Margin of Exposure (MOE) for Dioxin Non-Cancer Effects: Review and Evaluation of the EPA Draft Dioxin Reassessment

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- *Identification of critical effects data sets.*
- *Benchmark dose modeling*
  - *methodology*
  - *selection of target response levels*.
- *Extrapolation of acute TCDD studies to chronic exposure to a mixture of TEQ-contributing compounds*

- *Application of current TEFs, based on relative potency on an intake-dose basis, to body burdens of dioxin-like chemicals*
- *Interspecies differences in sensitivity*
- *Assessment of current and likely future exposure and body burden levels*.

Table 1. Summary of factors that influence the interpretation of the MOEs discussed in the Draft Reassessment

Risk Assessment Component	Approximate Magnitude of Unstated Conservatism in Estimated MOEs
Point-of-Departure Estimation	
Reliance on acute dose studies in pregnant animals to predict distribution to the fetus of chronic maternal body burden	2- to 3-fold
Reliance on studies of TCDD to predict effects of maternal body burden of other TEQ compounds on fetus	4-fold
Benchmark dose methodology choice (ED vs. BMD method)	3-fold
Reliance on benchmark dose-response level (1%) below observable LOAEL/NOAELs	2- to 3-fold
Application of intake-based TEFs to a body-burden-based risk assessment	Uncertain magnitude; varies by congener and endpoint
Lower sensitivity of humans compared to the most sensitive laboratory rodents	Uncertain magnitude (possible factor of 10 based on AhR ligand binding affinity)
Exposure Estimation	
Reliance on general population average body burdens to characterize body burdens of young adults of reproductive age	4-fold