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

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JUN 27 1996

OFFICE OF
INTERNATIONAL ACTIVITIES

MEMORANDUM

SUBJECT: Tebuconazole (Folicur): Reconsideration of the Reference Dose.

CASRN: 107534-96-3
EPA Chem. Code: 128997
Caswell No.: 463P

FROM: George Z. Ghali, Ph.D.
Manager, RfD/QA Peer Review Committee
Health Effects Division (7509C)
and
Alberto Protzel, Ph.D.
Toxicology Branch II
Health effects Division (7509C)

THRU: William Burnam
Chairman, RfD/QA Peer Review Committee
Health Effects Division (7509C)

TO: Connie Welch, PM 21
Fungicide-Herbicide Branch
Registration Division (7505C)

The Health Effects Division-RfD/Peer Review Committee met on April 4, 1996 to reconsider the Committee's position on the Reference Dose (RfD) for Tebuconazole in light of additional studies submitted to the Agency.

A. Background:

The Health Effects Division RfD/Peer Review Committee met on March 5, 1991 to evaluate data submitted in support of Tebuconazole registration with particular emphasis on the long term toxicity in rodent and non-rodent species, carcinogenicity in two species, and developmental and reproductive toxicity and to assess the Reference Dose for this chemical.

In this meeting, the RfD for this chemical was calculated based on a 1-year dietary study in beagle dogs (MRID No. 40700940) conducted with Tebuconazole at dietary levels of 0, 40, 200 or 1000/2000 ppm. The least-observable-effect level (LOEL) was 200

ppm (equivalent to 5 mg/kg/day) based on ocular lesions and hepatic toxicity in males and females at the mid- and high-dose levels. The no-observable-effect level (NOEL) was 40 ppm (1.0 mg/kg/day), which was used to calculate an RfD of 0.01 mg/kg/day, using an uncertainty factor (UF) of 100 to account for both the interspecies extrapolation and intraspecies variability.

Recently, a follow-up study (one-year) in beagle dogs conducted with Tebuconazole at dietary levels of 0, 100 or 150 ppm was submitted to the Agency. In this follow-up study in dogs, the LOEL was 150 ppm based on adrenal histopathology, and the NOEL was 100 ppm (equivalent to 2.96 and 2.94 mg/kg/day in both males and females, respectively).

B. Committee's Conclusions and Recommendations:

The Health Effects Division RfD/Peer Review Committee met on April 4, 1996 to evaluate the follow-up one-year study in beagle dogs (MRID Nos. 42030601, 42537201) conducted with tebuconazole and to determine its impact on the RfD of Tebuconazole.

In this meeting, the Committee recommended that the RfD for Tebuconazole be based on the follow-up study with a NOEL of 100 ppm (2.96 and 2.94 mg/kg/day in males and females, respectively) using an Uncertainty Factor (UF) of 100 to account for both the interspecies extrapolation and intraspecies variability. On this basis the RfD was calculated to be 0.03 mg/kg/day.

G. Individuals in Attendance:

Peer Review Committee members and associates present were William Burnam (Chief, SAB; Chairman, RfD/Peer Review Committee), George Ghali (Manager, RfD/Peer Review Committee), Karl Baetcke (Chief, TB I), Mike Ioannou (Acting Chief, TB II), Nancy McCarroll, Guruva Reddy, James Rowe, William Sette, Henry Spencer, and Rick Whiting.

Scientific reviewers (Committee or non-committee member(s) responsible for data presentation; signature(s) indicate technical accuracy of panel report)

Alberto Protzel

James Rowe

Respective Branch Chief or Acting Branch Chief (Committee member; signature indicates concurrence with the peer review unless otherwise stated)

Mike Ioannou

CC: Stephanie Irene
Debra Edwards
Albin Kocialski
Mike Ioannou
Alberto Protzel
James Rowe
Marion Copley
Beth Doyle
Amal Mahfouz (OW)
RfD File
Caswell File

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