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

FEB 17 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

**MEMORANDUM**

SUBJECT: RfD/Peer Review Report of Dichlormid

CASRN. 37764-25
Caswell No. 284A

FROM: George Z. Ghali, Ph.D.
Manager, RfD/Quality Assurance Peer Review
Health Effects Division (H7509C)

TO: Tina Levine, PhD
Registration Support Branch
Registration Division (H7508W)

The Health Effects Division RfD/Peer Review Committee met on January 06, 1994 to discuss and evaluate toxicology data submitted in support of Dichlormid registration and to assess the Reference Dose (RfD) for this chemical.

The toxicology data base for this chemical consisted of a subchronic feeding study in rats (00058467), two-subchronic feeding studies in dogs (MRID No. 41419401, 00058468) and a developmental feeding study in rats (00058469). The three subchronic studies were classified as Core-minimum data. The developmental toxicity study in rats was classified as Core-supplementary.

The Committee generally agreed with the reviewer's evaluation and interpretation of data and classification of the studies. The rat developmental toxicity study was considered to be deficient for the lack of maternal toxicity, lack of litter data, use of only two dose levels and exposure through diet. A new developmental toxicity study is required.

The Committee recommended that an RfD be established on the basis of a 90-day dog study with a NOEL of 5.0 mg/kg/day. Significant decreased body weight, degeneration of voluntary muscle fibers, and changes in clinical chemistry parameters (increased ALT, AST, CK, AP and decreased plasma creatinine), and increased liver weight were observed at the next higher dose level of 25 mg/kg/day. An uncertainty factor (UF) of 100 was used to account for the inter-species extrapolation and intra-species variability. An additional uncertainty factor of 10 was also used to account for

the extrapolation from subchronic to chronic exposure. On this basis the **RfD** was calculated to be **0.005 mg/kg/day.**

There was no evidence, based on the available data, that this chemical was associated with significant maternal and/or developmental toxicity.

The Committee debated the need for an additional uncertainty factor of 3 to compensate for the lack of an acceptable developmental toxicity study, but this additional uncertainty factor was not adopted. It should be noted that this chemical has not been reviewed and no ADI value has been generated for this chemical by the World Health Organization (WHO).

There are no chronic toxicity/carcinogenicity data available on this chemical. The registrant has previously indicated that it will voluntarily initiate long-term (chronic toxicity/ oncogenicity) studies for this chemical. However, because of structural similarity of dichlormid to known carcinogens, members of the Committee felt that chronic toxicity/carcinogenicity data are now becoming essential part of the data requirements in order to assess the carcinogenic potential and more effectively regulate this chemical.

A. Individuals in Attendance

1. Peer Review Committee Members and Associates present (Signature indicates concurrence with the peer review unless otherwise stated).

William Burnam

Reto Engler

Marcia Van Gemert

Karl Baetcke

Henry Spencer

William Sette

Roger Gardner

James Rowe

Esther Rinde

George Ghali

Rick Whiting

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

David Van Ormer

Albin Kocialski

3. Others:

D. McCall and P. Hurley of HED as observers.

CC: Penny Fenner-Crisp
Richard Schmitt
Kerry Dearfield
Esther Saito
Albin Kocialski
David Van Ormer
James Kariya
RfD File
Caswell File