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

JUL 8 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

Subject: EPA ID # 524-UGN: Dithiopyr - Review of Summary of Findings for Chronic Toxicity and Oncogenicity Studies with Dithiopyr (MON-7200 and MON-15100).

Tox. Chem. Number: 717C
Project Number: 1-0956
Submission Number: S392801

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Paul Chin 6/24/91

To: Joanne Miller, PM 23
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6/27/91 KB 7/3/91

I. CONCLUSION:

The Toxicology Branch I has reviewed the summary of findings for the following studies which were conducted to support a Japanese crop registration for dithiopyr:

1. MON 7200: 12-Month Oral Chronic Toxicity Study in Dogs (Study No. IET 87-0052/ET-87-162)
2. MON 7200: 24-Month Oral Chronic Toxicity and Oncogenicity Study in Rats (Study No. IET 86-0148/ET-86-361)
3. MON 7200: 18-Month Oral Oncogenicity Study in Mice (Study No. IET 87-0001/ET-87-8)

Based on the cursory review of the findings of the above studies, there are no treatment related oncogenic effects observed in oncogenicity studies in rats or mice with dithiopyr. Also, the summary of findings showed that liver toxicity is the major outcome of chronic toxicity studies in rats, mice or dogs with dithiopyr.

The no observable effect levels (NOEL) established from the above studies are as follows:

1. 12-Month Oral Chronic Toxicity Study in Dogs (Study No.IET 87-0052/ET-87-162). Dithiopyr was administered orally via gelatin capsule as a corn oil mixture to 3 groups of 6 male and 6 female beagle dogs at dose levels of 0.5, 5 and 25 mg/kg/day for 12 months.
   NOEL = 0.5 mg/kg/day based on the increased deposition of brown pigment in the livers of mid dose animals (5 mg/kg/day).
2. 24-Month Oral Chronic Toxicity and oncogenicity Study in Rats (Study No. IET 86-0148/ET-86-361). Dithiopyr was administered to 4 groups of 90 male and 90 female F-344 rats at dietary concentrations of 3, 10, 100 and 300 ppm for 24 months.
   NOEL = 10 ppm (0.36 and 0.43 mg/kg/day for males and females, respectively) based on liver and kidney weight increases in high dose animals (300 ppm), plasma chemistry alterations indicative of liver toxicity in the 100 and 300 ppm level animals, and histopathological evidence of liver and kidney toxicity in the 100 and 300 ppm level animals.
3. 18-Month Oral Oncogenicity Study in (Mice Study No. IET 87-0001/ET-87-8). Dithiopyr was administered to 3 groups of 70 male and 70 female CD-1 mice at dietary concentrations of 3, 30 and 300 ppm for 78 weeks.
   NOEL = 3 ppm (0.31 and 0.37 mg/kg/day for males and females, respectively) based on liver weight increases in 30 and 300 ppm level animals, histological evidence of cholestasis in 300 ppm level animals (both sexes), adrenal cortical cell swelling in 300 ppm level males, and increased pigment deposition in the adrenals of 300 ppm level females.

<u>The complete valuation of these studies can not be initiated until full reports are available</u>.

II. ACTION REQUESTED

Review the summary of findings for the following studies:

1. MON 7200: 12-Month Oral Chronic Toxicity study in Dogs (Study No. IET 87-0052/ET-87-162)
2. MON 7200: .24-Month Oral Chronic Toxicity and Oncogenicity Study in Rats (Study No. IET 86-0148/ET-86-361)
3. MON 7200: 18-Month Oral Oncogenicity Study in Mice (Study No. IET 87-0001/ET-87-8)

The above documents were submitted in the letter from Dennis Ward, Monsanto to Joanne Miller, Registration Division, dated March 12, 1991.

<u>cc:</u> Flora Chow, Science Analysis Coordination Branch, HED, H7509C

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