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

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MAR 16 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

Subject: Second Peer Review of Dichlorvos - Reevaluation Following the September 23, 1987 Science Advisory Panel Review.

From: Judith W. Hauswirth, Ph.D. Judith W. Hauswirth 2/4/88
Section Head, Section VI
Toxicology Branch/HED (TS-769C)

To: George LaRocca
Product Manager #15
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The Peer Review Committee met on September 29, 1987 to examine the issues raised by the Science Advisory Panel (SAP) with respect to the classification of the carcinogenicity of Dichlorvos.

A. Individuals in Attendance:

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

Theodore M. Farber	Theodore M. Farber
William L. Burnam	
Reto Engler	
John Quest	John A. Quest
Esther Rinde	Esther Rinde
Richard Levy	
Kerry Dearfield	
Judith W. Hauswirth	Judith W. Hauswirth

2. Scientific Reviewers: (Non-committee members responsible for presenation of data; signature indicate technical accuracy of panel report.)

Joycelyn Stewart	Joycelyn E Stewart
Albin Kocialski	Albin B. Kocialski
Irving Mauer	

Bernice Fisher

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

Anne Barton

Diane Beal

Richard Hill/Don Barnes —

Robert Beliles

B. Material Reviewed:

The SAP draft response memorandum (final dated October 1, 1987), The transcript of the NTP panel of experts meeting of July 14, 1987 and the National Toxicology Program Draft Report Abstracts for Seven Chemical Carcinogenesis Animal Bioassay dated July 1987 were reveiwed by the Committee.

C. Considerations:

The Panel did not agree with the Committee's overall assessment of the weight of the evidence on dichlorvos. The Committee classified dichlorvos as a category B_2 oncogen (probable human carcinogen), while the Panel felt that the evidence in both rats and mice was limited and classfied dichlorvos as a category C oncogen (possible human carcinogen).

Issue: Classification of dichlorvos as a category B_2 or C oncogen.

The Committee classified dichlorvos as a category B_2 oncogen based upon the results of NTP bioassays in B6C3F1 mice and Fischer 344 rats. The NTP was in general agreement with the Committee's classification concluding that dichlorvos demonstrated clear evidence of carcinogenicity in the male rat and in the female mouse. The SAP concluded that dichlorvos should be classified as a category C oncogen since 1) only benign tumors were induced by dichlorvos, 2) they were not dose-related and 3) dichlorvos was not mutagenic in in vivo assays (although it was mutagenic in several in vitro test systems both with and without metabolic activation).

Upon reconsideration, the Committee still concludes that the results of the NTP bioassays indicate that dichlorvos demonstrates sufficient evidence of carcinogenicity in the male rat and in the female mouse since 1) a dose-response relationship of statistical significance was seen for pancreatic adenomas (which have the potential to progress to malignancy) and mononuclear cell leukemia in male rats, 2) a dose-response relationship of statistical significance was seen in the female mouse for forestomach squamous cell papillomas which have the potential to progress to carcinomas, 3) the presence of some forestomach carcinomas (which are rare) was seen in the female mouse, 4) significant positive trend was seen for forestomach papillomas in male mice at a dose that did not achieve an MTD, 5) supporting evidence provided by a statistically significant increase in mammary tumors at the low dose in the female rat and an increase in lung tumors in the male rat which was associated with a significant trend, and 6) mutagenicity data was available indicating that dichlorvos is positive for mutagenicity in vitro in bacterial

and mammalian cells both with and without metabolic activation. The Committee, thereby, confirmed their initial classification of dichlorvos as a B_2 oncogen.