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Cancer Benchmark Dose Calculation for Fluorochemical-143 (FC-143): Ammonium Perfluorooctanoate

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Introduction

In a study conducted by the Riker Laboratories, Inc., 3M Company, during 1981-1983, fifty male and female Sprague-Dawley rats were fed ammonium perfluorooctanoate (FC-143) at 0, 30, and 300 ppm in the diet for two years. Also, an interim sacrifice was conducted at one year on 15 additional rats per sex for the controls and 300 ppm group.

There was a statistically significant increase for testicular tumors (epididymis Leydig cell adenoma) at the high dose with a significant dose response trend (P=0.007) associated with FC-143 in this study. Also, there was a statistically significant increase of mammary gland fibroadenoma at the high dose and a significant dose response trend (P=0.024) associated with FC-143 for this study. Thus, a benchmark dose (BMD_{10}), corresponding to an extra lifetime incidence of 10%, was estimated for testicular tumors and mammary gland fibroadenoma.

A lower 95% confidence limit on the benchmark dose ($LBMD_{10}$) has been suggested as a point of departure for low dose cancer risk assessment (U.S. EPA; 1996, 1999). If a nonlinear dose response is anticipated in the low dose range of human exposure, the $LBMD_{10}$ is divided by uncertainty factors for extrapolation from an effect level, animal to human extrapolation, and inter-individual sensitivity in order to arrive at a reference dose that likely is associated with at most a negligible lifetime cancer risk. In the absence of a nonlinear dose response, the default procedure is linear extrapolation from the $LBMD_{10}$ to zero for upper bound estimates of lifetime cancer risk at low doses.

Benchmark Dose for Testicular Tumors

The National Toxicology Program (NTP) has adopted the Poly-3 procedure (Bailer and Portier, 1988) for calculating the effective lifetime number of animals at risk for cancer, giving 44, 44, and 48 animals at risk of developing testicular tumors at doses of 0, 30, and 300 ppm, respectively, including the animals sacrificed at one year on the study. This gives age-adjusted testicular tumor incidence rates of 0/44, 2/44, and 7/48 at 0, 30, and 300 ppm, respectively. Using the U.S. EPA Benchmark Dose Software (www.epa.gov/ncea/bmds.htm) to fit the multistage model to these age-adjusted incidence rates gives estimates of BMD_{10} = 180 ppm and $LBMD_{10}$ = 100 ppm of FC-143 in the total diet for a lifetime for testicular tumors.

Benchmark Dose for Mammary Gland Fibroadenoma

The Poly-3 age–adjusted effective numbers of animals at risk for mammary gland fibroadenoma were 38, 37, and 43 for doses of 0, 30, and 300 ppm, respectively, including animals sacrificed at one year. The age-adjusted fibroadenoma incidence rates were 10/38, 19/37, and 23/43, for doses of 0, 30, and 300 ppm, respectively. Using the U.S. EPA Benchmark Dose Software (BMDS) to fit the multistage model to these incidence rates gave estimates of BMD_{10} = 93 ppm and LBMD = 45 ppm of FC-143 in the lifetime diet for mammary gland fibroadenoma.

References

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