

# Technical Memorandum

To: Teri L. Copeland, DABT

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Re: Toxicity Criteria for Titanium and Compounds, and for Tungsten and Compounds

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The available literature indicates that there is a wide range of toxicity associated with these metals and their compounds, and so appropriate caveats are needed in the use of derived toxicity criteria for both titanium and tungsten, and their associated compounds. These metals are commonly found in the earth's crust and the elemental metal forms are generally considered inert from a toxicological viewpoint, except for possible risk of pneumoconiosis at very high inhalation exposures to the fine metal dusts.

## **Titanium and Compounds:**

The 2004 EPA Region 9 PRG table lists titanium as having an oral RfD of 4.0E+00 mg/kg-d and an inhalation RfD of 8.6E-03, with associated soil PRGs of 1.0E+05 mg/kg (max) for both residential and industrial soils. However, a draft updated review of titanium (CAS No. 7440-32-6) and compounds from EPA Region 9 provides some more explicit caveats regarding the toxicology of titanium and compounds, and derives an RfC (3.0E-02 mg Ti/m<sup>3</sup>).

Although the oral RfD for titanium remained unchanged (4 mg/kg-d) in the draft updated review, the following specific caveats were added:

*“Because the proposed RfD is based on studies with animals exposed to TiO<sub>2</sub>, and there is limited information on the relative toxicity of other titanium compounds, caution is recommended in using the RfD for sites known to be contaminated with titanium tetrachloride, titanium dichloride or titanocenes, unless it is certain that these contaminating forms of titanium have been transformed into titanium dioxide. Information is available, as discussed in the Introduction of this paper, that these titanium compounds have different toxicological and biological properties than those of titanium metal or titanium dioxide. Nevertheless, the natural propensity of other titanium IV compounds to hydrolyse to titanium dioxide suggests that this RfD may have relevance to sites contaminated with forms of titanium other than titanium dioxide or titanium metal. In the absence of information to indicate which form of titanium is present at a particular site, it seems reasonable to use this RfD to characterize the potential nonneoplastic health risk from oral exposure to titanium.”*

The following caveats are provided for the RfC derivation of titanium and compounds:

*“Given the limited information that dusts of other titanium compounds (titan dust and titanium hydride) can produce pulmonary inflammation in rats and rabbits (see Shirakawa, 1985) and the mechanistic evidence that particle-induced pulmonary inflammation and tumor development in rats may be causally linked, especially when pulmonary clearance mechanisms are impaired, it appears reasonable to include dusts of titanium compounds other than titanium dioxide in this assessment. However, titanium tetrachloride and titanocenes are excluded from this classification, because of the evidence that they may have different biological properties than those of titanium metal and titanium dioxide. It should be emphasized that the available evidence suggests that oral exposure to titanium dioxide does not produce cancer in animals and that inhalation exposure to fine and ultrafine particulates is the most likely carcinogenic hazard to humans presented by titanium and titanium compounds.”*

The metallic compounds of titanium IV include titanium tetrachloride, phosphate, sulfate, and nitrate, titanous acid, calcium titanate, sodium titanate, and titanium dioxide. The most toxic of these compounds is titanium tetrachloride, an intermediate in one process for manufacturing titanium dioxide; the tetrachloride is a liquid under ambient conditions and is highly reactive and corrosive. These titanium IV compounds readily hydrolyze to form titanium dioxide in most environmental settings. At substantial levels in soils, titanium dioxide will appear as a white powder.

Titanium II compounds include titanium dichloride, black crystals that burn like tinder when heated in air, and titanium hydride, a metallic powder used in metallurgy as a source of hydrogen that is relatively stable at room temperatures. Other compounds include halides of titanium III, for which there is no toxicological data.

Given the above information, soil screening criteria for the Henderson project that are based on the RfD and RfC values cited above should be protective in most situations due to weathering over time, which in this case would convert the more reactive titanium compounds into the less toxic titanium dioxide. However, if there are pockets of deposited titanium wastes from TIMET or other manufacturers that include substantial amounts of titanium compounds other than the metallic form or the dioxide, a more conservative criterion might be more appropriate. One possibility would be to apply an additional safety factor of 100 to the soil screening criterion in order to address this uncertainty about the presence of other titanium compounds unless there is analytical data demonstrating that the titanium levels are associated with at least 90% titanium metal and/or titanium dioxide. This should be checked against normal background soil titanium levels in the region to assure that the more conservative soil screening level does not approach background levels.

