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

DATE: **October 8, 1997**

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

RABON

SUBJECT: **TETRACHLORVINPHOS - *FQPA REQUIREMENT*** - Report of the Hazard Identification Assessment Review Committee.

FROM: Jess Rowland
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THROUGH: K. Clark Swentzel K. Clark Swentzel 10/8/97
Chairman, Hazard Identification Assessment Review Committee
Toxicology Branch II, Health Effects Division (7509C)

TO: Mike Metzger
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Health Effects Division (7509C)

PC Code; 083701

BACKGROUND: On September 23, 1997, the Health Effects Division's Hazard Identification Assessment Review Committee met to evaluate the toxicology data base of Tetrachlorvinphos with special reference to the reproductive, developmental and neurotoxicity data. These data were re-reviewed specifically to address the sensitivity of infants and children from exposure to Tetrachlorvinphos as required by the Food Quality Protecting Act (FQPA) of 1996. The FQPA requirement was not addressed in the Reregistration Eligibility Document. The Committee's decisions are summarized below.

CC: Rick Whiting, Science Analysis Branch
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A. INTRODUCTION

The Health Effects Division's Hazard Identification Assessment Review Committee met to evaluate the toxicology data base of Tetrachlorvinphos with special reference to the reproductive, developmental and neurotoxicity data. These data were re-reviewed specifically to address the sensitivity of infants and children from exposure to Tetrachlorvinphos as required by the Food Quality Protecting Act (FQPA) of 1996. The FQPA requirement was not addressed in the Reregistration Eligibility Document.

B. RESULTS:

1. Neurotoxicity

- In an acute delayed neurotoxicity study, no clinical signs of neurotoxicity or neuropathology were seen in hens following two single oral doses of Tetrachlorvinphos at 2500 mg/kg, 21 days apart (cumulative dose, 5000 mg/kg) (MRID No.41905901). The Committee noted that this study did not assess the potential of Tetrachlorvinphos to inhibit neurotoxic esterase (NTE) in hens.

- In an acute neurotoxicity study, no treatment-related pathological lesions were seen in the central or peripheral nervous system following single oral doses at 0, 65. 325 or 650 mg/kg to female Sprague-Dawley rats. For neurotoxicity, the NOEL was 65 mg/kg and the LOEL was 325 mg/kg based on transient clinical signs characteristic of cholinesterase inhibition (MRID No.42912501).

- In a subchronic neurotoxicity study, Sprague-Dawley rats received dietary administration of Tetrachlorvinphos at 0, 200, 1000 or 5000 ppm (0, 10, 50, or 250 mg/kg/day, respectively) for 90-days. There was no evidence of neurotoxicity or neuropathological lesions in the central or peripheral nervous system. Cholinesterase activity was not measured. The NOEL was 5000 ppm (HDT); a LOEL was not established (MRID No. 43294101).

2. Developmental Toxicity

- The developmental toxicity studies in rats and rabbits showed no evidence of additional sensitivity of young rats or rabbits following pre-or postnatal exposure to Tetrachlorvinphos and comparable NOELs were established for adults and offspring.

- In a developmental toxicity study, pregnant Sprague-Dawley rats were given oral doses of Tetrachlorvinphos in 0.5% aqueous methylcellulose at 0, 75, 150, or 300 mg/kg/day during gestation days 6 through 15. For maternal toxicity, the NOEL was 75 mg/kg/day and the LOEL was 150 mg/kg/day based on decreased body weight gain. For developmental toxicity, the NOEL was 300 mg/kg/day (HDT); a LOEL was not established. There was no evidence of Teratogenicity (MRID Nos. 40152701 and 42520101).

- In a.developmental toxicity study, pregnant New Zealand rabbits received oral doses of Tetrachlorvinphos in carboxy methylcellulose at 0, 150, 375 or 750 mg/kg/day during gestation days 6 through 19. For maternal toxicity the NOEL was 375 mg/kg/day and the LOEL was 750 mg/kg/day based on mortality, abortions and red vaginal fluids. For developmental toxicity, the NOEL was 375 mg/kg/day and the LOEL was 750 mg/kg/day based on an increase in early resorptions/dam with a corresponding increase post implantation loss and a decrease in live fetuses/dam (MRID No. 00127831).

3. Reproductive Toxicity

- In a 2-generation reproduction study, Sprague-Dawley rats were fed diets containing Tetrachlorvinphos at 0,100, 500 or 2000 ppm (0, 5, 25 or 100 mg/kg/day , respectively) for two successive generations. There was no increased sensitivity of pups over the adults seen. For parental systemic toxicity, the NOEL was 500 ppm (25 mg/kg/day) and the LOEL was 2000 ppm (100 mg/kg/day) based on decreased body weight gains in males in the F_0 generation and in both sexes in the F_1 generation as well as increased mean adrenal gland weights in F_0 females. For reproductive toxicity, the NOEL was 2000 ppm (HDT); a LOEL was not established (MRID No.42054301).

4. Cholinesterase Inhibition

- Cholinesterase activity was not measured in the adults and offspring in the developmental toxicity studies or in the reproduction study. Therefore, no comparisons could be made for this endpoint between adults and offspring.

4. Developmental Neurotoxicity

- There are sufficient data available to adequately assess the potential for toxicity to young animals following pre-and/or post-natal exposure to Tetrachlorvinphos. These include acceptable developmental toxicity studies in rats and rabbits as well as a two-generation reproduction study in rats. In addition, no treatment-related neuropathology was seen in studies conducted in hens or rats (acute and subchronic). Therefore, based upon a weight-of-the-evidence consideration of the data base, the Committee determined that a developmental neurotoxicity study in rats is not required.

5. Reference Dose

- A Reference Dose (RfD) of 0.04 mg/kg/day was derived from the NOEL of 4.23 mg/kg/day and an Uncertainty Factor (UF) of 100. The NOEL was based on histopathological lesions of the liver and adrenal glands observed at 43.2 mg/kg/day in a 2-year feeding study in rats. The UF of 100 included a 10 to account for intra-species and a 10 for inter-species variations.

6. Data Gaps

- None

C. CONCLUSIONS

The Committee's conclusions on the Uncertainty Factors for acute and chronic dietary risk assessments are as follows:

1. Acute Dietary Risk Assessment

An acute dietary risk assessment is not required since a toxicological endpoint attributable to a single dose (exposure) was not identified in any of the oral toxicity studies.

2. Chronic Dietary Risk Assessment

The endpoint selected for chronic dietary risk assessment is based on histopathology observed at 43.2 mg/kg/day in a chronic toxicity/carcinogenicity study in rats. The NOEL was 4.23 mg/kg/day. A UF of 100 was applied to the NOEL; 10 to account for intra-species and a 10 for inter-species variations. Thus a RfD of 0.04 mg/kg/day was derived.

For chronic dietary risk assessments, the Committee determined that the **10 x** factor to account for enhanced sensitivity of infants and children **(as required by FQPA) should be removed. The present UF of 100 is adequate. Therefore, the RfD remains at 0.04 mg/kg/day.** A UF of 100 is adequate to ensure the protection of this population from exposure to Tetrachlorvinphos because there was no indication of increased sensitivity to young animals following pre-and/or post-natal exposure to Tetrachlorvinphos as shown below:

(i) Developmental toxicity studies showed no increased sensitivity of fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits.

(ii) A 2-generation reproduction toxicity study in rats showed no increased sensitivity of pups as compared to adults.