

Recommended Relative Potency Factors for 2,3,4,7,8-Pentachlorodibenzofuran: The Impact of Different Dose Metrics

Robert A. Budinsky,^{*,1} Dennis Paustenbach,[†] Donald Fontaine,^{*} Bryce Landenberger,^{*} and Thomas B. Starr[‡]

**The Dow Chemical Company, Midland, Michigan 48674; †ChemRisk, Inc., San Francisco, California 94105; and ‡TBS Associates, Raleigh North Carolina 27615–3700*

The recent National Toxicology Program (NTP) cancer bioassays for 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) and 2,3,4,7,8-pentachlorodibenzofuran (4-PeCDF) permit a reevaluation of the current TEF value of 4-PeCDF. The data also allow for the derivation of relative potency factors (RPFs) for cancer, which are based not only on administered dose but also on potentially more informative dose metrics, such as liver concentration, area under the liver concentration curve, and lifetime average body burden. Our analyses of these data indicate that chi-squared tests of observed versus predicted liver tumor incidence for 4-PeCDF reject the current TEF value of 0.5 value as too high. 4-PeCDF RPFs were derived using estimation methods that either did or did not assume parallelism of the 4-PeCDF and TCDD dose–response curves. The resulting parallelism-based RPFs for administered dose, liver concentration at terminal sacrifice, liver concentration AUC, and lifetime average body burden are 0.26, 0.014, 0.021, and 0.036, respectively. The administered dose RPF estimate is approximately one-half the current TEF value of 0.5. However, the use of administered dose fails to take into account pharmacokinetic differences between congeners and the generally acknowledged belief that body burden or some other measure of cumulative dose is more appropriate for estimating the health risk posed by persistent chemicals. The other three dose metrics do account for these important factors, and the corresponding RPFs are at least 10-fold lower than the current TEF for 4-PeCDF. In summary, our analyses support an administered dose TEF no greater than 0.25 and one in the 0.05–0.1 range for internal dose metrics such as lifetime average liver concentration or body burden.