## Tungsten and Compounds

There is relatively limited toxicological information available regarding tungsten and compounds (ATSDR, 2005). With respect to oral toxicity, short-term and intermediate duration studies in rodents have assessed primarily mortality from various tungsten compounds, with the lowest acute LD50 value of 240 mg/kg-d for sodium tungstate in mice. A lifetime study of sodium tungstate ingestion at 0.75 to 1 mg/kg-d in rats found no adverse effects (ATSDR, 2005). However, a study of metallic tungsten ingestion in rats found no effects at 7,650 mg/kg-d for 70 days.

Although the data are limited, the available findings demonstrate that metallic tungsten and other insoluble forms (tungsten dioxide, and tungsten carbide) may be considered biologically inert, while the soluble tungsten compounds (sodium tungstate, tungstic oxide, ammonium paratungstate) exhibit greater potential for toxicity via ingestion. The separate consideration of soluble and insoluble tungsten compounds has been used by OSHA and ACGIH in setting workplace exposure limits. Thus, despite very substantial database deficiencies, it seems most appropriate to develop separate oral RfDs based on insoluble and soluble tungsten compounds.

For tungsten metal and insoluble tungsten compounds, the NOEL of 7,650 mg/kg-d identified by Kinard and Van de Erve (1943) in rats fed metallic tungsten for 70 days can be utilized. Uncertainty factors for subchronic to chronic (10-fold), for rodent to human extrapolation (10-fold) and for limited toxicological database (10-fold), totaling 1000, would derive an oral RfD of 7.7E+00 mg/kg-d.

For soluble tungsten compounds, the lifetime feeding study of sodium tungstate in rats by Schroeder and Mitchener (1975) identified a NOEL of 0.75 mg/kg-d. Uncertainty factors for rodent to human extrapolation (10-fold) and for limited toxicological database (10-fold), totaling 100, would derive an oral RfD of 7.5 E-03 mg/kg-d.

There is even less toxicological data available for the inhalation route in regards to tungsten and compounds. A single subchronic study in rats exposed to tungsten carbide identified pulmonary fibrosis at an exposure concentration of 600 mg/m<sup>3</sup> for daily 1 hr exposures for 5 months (Mezentseva, 1967). The major toxic component of tungsten carbide cutting tools is noted to be the cobalt that provides a tough matrix in which the relatively brittle tungsten carbide is embedded. In addition, associations of tungsten carbide with pulmonary fibrosis or "hard metal disease" may also be related to the presence of cobalt and/or nickel in such occupational exposures (ATSDR, 2005).

Due to the lack of toxicological data on inhalation exposures, and the fact that OSHA standards are set in order to avoid pneumoconiosis and other toxic effects in humans, the derivation of separate RfCs for insoluble and soluble tungsten compounds based on the OSHA PELs is recommended. OSHA permissible exposure limits for insoluble tungsten and compounds is set at 5 mg/m<sup>3</sup> and for soluble

tungsten compounds is set at 1 mg/m<sup>3</sup>. An adjustment factor totaling 300 is recommended, including factors for workday-only to continuous exposure (10-fold), for limited toxicological database (10-fold), and for sensitive populations (3-fold). These assumptions derive an RfC of 1.7E-02 mg/m<sup>3</sup> for tungsten metal and insoluble compounds, and an RfC of 3.3E-03 mg/m<sup>3</sup> for soluble tungsten compounds. This should be checked against normal background soil tungsten levels in the region to assure that the associated soil screening level does not approach background levels.

For practical purposes in regards to the Henderson site, the total tungsten concentrations in soil can be screened against the soil level for soluble tungsten, and if it exceeds that level but not the value for insoluble tungsten then a determination of the fraction of soluble tungsten to total tungsten can be used to validate compliance. Also, the presence of tungsten levels above one of the screening criteria should also call attention to the need for data on nickel and cobalt levels in the same sample in order to assure protection in relation to risks of "hard metal disease" via inhalation of these common tungsten carbide-associated components.

## References

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