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

JAN 31 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: RfD/Peer Review Report of Alachlor

CASRN. 15972-60-8
EPA Chem. Code: 090501
Caswell No. 011

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

TO: Robert Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (H7505C)

Lois Rossi, chief
Reregistration Branch
Special Review and Reregistration Division (H7508W)

The Health Effects Division RfD/Peer Review Committee met on August 19, 1993 to discuss and evaluate the existing toxicology in support of Alachlor re-registration and to reassess the reference (RfD) dose for this chemical.

The RfD for this chemical was first assessed by the Health Effects Division RfD Committee on February 21, 1986 and subsequently verified by the Agency RfD Work Group on March 11, 1986 and again on March 27, 1991. At that time the RfD was based on a NOEL of 1 mg/kg/day for hemosiderosis and hemolytic anemia observed at 3 mg/kg/day in a one year feeding study in dogs. An Uncertainty Factor (UF) of 100 was used to account for the inter-species extrapolation and intra-species variability. On this basis the **RfD was** calculated to be **1. E-2 (0.01 mg/kg/day).** In the meeting of August 19, 1993 the Committee recommended that the RfD remain unchanged.

The Committee considered the chronic toxicity study in rats **(83-1a)**, the long term feeding toxicity study in dogs **(83-1b)**, the developmental toxicity studies in rats and rabbits **(83-3a and -3b)** and the reproductive toxicity in rats **(83-4)** to be acceptable and the data evaluation records to be adequate.

Since the carcinogenicity issue of Alachlor had already been addressed by the Health Effects Division Carcinogenicity Peer Review Committee (HED-CPRC), therefore, the carcinogenicity studies were not discussed by the RfD Peer Review Committee. The chemical was classified as a "Group B", probable human carcinogen (HED-CPRC report dated 06/26/1987).

There was no evidence, based on the available data, that the chemical was associated with significant developmental or reproductive toxicity under the testing conditions.

A. Individual in Attendance

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

William Burnam

Reto Engler

Marcia Van Gemert

Karl Baetcke

Henry Spencer

William Sette

James Rowe

Myron Ottley

George Ghali

Rick Whiting

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

Stephen Dapson

Mike Ioannou

3. Others:

Kerry Dearfield, Linda Kutney and Jennifer Wintersteen of HED as observers

CC: Penny Fenner-Crisp
Richard Schmitt
Kerry Dearfield
Marcia Van Gemert
Mike Ioannou
Stephen Dapson
James Kariya
Linda Kutney
RfD File
Caswell File

B. Material Reviewed

Material available for review included a reference dose summary document, data evaluation records for a long-term toxicity study in dogs **(83-1a)**, a chronic toxicity/carcinogenicity study in rats **(83-5 or 83-1b and -2a)**, developmental toxicity studies in rats and rabbits **(83-3a and -3b)** and a reproductive toxicity study in rats **(83-4)**, and a tox. one-liner.

1. Stout, L. D. (1984). A chronic study of alachlor administered in feed to Long-Evans rats. MRID No. 00091050, 40284001, HED Doc. No. 003753, 004091.

Core Classification: Core-minimum.

Committee's Conclusion and Recommendations:

The chemical was tested in Long-Evans rats at 0.5, 2.5 and 15 mg/kg/day. The NOEL/LOEL were considered to be 2.5 and 15 mg/kg/day based upon molting of retinal pigmentation and increased mortality rate in females and disseminated abnormal cellular foci in the liver of males. The Committee agreed with the reviewer's evaluation and interpretation of data. The study was considered acceptable and the data evaluation record was considered adequate. This study satisfies data requirement 83-1a of Sub-part F of the Pesticide Assessment Guideline for chronic toxicity testing in rats.

2. Naylor, M. W. et al. (1984). Chronic study of alachlor administered by gelatin capsule to dogs. MRID No. 00091050, 40284001, HED Doc. No. 003753, 004091.

Core Classification: Guideline.

Committee's Conclusion and Recommendations:

The chemical was tested in Beagle dogs at 1, 3 and 10 mg/kg/day. The NOEL/LOEL were considered to be 1 and 3 mg/kg/day based upon hemosiderosis seen in the kidney and spleen. The Committee agreed with the reviewer's evaluation and interpretation of data. The study was considered acceptable and the data evaluation record was considered adequate. This study satisfies data requirement 83-1b of Sub-part F of the Pesticide Assessment Guideline for chronic toxicity testing in dogs.

