UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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Subject: Acetochlor - Quantitative Risk Assessment, CD Rat Study

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

Caswell no.003B

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Summary

The unit risk, Q_1^* of acetochlor based upon male rat nasal tumors (adenomas and/or carcinomas) in terms of human equivalents $(mg/kg/day)^{-1}$ is 2.1×10^{-2}. The unit risk based upon the female rat nasal tumors (adenomas and/or carcinomas) in terms of human equivalents is 1.4×10^{-2} $(mg/kg/day)^{-1}$. The estimated risk based upon both sexes, combined by means of the geometric mean, is 1.7×10^{-2} $(mg/kg/day)^{-1}$ for acetochlor.

Background

In October,1991 the Peer Review Committee recommended that a quantitative risk assessment for acetochlor be estimated from the CD rat study by combining nasal tumor data for both sexes. The qualitative data evaluation (Acetochlor - Qualitative Risk Assessment - 2-Year CD Rat & CD-1 Mouse Dietary Studies, B.Fisher 9,91) indicated that incremental doses of acetochlor significantly affected survival in male rats, but not in the females. Significant dose related increases in tumors were for both sexes, in the combined nasal adenomas and/or carcinomas and in nasal adenomas. Both sexes of rats also had significant differences in the pair-wise comparison of controls and the highest dose group in nasal adenomas and in the combined nasal adenomas and/or carcinomas.

Dose-Response Analysis

Since male rats had statistically significant increases in mortality with dose increments of acetochlor, the estimate of unit risk, Q_1^* was obtained by the time-to-tumor Weibull model and for the females, with no significant mortality increases, by the Multi-Stage model (K.Crump, Toxver3 computer program).

The unit risk, $Q_1^*(mg/kg/day)^{-1}$ for rats was converted to human equivalents by the application of the interspecies surface area adjustment [(human weight/animal weight)$^{1/3}$], as recommended by the EPA Cancer Guidelines (F.R. 51; 33993-34014) and under the assumption that the adult weight of the rat is 0.400 kg. and the human is 60 kg.

The resulting unit risks, Q_1^*'s $(mg/kg/day)^{-1}$ are as follows:

	Animal	Human Equivalents
Male[a] rat nasal tumors (adenoma and/or carcinoma)	3.92×10^{-3}	2.08×10^{-2}
Female[b] rat nasal tumors (adenomas and/or carcinomas)	2.57×10^{-3}	1.37×10^{-2}
Both (geometric mean)		1.69×10^{-2}

[a] Time-to-Tumor Model
[b] Multi- Stage Model

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."