

**RISK ASSESSMENT OF 2,3,7,8-TCDD
USING A BIOLOGICALLY-BASED CANCER MODEL:
A RE-EVALUATION OF THE KOCIBA ET AL. (1978) BIOASSAY**

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ABSTRACT

The Moolgavkar-Knudson-Venzon (M-K-V) two-stage model for carcinogenesis was used to predict the risk-specific dose (RsD) based on the incidence of tumors reported by Kociba et al. (1978) for Sprague-Dawley rats exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD). In addition, the results from the recently completed histopathology re-evaluation of the same study by an independent Pathology Working Group (PWG,1990), using current National Toxicology Program (NTP) pathology criteria, were also evaluated using the M-K-V model. Preliminary estimates of the RsD at a 1×10^{-6} risk level based on the 1978 histopathology results were 10 fg/kg/day if carcinomas and hyperplastic nodules were combined and 150 fg/kg/day if only carcinomas were considered. In contrast, RsDs based on the histopathology re-examination using current pathology criteria were 80 fg/kg/day when adenomas and carcinomas were combined and 400 fg/kg/day if only hepatic carcinomas were considered. Since the M-K-V model is intended only to be used for malignant tumors, the most appropriate RsD is 400 fg/kg/day (10^{-6} risk). This value is approximately 60-fold greater than USEPA's RsD (10^{-6} risk) of 6.4 fg/kg/day. In light of the more biologically relevant basis of the M-K-V model, these results can be expected to be more valid than those derived from statistically based models.

KEY WORDS

2,3,7,8-TCDD, dioxin, M-K-V model, cancer risk, biologically-based model