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

JUN 24, 1991

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No. 707-145, 165, and 174
Oxyfluorfen; Goal; HED Peer Review
on Oxyfluorfen; Company Response

Caswell No. 188AAA
Project No. 0-1924
Record No. 5382050

FROM: William Dykstra, Ph.D.
Review Section I, TB-I, IRS
Health Effects Division, H7509C

William Dykstra
6/26/90

TO: Steven Robbins, PM Team # 23
HFB,
Registration Division, H7505C

THRU: Roger Gardner, Acting Section Head
Review Section I, TB-I, IRS
Health Effects Division, H7509C

Reviewed
06/14/91
(for RG)
Karl Baetcke
6/14/91

Requested Action:

Review company's comments regarding the inappropriate use of quantification of cancer risk for oxyfluorfen.

Conclusion and Recommendation:

1. The HED Peer Review Committee considered the entire oxyfluorfen data base, SAR activity and its judicious use of the Q_1* has not been successfully challenged, in the opinion of TB-I, by the registrant. The registrant's dietary risk assessment should be deferred to DEB or DRES for further comment.

Review:

1. Letter of June 13, 1990 from William Lynch, Ph.D. to Joanne Miller of EPA.

~~109~~
1

In the letter, Dr. Lynch states:

"The Health Effects Division Peer Review Committee has concluded that oxyflyuorfen is a Category C - Possible Human Carcinogen based on hepatocellular adenomas and carcinomas in male mice and recommended that quantitation of risk should be performed based on the significant positive dose-related trend in liver tumors in male mice.

It is our judgment that the evidence for oxyfluorfen carcinogenicity in the male mouse is equivocal since statistically significant differences, are, or are not, obtained depending on which pathologists findings are used and which control group the treated groups are compared with. Furthermore, the evidence for a significant trend in tumor incidence, which prompts a call for quantitative risk assessment, is certainly undermined by the absence of any liver tumors at the lowest dose of oxyfluorfen." End of quotation

TB Response:

Dr. Lynch apparently has not understood that the decision to utilize a Q_1* for oxyfluorfen was based not only on the significant dose-related trend for liver tumors, but additionally, on the increased incidence of carcinomas in treated groups, the positive mutagenicity data, and the strong evidence of carcinogenicity based on SAR. Additionally, the vote of the Committee members which resulted in a consensus to utilize the Q_1* may have included other individual scientific reasons of Committee members which were not detailed in the HED document. Clearly, oxyfluorfen is a carcinogen and a Q_1* is fully warranted.

Note to PM #23:

The registrant's dietary risk estimates based on the company's data should be deferred to DEB or DRES.