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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: Fortress: Response to Registrant's Submission Regarding the Toxicity and Potential for Cholinesterase Inhibition of Diethylphosphate (DEP) and Diethylthiophosphate (DETP).

Tox. Chem. No.: 663P.
EPA Record No.: 244011.
Project No.: 9-1343.

TO: Dennis Edwards, PM Team #12
Registration Division (H7505C)

FROM: Sanford W. Bigelow, Ph.D. 5/16/89
Review Section 2, IRB
Health Effects Division (H7509C)

THRU: Marion P. Copley, D.V.M., Section Head Marion Copley 5/25/89
Review Section 2, IRB
Health Effects Division (H7509C)

Action Requested:

HED has reviewed toxicology data on DEP and DETP submitted by DuPont. This toxicology data was obtained from a search of the literature and computer databases.

Conclusions:

HED finds that the potential for DEP or DETP to cause cholinesterase inhibition is limited (1,000 fold less) relative to the putative parent compound, chlorethoxyphos (Fortress) and that this inhibition correlated well with their potential for acute lethality. All three compounds have negative mutagenic potential. HED concludes that the acute toxicity of DEP and DETP is not a relative concern to that of chlorethoxyphos.

HED also finds that the enclosed Memorandum of Discussion accurately reflects the topics related to the toxicology of DEP and DETP discussed at the March 15, 1989 meeting. HED finds that another meeting with DuPont may be unnecessary to discuss matters related to the acute toxicity of DEP and DETP.

Summary of Submitted Toxicology Data on DEP and DETP.

Three main toxicological endpoints for DEP and DETP were presented, the LD_{50} values, mutagenicity and cholinesterase inhibition, the putative mechanism of organophosphate toxicity. Toxicological endpoints for DEP and DETP were compared to those of chlorethoxyphos (Fortress).

Acute lethality. The acute lethality (LD_{50}) for DEP ranges from 1.2-6 g/kg (Lehman et al. 1949. Assoc. Food Drug Officials Q. Bull. 13:65-70, as abstracted in Chemical Abstracts). No acute lethality data was provided for DETP. The LD_{50} value for chlorethoxyphos is 1.8 mg/kg in female rats and 4.8 mg/kg in male rats (MRID No. 408837-11). The acute lethality of DEP and DETP should be comparable based on similar chemical structure and that the monothio analogs of organophosphates are relatively inactive cholinesterase inhibitors (Eto, M. 1974. Organophosphorus pesticides: Organic and biological chemistry. CRC Press, Inc., Cleveland, OH, p 147). Based on this data, chlorethoxyphos is 1,000 fold more acutely toxic than DEP or DETP.

Mutagenicity. When tested, both DEP and DETP produced negative mutagenicity test results (Fahring, R. 1974. IARC Sci. Publ. 10:161-181 and Wild, D. 1975. Mutation Res. 32:133-150). Chlorethoxyphos, when tested, also produces negative mutagenicity results (MRID Nos. 408837-25, 408837-26, 408837-27, 408837-28, 408837-29, 408837-30, 408837-31). All three compounds have negative mutagenic potential.

Cholinesterase inhibition. DEP and DETP have been found to inhibit human plasma cholinesterase activity at concentrations of 9.4 and 0.7 millimolar, respectively, whereas paraoxon inhibits cholinesterase activity at concentrations of 800 nanomolar (Daughton, C.G. et al. 1976. J. Agric. Food Chem. 24:236-241).

In sum, the ability of DEP, DETP and chlorethoxyphos to inhibit cholinesterase activity correlates well with their potential for acute lethality. All three compounds are not mutagenic in the studies reported.

cc: E. Regelman, Environmental Fate and Ground Water Branch (H7507C)
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M. Camardese, Ecological Effects Branch (H7507C)

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