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2-28-97

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

FEB 28 1997

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: Propazine, Quantitative Risk Assessment -Revised Q_1^*, (3/4's Interspecies Scaling Factor), Two-Year Sprague-Dawley Rat Dietary Study
P.C. no. 080808

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Summary

The revised unit risk, $Q_1^*(mg/kg/day)^{-1}$ of Propazine, based upon female rat mammary gland (adenomas and/or adenocarcinomas) tumor rates is $4.45x10^{-2}$ 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 for the 105 week study, were 0, 3, 100 and 1000 ppm. of Propazine. The corresponding tumor rates were 6/57, 17/58, 11/59 and 121/55 respectively.

Background

In August, 1996 (third meeting), the Carcinogenicity Peer Review recommended that a quantitative risk assessment for Propazine be recalculated from the mammary gland tumors observed in the re-read slides of the 1981 Dietary Study of the Sprague-Dawley female rats.

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

The memorandum, Revised Propazine Qualitative Risk Assessment Based on 1995 Re-Read of female mammary gland slides from 1981 Sprague-Dawley Rat Dietary Study, L.Brunsman (8/96), indicated that there was a significant decreasing trend in survival with dose increments of Propazine.

Female rats had a dose related significant ($p<.01$) increasing trend in mammary gland (adenomas and/or adenocarcinomas) tumor rates and also significant ($p<.01$) differences in the pair-wise comparisons of the 3 and the 1000 ppm. dose groups, each with the control group.

Dose-Response Analysis

The estimate of unit risk, Q_1^*, was based upon mammary gland (adenoma and/or adenocarcinoma) tumor rates in female rats. Since female rats had significantly increased mortality with incremental doses of Propazine, the estimate of the unit risk, Q_1^*, were obtained by the application of the Multi-Stage Weib model (Tox_Risk program, version 3.5 - K.Crump).

For the conversion to human equivalents, weights of .35 kg for the rats, 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."