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

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Cyanazine; Quantitative Estimate of Carcinogenic Risk: Oral Slope Factor

FROM: Reto Engler
CRAVE Co-Chair
Office of Pesticide Programs
Health Effects Division (H 7509 C)

THROUGH: Penelope Fenner-Crisp
Director Penelope A. Fenner-Crisp 6/14/93
Health Effects Division (H 7509 C)

TO: Jim Cogliano
CRAVE Co-Chair
Human Health Assessment Group
Office of Health and Environmental Assessment (RD-689)

At the CRAVE meeting of June 3, 1993 the calculation of the oral slope factor for Cyanazine was discussed at great detail. At the time the Office of Pesticide Programs (OPP) had calculated the oral slope factor the interim sacrifice animals were included in the calculation, because some (i.e. a total of three animals) of these animals already had the relevant tumor[1].

The OPP agrees that interim sacrifice animals should in general not be included in the calculation of a slope factor for a lifetime exposure, regardless of whether or not some of these animals already have the relevant tumor. Early appearance of tumors should, however, be used in the weight of the evidence evaluation, or if appropriate the tumor incidence at the one year sacrifice can be used to calculate a projected lifetime slope factor using the customary adjustments for the shorter duration of exposure to the test substance. In short we agree that the oral slope factor of 1.0 (rounded from 1.01) per mg/kg/day is more appropriately reflecting the current practice of computing such factors, than the slope factor of 0.84 per mg/kg/day previously calculated by OPP.

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[1] To the best recollection of some of us this was also done in part because it was believed that it was agency policy to include interim sacrifice animals if in fact the first tumor appeared before the interim kill.

At the CRAVE meeting we nevertheless argued that CRAVE could and probably should verify cancer assessments, including slope factors, done by the program offices particularly if these assessments were already used extensively in regulatory decisions, and if the assessment is not seriously flawed. The slope factor of 0.84 has been used by OPP for the assessment of dietary risks (DRES memo of November 13, 1993), however, to date no regulatory decisions, such as accepting or rejecting certain food uses or altering agricultural use patterns have been made using the slope factor of 0.84. We therefore believe that this is an appropriate moment for OPP to start using the slope factor of 1.0 in accordance with the CRAVE assessment. We support that this value is verified for use on IRIS and that the slope factor of 0.84 should not be mentioned.

Beyond the present cancer assessment of Cyanazine (and the analogues) we believe that there is a strong likelihood that future research and testing could support the hypothesis that these chemicals produce mammary tumors via a mechanism that disturbs the hormonal balance of the exposed animals. If in the future we should conclude that the hypothesis has been shown to be true we would present our assessment to peer review and CRAVE for verification.

cc:

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