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

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July 15, 1992

MEMORANDUM

SUBJECT: Post SAP Carcinogenicity Peer Review Meeting on
Dimethoate, Bromoxynil and Triallate
and
Re-consideration of the Classification of Aliette and
Cyromazine/Melamine

FROM: Esther Rinde, Ph.D.
Manager, Carcinogenicity Peer Review
Health Effects Division (H7509c)

TO: Addressees

Attached for your review are the Peer Review Memos and SAP Reports for Dimethoate, Bromoxynil and Triallate.

A meeting to re-consider the carcinogenicity classification of Dimethoate, Bromoxynil and Triallate, in light of the SAP's comments, is scheduled for Wednesday July 29, 1992, from 10:00 to 11:00 am in Room 817, CM2.

Following that discussion, from 11:00 am to 12:00 noon, we will discuss and re-consider the Aliette and Cyromazine/Melamine classifications. The Peer Review Memos for Aliette and Cyromazine/Melamine are circulating for signatures concurrently, because of complex issues common to both. Members were asked to provide comments, which are being collected and will be distributed and used in the discussion.

Addressees

P. Fenner-Crisp	G. Ghali
W. Burnam	B. Fisher
R. Engler	J. Du
R. Hill	Y. Woo
K. Baetcke	J. Quest
L. Brennecke	E. Saito (for microfiche-with one-liner)
M. Van Gemert	A. Clevenger
M. Copley	E. Andersen
K. Dearfield	W. Phang
J. Parker	J. Rowe
H. Pettigrew	S. Dapson
W. Sette	M. Ioannou
J. Stewart	R. Gardner
C. Swentzel	J. Rowland

FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT
SCIENTIFIC ADVISORY PANEL

A Set of Scientific Issues Being Considered by the Agency in
Connection with the Peer Review Classification of Dimethoate
as a Group C Carcinogen

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) has completed review of a set of scientific issues regarding the Environmental Protection Agency Peer Review Committee's classification of Dimethoate as a Group C Carcinogen. The review was conducted in an open meeting held in Arlington, Virginia, on June 25, 1992. The meeting was chaired by Dr. Edward Bresnick. Other Panel members present were Drs. Marion Anders, Harihara M. Mehendale, Curtis Travis and Ernest E. McConnell. In addition Dr. Joe Grisham, University of North Carolina, and Dr. Richard A. Griesemer, National Institute of Environmental Health Sciences served as Ad Hoc experts to the FIFRA SAP.

Public notice of the meeting was published in the Federal Register on June 5, 1992.

There were no oral or written comments provided to the Agency.

In consideration of all matters brought out during the meeting and careful review of all documents presented by the Agency, the Panel unanimously submits the following report.

REPORT OF PANEL RECOMMENDATIONS

Issue # 1: The Agency requests comments from the Scientific Advisory Panel regarding the Peer Review Committee's weight of the evidence evaluation for the following responses:

a. The hemolymphoreticular tumors (lymphomas, reticulosarcomas and leukemias) and the combination of these tumors in male B6C3F1 mouse.

Response

The SAP feels that the relationship of hemolymphoreticular tumors (lymphomas, reticulosarcomas and leukemias) to exposure to dimethoate is equivocal because:

1. The response was relatively low and consistent with historical control.
2. The control group incidence seemed unusually low compared to contemporary historical control data.
3. The response occurred only in one sex (males)
4. The response was dose related, but evident only in the high dose group.
5. The inclusion of reticulum cell sarcomas with other lymphoid neoplasms may not be appropriate, dependent upon the origin or location of such neoplasms. The Agency was not able to clarify the situation to the satisfaction of the SAP. Thus, there was insufficient information to make that determination.

However, the SAP felt the study is limited in its sensitivity to detect carcinogenic activity because of the short duration of the study (78 weeks). The B6C3F1 strain has good survival (75%) at 24 months and studies need to be at least that long in this strain.

Issue # 1b: The angiogenic tumors (spleen and skin hemangiomas/hemangiosarcomas, and lymph angiomas/angiosarcomas and the combination of these tumors in male Wistar rats.

Response

The SAP agrees with the Agency that it is appropriate to combine endothelial tumors in various tissues/organs to determine a potential chemical effect. However, the SAP had some concern as to whether these lesions are truly neoplastic since they were found almost exclusively in a single organ/tissue. Answers to questions regarding their occurrence in multiple organs in the some animal were not clearly articulated by the Agency. Classic hemangiosarcomas typically involve several tissues. Nevertheless, the SAP felt that the data available to it would support the Agency's view that the vascular neoplasms are treatment related. The SAP recommends that the Agency make an effort to better define multiple organ involvement when such occurs, as with the above types of tumors.

Issue #2: The Agency requests comments from the Scientific Advisory Panel regarding the cancer classification of Dimethoate as a Group C, Possible Human Carcinogen, in accordance with the Agency's Risk Assessment Guidelines.

Response

After much discussion, the SAP agrees with the Agency that the appropriate classification for dimethoate is Group C based on the treatment related increase in vascular neoplasms in male rats. The lymphoma response observed in male mice was equivocal, and thus neither strengthened nor detracted from the Agency's weight of

evidence. However, there was concern for the conflicting results of two mouse carcinogenicity studies and the Agency's choice of one over the other for classification was not clear.

FOR THE CHAIRMAN:

Certified as an accurate report of Findings:



Robert B. Jagger
Designated Federal Official
FIFRA Scientific Advisory Panel

Date: July 10, 1992