

EPA's Proposed Reference Dose for TCDD

EPA has proposed a draft "reference dose" (RfD) for 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) ("dioxin"). An RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

EPA's proposed value – 0.7 pg/kg-d – is more than three times lower than the World Health Organization Tolerable Daily Intake (TDI) value of 2.3 pg/kg-d used internationally for dioxins. EPA's draft RfD is based on data from two studies of persons exposed to a large release of dioxin in an accident in Seveso, Italy, in 1976. In one study, slight alterations of thyroid hormone levels in newborn infants were associated with maternal blood levels of dioxins. In the other, sperm levels in males exposed as children were inversely associated with childhood dioxin levels.

EPA's overall approach to deriving an RfD using these datasets is generally appropriate. Specific science policy choices, however, result in an RfD value that is overly conservative. These choices fall into three categories:

1. EPA ignores non-TCDD dioxins in the studied population. EPA assumes that all "dioxin-like" compounds produce the same effects with different potencies. Persons in the Seveso population had high levels of non-TCDD dioxin-like compounds, but EPA counted only TCDD in their quantification of the starting point, or point of departure (POD) for deriving the RfD. Accounting for non-TCDD dioxin-like compounds would increase the estimated exposure level for the two key studies by 50% and 125%. **This would result in an increase in the resulting RfD values by a factor of 1.5 to 2.**

2. EPA over interprets the observed effects. Neither the subtle alterations in thyroid hormone levels nor the changes in sperm parameters observed in these studies rise to the level of clinically relevant changes. However, in both cases, EPA counts the observed changes as fully adverse effects, assigning a 10-fold uncertainty factor in the RfD derivation to account for these. EPA policy allows for assigning a partial uncertainty factor of 3 to effects considered to be "minimally adverse." **This change would result in a 3-fold increase in the derived RfD.**

3. EPA underestimates children's exposures in Seveso. EPA's estimation of daily doses required to achieve the blood levels seen in the children in Seveso is too low, and conflicts with other published information for these children. **Correctly estimating these exposures would increase the derived RfD by a factor of 2 to 3.**

If these technical issues were corrected, the derived RfD would be approximately 3 to 10.