6-10-92

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

MEMORANDUM

SUBJECT: Report of the third RfD/Peer Review of Dichlorvos (DDVP).
Tox. Chem. No. 328
CAS No. 62-73-7
EPA Chem. Code: 084001
Reg. Group: List A (3 SR)

FROM: George Z. Ghali, Ph.D. G. Ghali 6.10.92
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

TO: George LaRocca, PM 13
Insecticide and Rodenticide Branch
Registration Division (H7509C)
and
Lois Rossi, Chief
Reregistration Branch
Special Review and Reregistration Division (H7508W)

The Health Effects Division RfD/Peer Review Committee met on May 1, 1992 to evaluate data submitted in support of Dichlorvos (DDVP) registration with particular emphasis on long term toxicity in rodent and non-rodent species, and developmental and reproductive toxicity.

Since the chemical has been classified by the HED Cancer Peer Review Committee as a Group C, possible human carcinogen (cancer peer review report dated 09/18/1989), there was no need to discuss material related to the carcinogenicity issue. However, the chronic toxicity phase of the rat and mouse chronic toxicity/carcinogenicity studies have been considered by the RfD/ Peer Review Committee for possible impact on the RfD.

The Committee also reviewed a new developmental toxicity study in rats (MRID No. 41951501) submitted to the Agency in 1991. The Committee agreed with the reviewer interpretation and conclusions. The study is acceptable and the data evaluation record is adequate. Our search of the Pesticide Document Management System (PDMS) also indicated that a developmental toxicity study in rabbits (MRID No. 41802401) was submitted to the Agency in 1991. However, according to HED records, it appears that this study has not been received or reviewed by the Health Effects Division. A reproduction study was also presented to the Committee and was considered supplementary.

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It was not known to the Committee at that time whether a new study was requested. The Committee recommended that if a new study to is be submitted, it should include measurement of cholinesterase inhibition.

The RfD for this chemical is currently on IRIS as 0.0008 mg/kg/day based upon a "no-observable effect level" of 0.08 mg/kg/day for increased liver weight and enlarged hepatocytes observed at 0.8 mg/kg/day observed in a two-year feeding study in dogs (Jolley, N. P. et al., 1967) using an uncertainty factor of 100. This study has been declared invalid (H. Spencer, memo dated Nov. 5, 1990; W. Greer, memo dated Dec. 3, 1990). A new chronic feeding study in dogs (MRID No. 41593101) was submitted to the Agency demonstrating a "no-observable effect level" of 0.05 mg/kg/day for plasma and RBC cholinesterase inhibition in males and females and brain cholinesterase inhibition in males observed at 1 mg/kg/day.

The Committee recommended that the RfD be revised to 0.0005 mg/kg/day to reflect the changes in the toxicology profile for this chemical. The new RfD was based upon a "no-observable effect level" of 0.05 mg/kg/day demonstrated in the new long-term feeding study in dogs using an uncertainty factor of 100 to account for the intra- and inter-species differences.

A. Individuals in Attendance

1. Peer Review Committee (signature indicates concurrence with the peer review unless otherwise stated).

William L. Burnam

Henry Spencer

James Rowe 6/26/92

Stephen Dapson

Gary Burin

George Ghali

Rick Whiting

2. Peer Review Members in Absentia (committee members who were unable to attend the discussion; signatures indicate concurrence with the overall conclusions of the committee).

Reto Engler

Karl Baetcke

Marcia Van Gemert

Laurence Chitlik

Esther Rinde —

Roger Gardner 6/26/92

3. Scientific Reviewer (committee or non-committee members responsible for data presentation; signatures indicate technical accuracy of panel report).

Joycelyn Stewart

B. MATERIAL REVIEWED:

The material available for review consisted of an IRIS RfD/RfC summary document and data evaluation records (DER's) of the following Studies:

1. Markiewicz, V. (1990). A 52-Week chronic toxicity study on DDVP in dogs. Unpublished study No. 2534-102 conducted by Hazleton Laboratory America, Inc., Report dated August 6, 1990, submitted to the Agency by AMVAC Chemical Corporation. MRID No. 415931-01, HED Doc. No. 008178.

Core Classification: Guideline.

Committee's conclusions and recommendations:

The Committee agreed with the reviewer's evaluation and interpretation of data. The Study is acceptable and satisfies Guideline requirement 83-1 for chronic toxicity testing for non-rodent species under Subpart F of the Pesticide Assessment Guideline.

2. Tyl, R., Marr, M., Myers, C. (1991). Developmental toxicity evaluation of DDVP administered by gavage to CD (Sprague Dawley) rats. Unpublished study No. 60C-4629-10/20, conducted by Research Triangle Institute, report dated February 22, 1991, submitted to the Agency by AMVAC Chemical Corporation. MRID No. 41951501, HED Rec. No. 009305.

Core Classification: Minimum data.

Committee's conclusions and recommendations:

The Committee agreed with the reviewer's evaluation and interpretation of data. The Study is acceptable and satisfies Guideline requirement 83-3 for developmental toxicity testing for one species under Subpart F of the Pesticide Assessment Guideline.

3. Whithrup, S., Caldwell, J., and Hull, L. (1965). The effects exerted upon the fertility of rats, and upon the viability of their offspring by introduction of Vapona (R) insecticide into their diets. (Unpublished study conducted by University of Cincinnati, Dept. of Preventive Medicine and Industrial Health, submitted to the Agency by Shell Chemical Company. MRID No. 00050012, HED Doc. No, 007765.

Core Classification: Supplementary data.

Committee's conclusions and recommendations:

The Committee agreed with the reviewer's evaluation and interpretation of data. The Study does not satisfy Guideline

requirement 83-4 for reproductive toxicity testing under Subpart F of the Pesticide Assessment Guideline.

It was not known to the Committee at that time whether a new study was requested. The Committee recommended that if a new study is to be submitted, it should include measurement of cholinesterase inhibition.

CC: Penny Fenner-Crisp
Richard Schmitt
Kerry Dearfield
Albin Kocialski
Flora Chow