound. b. Oxamyl has been shown to be acutely toxic by inhibiting cholinesterase activity. The oral LD_{50} was approximately 3 mg/kg for rats. The results of a chronic feeding/ oncogenicity study showed that rats which received oxamyl at dietary concentrations of 25 to 150 ppm did not produce any tumor incidence or significant chronic toxicity other than cholinesterase inhibition in rats of the two highest dose groups. The cholinesterase inhibition did not result in any deaths (MRID No. 419631-01). One of important objectives of a metabolism study is to provide a certain understanding of the mechanism of the chronic toxicity of a chemical. In the absence of any significant chronic toxicity, waiving the requirements for a low-dose and a repeated low-dose metabolism studies would not limit the understanding of the toxicity of oxamyl.		010017

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