

**BASIS FOR A PROPOSED REFERENCE DOSE (RfD) FOR DIOXIN OF 1–10 PG/KG-DAY: A WEIGHT OF EVIDENCE EVALUATION OF THE HUMAN AND ANIMAL STUDIES**

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*The dioxins have been perhaps the most studied of all chemicals to which humans are routinely exposed. It has been reported that more than 5000 scientific papers have been published that have evaluated the toxicology of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Although the cancer hazard posed by this chemical has probably received the bulk of attention over the past 20 years, the U.S. Environmental Protection Agency (EPA) and the recent U.S. EPA Science Advisory Board (SAB) that reviewed the "Reassessment" have suggested that the noncancer hazard may well be more important than the cancer hazard at current background doses to the general public. The World Health Organization (WHO) and U.K. Food Standards Agency (FAO) committee (JECFA) on dioxins has reached similar conclusions. This article reviews the published studies involving laboratory animals and humans that address the noncancer effects. Based on our review, developmental toxicity is the most sensitive effect of TCDD consistently seen in mice and rats. Specifically, of the various studies, a no-observed-adverse-effects level (NOAEL) of 13 ng/kg (maternal body burden) was identified as the most pertinent for deriving a reference dose (RfD) for humans. Although more than a dozen different adverse effects have been reported in various studies of humans over the past 25 years, the most consistent clinically important adverse effect of human exposure appears to be chloracne. Following a review of all published studies, we concluded that the best estimate of a LOAEL for production of chloracne is approximately 160 ng/kg (body burden). Based on our analysis, an RfD of between 1 and 10 pg/kg-d (TCDD TEQ) is consistent with the objectives of this risk criterion. Maintaining a lifetime average daily dose below this concentration, based on what is known today, should prevent noncancer effects in virtually all persons. This value is consistent with the JECFA recommendation of 70 pg/kg-mo.*