UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: Imazalil, Quantitative Risk Assessment, Two-Year Charles River SPF Swiss Albino Mouse Dietary Study

Caswell No. 497B

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Summary

The estimated unit risk, $Q_1^*(mg/kg/day)^{-1}$ of Imazalil, based upon the male mouse hepatocellular (adenomas, and/or carcinomas) tumors is 6.20×10^{-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 dose levels used in the 100 week study were 0, 50, 200, and 600 ppm of Imazalil. The corresponding tumor rates for the male mice were 10/50, 8/47, 17/50, and 22/48 respectively.

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

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Background

In August, 1994, the Carcinogenicity Peer Review Committee recommended that a quantitative risk assessment for Imazalil be estimated from male mouse liver (adenomas and/or carcinomas) tumor rates.

The statistical evaluation (Imazalil Qualitative Risk Assessment Based on Charles River SPF Swiss Albino Mouse Dietary Study, L.Brunsman 7/94) indicated no significant dose related differential mortality in the male mice.

Male mice had a dose related significant ($p<.01$) increasing trend in hepatocellular (adenomas and/or carcinomas) tumor rates and also a significant difference in the pair-wise comparison of the 600 ppm dose group and the controls.

Dose-Response

Since mortality was not affected differentially with increasing doses of Imazalil, the estimate of the unit risk, Q_1^*, in human equivalents was obtained by the application of the Multi-Stage model (Tox_Risk program, version 3.5 - K.Crump). An estimate of the risk was calculated from male mouse hepatocellular (adenomas and/or carcinomas) tumor rates.

The resulting estimates of unit risk, Q_1^*, were converted to human equivalents by the use of weights of .03 kg for the mice and 70 kg for humans and the 3/4's scaling factor for interspecies extrapolation.

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."