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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: Fenbuconazole, Quantitative Risk Assessment, Two-Year Rat (Charles River Sprague-Dawley, MRID Nos. 416353-01 & 416353-02) Dietary Study

Caswell no.723Q

From: Bernice Fisher, Biostatistician
Statistics Section
Science Analysis Branch
Health Effects Division (7509C)

Bernice Fisher 2/2/94

To: SanYvette Williams, Pharmacologist
Review Section IV
Toxicology Branch II
Health Effects Division (7509C)

Thru: Hugh Pettigrew, Ph.D., Section Head
Statistics Section
Science Analysis Branch
Health Effects Division (7509C)

Hugh M. Pettigrew 2/7/94

Summary

The unit risk, $Q_1^*(mg/kg/day)^{-1}$ of Fenbuconazole, based upon male rat thyroid follicular cell (adenomas and/or carcinomas) tumor rates is 1.65×10^{-2} $(mg/kg/day)^{-1}$ in human equivalents. The data on tumor rates and dose levels represent combined data from two rat studies. The dose levels used, from the combined studies were 0, 8, 80, 800 and 1600 ppm. of Fenbuconazole. The corresponding combined tumor rates were 5/113, 5/58, 3/57 13/116, and 10/55 respectively.

Background

In August, 1993 the Peer Review Committee recommended that a quantitative risk assessment for Fenbuconazole be estimated from the combined high and low dose studies of rats for male thyroid follicular(adenomas and/or carcinomas) tumor rates.

The statistical evaluation (Fenbuconazole-Qualitative Risk Assessment-Based on Charles River Sprague-Dawley Rat and CD-1 Mouse Dietary Studies, L.Brunsman 7/93) indicated that there was no significant differential mortality with dose increments of Fenbuconazole in the low dose study and a decrease in mortality (although not statistically significant) in the high dose group. The male rats, both the high and low dose studies had significantly increasing trends in thyroid follicular cell (adenomas and/or carcinomas) tumor rates with dose increments of Fenbuconazole.

Dose-Response

Since mortality did not significantly increase in either of the two rat studies with incremental doses of Fenbuconazole in males, the estimate of the unit risk, Q_1^* was obtained by the application of the Linearized Multi-Stage model (Tox_Risk program, version 3.1- K.Crump).

An estimate of risk, Q_1^* was calculated for both the high and low dose studies separately for the thyroid follicular cell (adenomas and/or carcinomas) tumor rates and also for the combined data from both studies for the same tumor rates.

The results of the estimate of unit risk, Q_1^* are as follows:

Species:Strain,	tumor	Q_1^* $(mg/kg/day)^{-1}$ in Human Equivalence
Rat:Charles River Sprague-Dawley	Thyroid follicular cell(adenoma &/or carcinoma)	
Male- low dose		3.00×10^{-2}
Male- high dose		1.52×10^{-2}
Males- combined doses		1.65×10^{-2}

It is to be noted that Q_1^* $(mg/kg/day)^{-1}$ is an estimate of the upper bound on risk and that (as stated in the EPA Risk Assessment Guidelines) "the true value of the risk is unknown, and may be as low as zero."