

The Tungsten Reference Dose (RfD)

Tungsten is a rare metal used in many industrial applications, especially machine tools, catalysts, and superalloys. The 2015 Provisional Peer-Reviewed Toxicity Values (PPRTV) for Soluble Tungsten Compounds used rat gavage studies to identify increased glandular stomach cell metaplasia as the critical effect for deriving toxicity values for soluble tungsten substances. However, gavage dosing delivers a bolus directly to the stomach, prolonging contact with stomach tissue and exposing the substance to different local conditions, such as lower pH, that may promote localized lesions. On that basis, the subchronic and chronic provisional Reference Doses (p-RfDs) were derived from a BMDL10 of 2.3 mg W/kg-day in a 90-day gavage study, with uncertainty factors of 300 and 3,000, producing values of 0.008 and 0.0008 mg W/kg-day, respectively. New subchronic and chronic drinking-water rodent studies sponsored by the U.S. National Toxicology Program on sodium tungstate instead identify the kidney as the target organ in both sexes of rats and mice, based on renal cortical tubule regeneration; stomach lesions were not reported. This shift from the stomach to the kidney is supported by evidence from other ubiquitous metal kidney toxicants, including arsenic, cadmium, and lead, which contribute to chronic kidney disease. Because the kidney reabsorbs and accumulates divalent metals, it is often an early target of heavy metal toxicity. Using the drinking-water studies and model-selection procedures consistent with current EPA (2012) guidance, subchronic and chronic RfDs of 0.1 and 0.01 mg W/kg-day, respectively, were estimated from BMDL10 values of 5.9 mg/kg-day for subchronic exposure and 0.6 mg/kg-day for chronic exposure, with an uncertainty factor of 30. Based on this assessment, the oral p-RfD values for soluble tungsten substances should be reconsidered in light of newly available data, including the use of glandular stomach lesions as the critical effect.