Status of the Reassessment of Vanadium Pentoxide
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Vanadium occurs naturally in the environment and several vanadium-containing compounds are produced as a result of industrial processes. There are a number of different forms of vanadium, including, but not limited to, vanadium pentoxide, vanadyl sulfate, sodium metavanadate, sodium orthovanadate, and several of the forms of vanadium can interconvert. There are data to indicate that exposure to vanadium-containing compounds, including vanadium pentoxide, may be toxic to humans.

An IRIS assessment for vanadium pentoxide is currently on the IRIS database (posted in 1987) that includes an evaluation of potential toxicity by the oral route of exposure and a noncancer reference dose (RfD). A draft IRIS reassessment for vanadium pentoxide was released for public comment and external peer review in September 2011. The archived external peer review draft IRIS Toxicological Review and the final peer review report can be found at http://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=236587 .

As a result of discussions during the development of the IRIS multi-year agenda (http://www.epa.gov/iris/iris-agenda) that was released by the EPA in December 2015, it was determined that an evaluation of the potential toxicity of multiple vanadium-containing compounds, including vanadium pentoxide, was a cross-Agency high priority need. For this reason, EPA has decided that the reassessment of vanadium pentoxide toxicity would benefit from a concurrent, systematic, evaluation of all of the available vanadium speciation and toxicity information. Looking at a broader array of vanadium compounds may also inform the evaluation of potential toxic effects and data gaps that were identified during the development of the draft vanadium pentoxide assessment. Therefore, the draft vanadium pentoxide assessment will not be finalized at this time. The information in the draft assessment and the recommendations of the external peer review panel will inform the upcoming and more inclusive assessment for vanadium-containing compounds.

The draft vanadium pentoxide reassessment was initiated prior to the implementation of the newer IRIS assessment format and did not incorporate some of the more recent enhancements to the IRIS assessment process (http://www.epa.gov/iris/basic-information-about-integrated-risk-information-system#process). The new assessment of vanadium-containing compounds will benefit from undergoing scoping and problem formulations steps, the application of systematic review methodology to assess human health hazards, and a peer review conducted through the standing Science Advisory Board's Chemical Assessment Advisory Committee (SAB CAAC).

The noncancer effects of exposure to vanadium pentoxide have been studied. However, few studies are available to inform the potential for oral toxicity from exposure to vanadium pentoxide. A chronic oral

reference dose (RfD) of 9 x 10^{-3} mg/kg-day has been derived by the IRIS Program (1987) and is based on decreased hair cystine levels in rats as reported by Stokinger et al. (1953). There are multiple human and animal studies available on the toxicity of vanadium pentoxide by the inhalation route of exposure. According to EPA's *Provisional Peer-Reviewed Toxicity Values for Vanadium Pentoxide* (USEPA, 2008), upper and lower respiratory tract toxicity has been consistently reported in acute, subchronic and chronic exposure studies in mice, rats, monkeys and humans, with LOAEL values ranging from 0.1 to 5 mg/m^3. The effects of chronic inhalation of vanadium pentoxide have been assessed in a single 2-year, multi-dose exposure study in rats and mice (NTP, 2002). Irritation of the upper and lower respiratory tract has been reported in several acute and subchronic occupational and case studies of workers exposed to vanadium pentoxide in fuel-oil ash and vanadium dust. A chronic provisional inhalation reference concentration (RfC) of 7 x 10^{-6} mg/m^3 has been derived (USEPA, 2008) based on the occurrence of respiratory lesions in rats and mice that were observed in the NTP (2002) study.

The carcinogenic potential of vanadium pentoxide by the inhalation route of exposure has been evaluated by several health agencies. USEPA (2008) determined that there was suggestive evidence of carcinogenic potential for vanadium pentoxide following inhalation exposure based on the findings of the NTP (2002) study. NTP (2002) found *some evidence of carcinogenic activity* of vanadium pentoxide in male rats, *equivocal evidence of carcinogenic activity* in female rats, and *clear evidence of carcinogenic activity* in male and female mice based on increased incidences of alveolar/bronchiolar neoplasms. The International Agency for Research on Cancer classified vanadium pentoxide in group 2B (possibly carcinogenic to humans) based on inadequate evidence in humans and sufficient evidence in animals (IARC, 2006).

For more information on the potential toxicity of vanadium pentoxide, please see the following assessments and studies that have been conducted by EPA and other national and international health agencies:

- ATSDR. (Agency for Toxic Substances and Disease Registry). (2012) Toxicological Profile for Vanadium. Atlanta, GA. http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=276&tid=50
- USEPA. (Superfund Health Risk Technical Support Center, National Center for Environmental Assessment, US Environmental Protection Agency). (2008) Provisional Peer-Reviewed Toxicity Values for Vanadium Pentoxide (CASRN 1314-62-1). Cincinnati, OH. http://hhpprtv.ornl.gov/issue_papers/VanadiumPentoxide.pdf
- IARC. (International Agency for Research on Cancer). (2006) Cobalt in hard metals and cobalt sulfate, gallium arsenide, indium phosphide and vanadium pentoxide. Lyon, France. http://monographs.iarc.fr/ENG/Monographs/vol86/index.php

- NTP. (National Toxicology Program). (2002) NTP toxicology and carcinogenesis studies of vanadium pentoxide (CASRN 1314-62-1) in F344/N rats and B6C3F1 mice (inhalation). Washington, DC. https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr507.pdf
- Stokinger, H.E., W.D. Wagner, J.T. Mountain, F.R. Stocksill, O.J. Dobrogorski and R.G. Keenan. 1953. No title given. Unpublished results. Division of Occupational Health, Cincinnati, OH. (Cited in: Patty's Industrial Hygiene and Toxicology, 3rd ed., 1981).