3-15-95

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

#723Q

MAR 15 1995

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: Fenbuconazole, Quantitative Risk Assessment -Revised Q_1^*, (3/4's Interspecies Scaling Factor), Two-Year Charles River Sprague-Dawley Rat Dietary Studies

Caswell No.723Q
PCCODE : 129011

From: Bernice Fisher, Biostatistician
and
Hugh Pettigrew, Section Head
Statistics Section
Science Analysis Branch/HED (7509C)

3/14/95

To: Debra Edwards, Chief
Chemical Coordination Branch/HED (7509C)

Thru: William L. Burnam, Chief,
Science Analysis Branch/HED (7509C)

The revised unit risk, $Q_1^*(mg/kg/day)^{-1}$ of Fenbuconazole, based upon male rat thyroid follicular cell (adenomas and/or carcinomas) tumor rates is $1.06x10^{-2}$ in human equivalents (converted from animals to humans by use of the 3/4's scaling factor-1994,Tox_Risk,3.5-K.Crump)[a]. The data on tumor rates and the 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. The memorandum, Fenbuconazole- Qualitative Risk Assessment-Based on Charles River Sprague-Dawley Rat and CD-1 Mouse Dietary Studies, L.Brunsman 7/93) contained the underlying data and statistical evaluation that was used for the above revision of the unit risk of Fenbuconazole.

[a] See Memo - Deriving Q_1^*s Using the Unified Interspecies Scaling Factor, P.A. Fenner-Crisp, Director-HED, 7/1/94.

cc: Caswell file
B.Doyle
M.Van Gemert
C.Swentzel

Background

At a March 14,1995 meeting with Rohm and Haas, William Burnam, Drs Karl Baeckte, Marcia Van Gemert among others from HED, and Jim Stone and Ms. Giles-Parker of RD, etc agreed that the Fenbuconazole unit risk, Q_1^*, should be recalculated based upon the new 3/4's power scaling factor instead of the previous 2/3's power.

Dose-Response Analysis

The estimate of unit risk, Q_1^*, was based upon thyroid follicular cell (adenoma and/or carcinoma) tumor rates in male rats obtained from combined data of a high and low dose study.

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^*, were obtained by the application of the Linearized Multi-Stage model(Tox_Risk program, version 3.5 - K.Crump).

The resulting estimate of unit risk, Q_1^*, is as follows:

Species,Strain,Sex	Tumor	Q_1^* $(mg/kg/day)^{-1}$
Rat,Charles River,Male Sprague-Dawley	Thyroid Follicular Cell (Ad &/or Ca)	1.06×10^{-2}

For the conversion to human equivalents, weights of .35 kg for the mice, 70 kg for humans and the 3/4's scaling factor were used.

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."