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

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MEMORANDUM August 19, 1999

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Thiabendazole™ Quantitative Risk Assessment (Q_1^*) Based On Sprague-Dawley Crl:CD BR Rat Chronic Dietary Study Using mg/kg b.w.$^{\hat{}3/4}$'s/day Cross Species Scaling Factor

P.C. Code 060101

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The most potent unit risk, $Q_1^*(mg/kg/day)^{-1}$, of those calculated for Thiabendazole is that for female rat thyroid follicular cell adenoma and/or carcinoma combined tumor rates at 7.11×10^{-3} in human equivalents. The dose levels used from the 105-week dietary study were 0, 10, 30, and 90 mg/kg/day. The corresponding tumor rates were 4/82, 0/36, 1/43, and 5/44, respectively.

Background

On May 26, 1999, the Cancer Assessment Review Committee met to classify the carcinogenic potential of Thiabendazole. Quantifications of risk have subsequently been estimated for male and female rat thyroid follicular cell tumors. The most potent unit risk, Q_1^*, of the these will be used for further calculations by the Agency. In this case, the most potent unit risk, Q_1^*, is that for female rat thyroid follicular cell adenoma and/or carcinoma combined tumor rates at 7.11×10^{-3} in human equivalents.

All unit risks have been converted from animals to humans by use of the $^3/_4$'s scaling factor (Tox_Risk program, Version 3.5, K. Crump, 1994)[1]. For the conversion to human equivalents, weights of 0.35 kg for the rat and 70 kg for humans were used.

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

It is to be noted that the 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."

Dose-Response Analysis

The statistical evaluation of mortality (Malathion Qualitative Risk Assessment Based On Sprague-Dawley Crl:CD BR Rat Dietary Study, L. Brunsman, 8/19/99) indicated significant increasing trends with increasing doses of Thiabendazole in female rats. Therefore, the estimate of unit risk, Q_1^*, for female rats was obtained by the application of the time-to-tumor Weibull model (Tox_Risk program, Version 3.5, K. Crump, 1994). Male rats showed no significant incremental changes in mortality with increasing doses of Thiabendazole. The unit risk, Q_1^*, for male rats was obtained by the application of the Multi-Stage model (Tox_Risk program, Version 3.5, K. Crump, 1994).

Female rats had significant increasing trends in thyroid follicular cell adenomas and adenomas and/or carcinomas combined, both at $p < 0.05$. There was a significant difference in the pair-wise comparison of the 90 mg/kg/day dose group with the controls for thyroid follicular cell adenomas at $p < 0.05$.

Male rats had significant increasing trends, and significant differences in the pair-wise comparisons of the 90 mg/kg/day dose group with the controls, for thyroid follicular cell adenomas and adenomas and/or carcinomas combined, all at $p < 0.01$. There were also significant differences in the pair-wise comparisons of the 30 mg/kg/day dose group with the controls at $p < 0.01$ for thyroid follicular cell adenomas and at $p < 0.05$ for thyroid follicular cell adenomas and/or carcinomas combined.

Additional Q_1^* Calculations

The unit risk, Q_1^* $(mg/kg/day)^{-1}$, of Thiabendazole based upon male rat thyroid follicular cell adenoma and/or carcinoma combined tumor rates is 1.83×10^{-3} in human equivalents. The dose levels used from the 105-week dietary study were 0, 10, 30, and 90 mg/kg/day. The corresponding tumor rates were 1/97, 1/46, 5/47, and 6/46, respectively.