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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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Subject: Cyproconazole, Quantitative Risk Assessment,
CD-1 Mouse Dietary Study

Caswell no.272E

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Summary

The unit risk, $Q_1^*$ $(mg/kg/day)^{-1}$ of cyproconazole in terms of human equivalents is $5.2 \times 10^{-2}$. The estimate of the risk is based upon the geometric mean of male and female mice with discernable 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 of both male and female mice. 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 increased mortality was not affected by incremental doses of cyproconazole in either male or 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 by 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 and then combined geometrically to represent the risk of cyproconazole.

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

| Species:Strain, | tumor | $Q_1^*$ $(mg/kg/day)^{-1}$ |
|---|---|---|
| Mouse CD-1, | Liver tumors (adenomas &/or carcinomas) | in Human Equivalence |
| Female | | $8.87 \times 10^{-2}$ |
| Male | | $3.02 \times 10^{-1}$ |
| Geometric Mean | | ~~$5.17 \times 10^{-2}$~~ $1.6 \times 10^{-1}$ |

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."