10-2-91

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

OCT 2 1991

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MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: Transmittal of the Final FIFRA Scientific Advisory Panel Report on the September 18, 1991, Meeting

FROM: Robert B. Jaeger RBJ 10/2/91
Designated Federal Official
FIFRA Scientific Advisory Panel

TO: Douglas D. Campt
Director
Office of Pesticide Programs

The above mentioned meeting of the FIFRA Scientific Advisory Panel (SAP) was an open meeting held in Arlington, Virginia to review the following topics:

1. A set of Scientific Issues Regarding the Agency Peer Review Committee's Classification of Prodiamine as a Group C Carcinogen.

2. A set of Scientific Issues Regarding the Agency Peer Review Committee's Classification of Metolachlor as a Group C Carcinogen.

3. A set of Scientific Issues Regarding the Agency Peer Review Committee's Classification of Triphenyltin Hydroxide (TPTH) as a Group B_2, Probable Human Carcinogen.

4. A set of Scientific Issues Regarding the Agency Peer Review Committee's Review of a Dose-Response Risk Assessment for the Carcinogenic Effects of Ethylene Thiourea (ETU) in Rats and MIce.

Please find attached the Panel's final report on the agenda items discussed at the meeting.

Attachment

cc: Panel Members
Linda J. Fisher
Victor J. Kimm
Susan Wayland
Penny Fenner-Crisp
Mike Ioannou
Steve Dapson
John Doherty
Reto Engler
Don Barnes
Al Heier
Mary Beatty

Freedom of Information (Susan Lawrence)

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 Triphenyltin Hydroxide (TPTH) as a Group B_2, Probable Human Carcinogen

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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 Triphenyltin Hydroxide (TPTH) as a Group B_2, Probable Human Carcinogen. The review was conducted in an open meeting held in Arlington, Virginia, on September 18, 1991. Panel members present for the review were Dr. Edward Bresnick (Chairman), Dr. Mont Juchau, Dr. Peter Magee, and Dr. Curtis Travis (Dr. John Wilson was recused from these discussions and was not present in the meeting room). In addition, Dr. Edmund Crouch of Cambridge Environmental, Inc, Dr. Richard Griesemer and Dr. Christopher Portier of the National Institute of Environmental Health Sciences, served as Agency representatives; and Dr. Dale Hattis of Clark University, and Dr. Ernest McConnell of Raleigh, NC served as Special Government Employees on the Panel.

Public notice of the meeting was published in two Federal Registers on Friday, August 23, and Friday, September 13, 1991.

Oral presentations were made by Dr. James Lamb and Dr. Judith Hauswirth of Jellinek, Schwartz, Connolly and Freshman, Inc.; and Dr. Bert Volger of Hoechst Roussel Agri-Vet Company.

Written comments were received from Jellinek, Schwartz, Connolly and Freshman, Inc.

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

The Agency requested comments from the Panel relative to the Peer Review Committee's recommendations for the carcinogenicity evaluation of triphenyltin hydroxide (TPTH).

Specifically:

1. Does the Panel have reservations regarding the significance of the following tumor types in the weight-of-the-evidence:

   - o fatal pituitary adenomas in female Wistar rats;
   - o Leydig cell tumors in Wistar rats; and
   - o hepatocellular tumors (benign and/or malignant) in male and female NMRI mice?

2. Does the Panel agree with the Agency's classification of TPTH as a B_2 carcinogen?

Panel Response:

The Panel agreed that TPTH is carcinogenic in experimental animals based on the following evidence. Significant increases were noted in the incidence of liver tumors in mice of both sexes exposed to the TPTH. In both cases the increases involved adenomas, without significance in the numbers of carcinomas. However, the combined incidences were significant. The data in the females were more impressive because of the absence of liver tumors in the control animals and their known very low incidence in females of the NMRI strain used in the study.

Female Wistar rats showed a significant increase in the incidence of pituitary adenomas at the highest and next lower dose with a positive trend. However, these findings were considered equivocal because of the very high spontaneous incidence of these tumors in the female Wistar rat and the fact that a very high proportion of untreated female rats of this strain develop tumors in old age.

The analysis of fatal pituitary tumors in female rats was considered to be flawed; the Panel believed that a survival-adjusted analysis should have been done.

It was noted that the numbers of male rats examined for pituitary tumors was considerably smaller than for the testicular tumors thus prohibiting the drawing of valid conclusions as to the incidence of pituitary tumors in this sex. However, in the male rats, clear evidence was present for the induction of Leydig cell tumors in the testis.

On the basis of the tumorigenicity in the rat (Leydig cell tumors) and in both the male and female mouse (liver tumors), the Panel agreed with the Peer Review Committee that TPTH should be classified as a B_2 carcinogen.

FOR THE CHAIRMAN:

Certified as an accurate report of Findings:

Robert B Jaeger — 10/2/91

Robert B. Jaeger (date)
Designated Federal Official
FIFRA Scientific Advisory Panel