

**A Critical Evaluation of the Use of Mutagenesis, Carcinogenesis, and
Tumor Promotion Data in a Cancer Risk Assessment of
2,3,7,8-Tetrachlorodibenzo-*p*-dioxin**

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Regulatory agencies in the Western Hemisphere are currently assessing the potential human health risks of environmental contamination by 2,3,7,8 tetrachlorodibenzo-*p*-dioxin (TCDD). Some U.S. agencies such as the Environmental Protection Agency (EPA) and Centers for Disease Control (CDC) have assumed that TCDD behaves as a tumor initiator in animals and have used linear low-dose mathematical extrapolation models for estimating any human risk. In contrast, the Ontario Ministry of the Environment, the State Institute of National Health of The Netherlands, and the Federal Environmental Agency of the Federal Republic of Germany have concluded that TCDD does not have initiator activity; these agencies have advocated a risk extrapolation approach which applies a safety factor to a no-observable-effect level. Estimations of the potential risk obtained by these two approaches can differ by three to four orders of magnitude and have a major impact on the allocation of resources within the affected countries. This paper critically reviews the TCDD bacterial, animal, and human data on mutagenesis, carcinogenesis, and tumor promotion and concludes that the scientific evidence does not support risk estimations which are based on TCDD as a tumor initiator. Rather, the animal data overwhelmingly support TCDD as a tumor promoter. Risk estimations which incorporate tumor promotion activity more accurately reflect the scientific understanding of TCDD's mechanism of action and provide better estimates of its risk.