3. Tasker, E. J. (1980). Teratology study in rats. MRID No. 00043645, HED Doc. No. 003993, 001021.

Core Classification: Core-minimum.

Committee's Conclusion and Recommendations:

The chemical was tested in Charles River COBS CD albino rats at 50, 150 and 400 mg/kg/day. The maternal NOEL/LOEL were considered to be 150 and 400 mg/kg/day based upon increased death rate, increased clinical signs, decreased body weight gain for the dosing period and for the entire gestation period. Developmental NOEL was considered to be 400 mg/kg/day, the highest dose tested. Slight developmental toxicity was noted in the form of slightly reduced litter size, slightly increased post-implantation loss and slightly decreased mean fetal weight. The Committee generally agreed with the reviewer's evaluation and interpretation of data, but considered the developmental toxicity effects, if any, to be very weak. The study was considered to be acceptable and the data evaluation records to be adequate, except for minor discrepancy between the NOEL/LOEL for developmental toxicity on page 8 of the data evaluation record and page 2 of the cover memo. This study satisfies data requirement 83-3a of Sub-part F of the Pesticide Assessment Guideline for developmental toxicity testing in the rat.

4. Schroeder, R. E. (1988). A teratology study in rabbits with alachlor. MRID No. 40579402, HED Doc. No. 006886.

Core Classification: Core-minimum.

Committee's Conclusion and Recommendations:

The chemical was tested in New Zealand white rabbits at 50, 100 and 150 mg/kg/day. The maternal NOEL/LOEL were considered to be 100 and 150 mg/kg/day based upon reduced body weight gain during the dosing period with a rebound increase in body weight gain in the period following dosing. Developmental toxicity NOEL was considered to be 150 mg/kg/day, the highest dose tested. The Committee generally agreed with the reviewer's evaluation and interpretation of data. The study was considered to be acceptable and the data evaluation records to be adequate. This study satisfies data requirement 83-3b of Sub-part F of the Pesticide Assessment Guideline for developmental toxicity testing in the rabbit.

5. Monsanto (1981). A three-generation reproduction study in rats with alachlor. MRID No. 0075062, HED Doc. No. 0013338.

Core Classification: Core-minimum.

Committee's Conclusion and Recommendations:

The chemical was tested in Sprague-Dawley rats at 3, 10 and 30 mg/kg/day. The reproductive toxicity NOEL/LOEL were considered to be 10 and 30 mg/kg/day based upon kidney discoloration and increased absolute and relative kidney weights. The Committee generally agreed with the reviewer's evaluation and interpretation of data. It was suggested that the decreased absolute and relative ovarian weights consistently observed in all three generations be added to the conclusions in the one-liner of this study. The study

was considered to be acceptable and the data evaluation records to be adequate. This study satisfies data requirement 83-4 of Subpart F of the Pesticide Assessment Guideline for reproductive toxicity testing in the rat.

C. Conclusions and Recommendation

1. Reference Dose

The RfD for this chemical was first assessed by the Health Effects Division RfD Committee on February 21, 1986 and subsequently verified by the Agency RfD Work Group on March 11, 1986 and again on March 27, 1991. At that time the RfD was based on a NOEL of 1 mg/kg/day for hemosiderosis and hemolytic anemia observed at 3 mg/kg/day in a one year feeding study in dogs. An Uncertainty Factor (UF) of 100 was used to account for the inter-species extrapolation and intra-species variability. On this basis the **RfD** was calculated to be **1 E-2 (0.01 mg/kg/day)**. In the meeting of August 19, 1993 the Committee recommended that the RfD remain unchanged.

2. Data Base

The Committee considered the chronic toxicity study in rats **(83-1a)**, the long term feeding toxicity study in dogs **(83-1b)**, the developmental toxicity studies in rats and rabbits **(83-3a and -3b)** and the reproductive toxicity in rats **(83-4)** to be acceptable and the data evaluation records to be adequate.

3. Carcinogenicity

Since the carcinogenicity issue of Alachlor had already been addressed by the Health Effects Division Carcinogenicity Peer Review Committee (HED-CPRC), therefore, the carcinogenicity studies were not discussed by the RfD Peer Review Committee. The chemical was classified as a "Group B", probable human carcinogen (HED-CPRC report dated 06/26/1987).

4. Developmental and Reproductive Toxicity

There was no evidence, based on the available data, that the chemical was associated with significant developmental or reproductive toxicity under the testing conditions.