



188AAA

CASWELL FILE

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Subject: Oxyfluorfen (Goal) - Quantitative Risk Assessment,
20 Month Dietary Study of Charles River CD Male Mice

Caswell no. 188AAA

From: Bernice Fisher, Biostatistician
Science Support Section
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

Bernice Fisher 9/18/89

To: William Dykstra, Ph.D., Pharmacologist
Review Section I
Toxicology Branch I - Insecticide/Rodenticide Support
Health Effects Division (H7509C)

Thru: *for* John A. Quest, Ph.D., Section Head
Science Support Section
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

Kerry D. Deafield 9/18/89

Summary

The unit risk, Q_1^* , of oxyfluorfen is $1.28 \times 10^{-1} (\text{mg/kg/day})^{-1}$ in human equivalents. This estimate of Q_1^* is based upon male liver (adenoma and/or carcinoma) tumors in Charles River CD-1 mice with dose levels of 0 (untreated), 2, 20, and 200 ppm.

Mortality was significantly decreased with dose increments of oxyfluorfen. No other significant differences were found in these data. There was a significant dose related trend in male liver tumor (adenoma and/or carcinoma) rates. See the memorandum on "Oxyfluorfen (Goal) - Qualitative Risk Assessment, B. Fisher, 10/28/88" for further details about the selection of male liver tumors for use in the quantitative risk assessment process.

Dose-Response Analysis

The Peer Review Committee on oxyfluorfen categorized it as a [C_q] carcinogen and recommended that the male mouse liver tumor (adenoma and/or carcinoma) rates be used to estimate the unit risk, Q_1^* because of the fact that these tumors exhibited a significant increasing dose related trend.

Since there was no statistical evidence of a significant increase in dose related mortality in the males, the estimate of the unit risk, Q_1^* of oxyfluorfen based upon liver tumor data, was calculated by the use of the Global86 (Multi-Stage process) computer program of K.Crump. The unit risk calculated from the male data in ppm doses was converted to mouse mg/kg/day by the use of Lehman's Tables and then to human equivalents by the use of interspecies surface area adjustments as recommended by EPA Cancer Guidelines (1986).

The resultant estimate of Q_1^* is as follows:

male liver tumor (adenoma and/or carcinoma)	Mouse, Q_1^* (mg/kg/day) ⁻¹ 9.58 x 10 ⁻³	In Human Equivalents 1.28 x 10 ⁻¹
---	---	---

It is to be noted that Q_1^* is an estimate of the upper (95%) bound on risk and that (as stated in the EPA Guidelines) the "true value of the risk is unknown and that the lower limit of the risk may be as low as zero".

2

References

Howe, R.B., Crump, K.S. and Van Landingham, C. (1986)
A Computer Program to Extrapolate Quantal Animal
Toxicity Data to Low Doses (unpublished report), 25pgs.