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Subject: Cyproconazole, Revised Quantitative Risk Assessment,
CD-1 Mouse Dietary Study

Caswell no.272E

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Summary

The revised unit risk, Q_1^* (mg/kg/day)⁻¹ of cyproconazole in terms of human equivalents is 3.0×10^{-1} . The estimate of the risk is based upon the higher estimated risk in males as compared with female mice each with significant dose related increasing liver tumors (adenomas and/or carcinomas) in the 2-year dietary study. The dose levels used in the study were 0, 5, 15, 100 and 200 ppm. of cyproconazole.

Background

In June, 1990 the Peer Review Committee recommended that a quantitative risk assessment for cyproconazole be estimated from the combined liver tumor (adenomas and/or carcinomas) rates in both male and female mice and to use "the steeper dose response for the purpose of risk assessment" (Dose Response Assessment of the Carcinogenic Effects of Cyproconazole at Low doses etc, Reto Engler memo of 6/29/90). This decision was reaffirmed in the second peer review meeting of January, 1992.

The statistical evaluation (Cyproconazole-Qualitative Risk Assessment, Mouse (CD-1) Study, B.Fisher 5/90) indicated that there was significant decreased mortality with incremental doses of cyproconazole in both male and female mice. The significant dose related increases in tumors were in both male and female liver tumors (adenomas and/or carcinomas).

Dose-Response

Since there was differential survival with incremental doses of cyproconazole in both sexes, the estimate of the unit risk, Q_1 was obtained by the application of the Time-to-Tumor model (Tox_Risk program, version 3.1- K.Crump). An estimate of risk, Q_1 was calculated for each sex on the liver tumor (adenomas and/or carcinomas) rates.

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

Species:Strain, tumor	Q_1^* (mg/kg/day) ⁻¹ in Human Equivalence
Mouse CD-1, Liver tumors (adenomas &/or carcinomas)	
Female	8.87×10^{-2}
Male	3.02×10^{-1}

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."

This memo supersedes the earlier quantitative risk assessment memo of 5/14/92.