3-26-90

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

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Cholinesterase Peer Review Committee Meeting of 3/1/90 on Malathion Chronic Dog Study

FROM: Brian Dementi, Ph.D., D.A.B.T. Brian Dementi 3/26/90
Review Section I
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

TO: Penelope A. Fenner-Crisp, Ph.D., Director
Health Effects Division (H7509C)

THRU: Karl Baetcke, Ph.D.
Chief, Toxicology Branch I
Insecticide, Rodenticide Support
Health Effects Division (H7509C)

THRU: Roger Gardner, Acting Section Head
Review Section I
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (H7509C)

A. Individuals in Attendance:

1. Peer Review Committee: (Signatures indicate concurrence with the peer review unless otherwise stated.)

Penny Fenner-Crisp	
Karl Baetcke	3/28/90
Karen Hammernik	3/29/90
Roger Gardner	
Paul Chin	3/29/90
William Burnam	
Thoa Nguyen	
Robert Zendzian	3/29/90
Brian Dementi	3/26/90

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B. Conclusions of Peer Review Committee

The Cholinesterase Peer Review Committee convened on March 1, 1990 to consider the malathion registration standard requirement for a repeat chronic toxicity study in the dog.

At issue was the malathion chronic dog study performed by Tegeris Laboratories, Inc. (MRID No.: 40188501, 4/30/87), reviewed in Tox Branch in October, 1987. This study was classified core-supplementary, in part because a NOEL was not identified for cholinesterase inhibition. Additional effects for which a NOEL was not identified included: increased liver and kidney weights, elevated platelet count, decreased creatinine, decreased BUN and inhibition of SGPT. The need for definitive cholinesterase data was considered to be particularly important.

After discussing the various aspects of the cholinesterase responses in the dog study, the committee deemed it unlikely that malathion would inhibit cholinesterase in the dog at levels even approaching these low levels at which cholinesterase was inhibited in the human study (Moeller and Rider, 1962). For example, in the dog study, plasma and erythrocyte cholinesterases were inhibited at all doses. The lowest dose tested was 62.5 mg/kg/day, where cholinesterase inhibition approximated 25%. By contrast, the LEL for cholinesterase inhibition in the human study was only 0.34 mg/kg/day.

The Committee affirmed the need to obtain definitive cholinesterase data, but decided it would be more appropriate to obtain that data in the malathion and malaoxon combined rat chronic/oncogenicity studies now required of the Registrants. Though there is the cholinesterase data available in humans, additional data is being requested in the rat in order to confirm findings in both males and females, on brain cholinesterase as well as plasma and erythrocyte cholinesterase and using a test material of known high purity.

The Committee decided that the other than cholinesterase findings in the chronic dog study were not of sufficient concern to require an additional chronic dog study. The Committee's basic conclusion that another chronic dog study will not be necessary conforms with the Registrant's Malathion Reregistration Task Force June 27, 1988 response to the registration standard, claiming another dog study should not be required.

Reregistration Division should be advised that the Tegeris Labs Chronic Dog Study, now classified as core-supplementary will satisfy the Section 83-1 data requirement, non-rodent chronic toxicity.