**MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY**

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**INTEROFFICE COMMUNICATION**

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TO: File for Titanium (CAS # 7440-32-6)

FROM: Keisha Williams, Air Quality Division

DATE: February 22, 2019

SUBJECT: Screening Level for Titanium

The initial threshold screening level (ITSL) for acute exposure to titanium is 24 µg/$m^3$ (8-hour averaging time) based on the Michigan Department of Environmental Quality (MDEQ), Air Quality Division (AQD) Rule 336.1232 (1) (c).

The following references or databases were searched to identify data to determine the screening level: United States Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS), ChemView: the EPA's database on chemical health and safety data for chemicals subject to the Toxic Substances Control Act (TSCA), the TSCA documents in the National Technical Reports Library (NTRL) database, the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV), National Institute of Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, Agency for Toxic Substances and Disease Registry (ATSDR) Minimal Risk Levels, International Agency for Research on Cancer (IARC) Monographs, the American Chemical Society's SciFinder database, Health Effects Assessment Summary Tables (HEAST), National Toxicology Program (NTP) Status Report, EPA Superfund Provisional Peer Reviewed Toxicity Values, EPA Acute Exposure Guideline Levels (AEGLs) for Airborne Chemicals, EPA High Production Volume Database, United States Department of Labor Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELs), the Organisation for Economic Co-operation and Development's Existing Chemicals Database, the Canadian Centre for Occupational Health and Safety's Registry of Toxic Effects of Chemical Substances (RTECS), the Toxnet databases: Hazardous Substances Data Bank (HSDB) and Toxline, Spacecraft Maximum Allowable Concentrations (SMACs), California Office of Environmental Health Hazard Assessments Reference Exposure Levels, Texas Commission on Environmental Quality (TCEQ) Effects Screening Levels (ESLs), German maximale Arbeitsplatz-Konzentration (MAK) values, and European Chemicals Agency Registered Substances Dossiers.

Titanium has been used in several industries, including surgical appliances, manufacture of electrodes and lamp filaments, manufacture of welding rods, in the paint and dye industry, and in manufacturing of metal alloys (HSDB, 2002).

There is relatively little toxicity information on the metal titanium. Titanium has been grouped with titanium dioxide ($TiO_2$) in regard to its toxicity as seen with the TCEQ ESLs (TCEQ, 2003). Furthermore, studies show that titanium rapidly hydrolyzes at its surface to produce a layer of $TiO_2$ (Vaquila, 1999). In regard to the current ITSL for $TiO_2$ (CAS # 13463-67-7), documentation

on the current health benchmark (the NIOSH REL), on which the ITSL is based notes, "…The weight of evidence suggests that the tumor response observed in rats exposed to fine and ultrafine $TiO_2$ results from a secondary genotoxic mechanism involving chronic inflammation and cell proliferation. Rather than via genotoxicity of $TiO_2$ itself. This effect appears related to the physical form of the inhaled particle (i.e., particle surface area) rather than the chemical compound itself" (NIOSH, 2011).

As noted in the titanium dioxide ITSL justification, "The RELs of 2.4 $mg/m^3$ for fine (respirable) $TiO_2$ and 0.3 $mg/m^3$ for ultrafine (<0.1µm) $TiO_2$ are designed to prevent pulmonary inflammation, and thus prevent the development of secondary toxicity (lung tumors)." (MDEQ, 2015). The $TiO_2$ ITSL for fine (respirable) particulate matter will be adopted for the titanium ITSL.

**Therefore, the acute ITSL is 24 $\mu g/m^3$, 8-hour averaging time.**

**References**


Act 451 of 1994, Natural Resources and Environmental Protection Act and Air Pollution Control Rules, Michigan Department of Environmental Quality.

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MDEQ. 2015. Memo from Michael Depa to File for Titanium Dioxide (CAS # 13463-67-7). Subject: Screening level Updates. July 28, 2015.

NIOSH. 2011. Current Intelligence Bulletin 63: Occupational Exposure to Titanium Dioxide. United States Department of Health and Human Services.

TCEQ. 2003. Tox ESL-Summary Report for Titanium and Titanium (IV) Dioxide. Accessed from the Texas Air Monitoring Information web interface on January 3, 2019.
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Vaquila, I.; Vergara, L. I.; Passeggi Jr, M. C. G.; Vidal, R. A.; Ferron, J. 1999. Chemical reactions at surfaces: titanium oxidation. Surface and Coatings Technology, 122(1), 67-71.


KW:lh

**MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY**

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**INTEROFFICE COMMUNICATION**

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July 28, 2015

To: File for Titanium Dioxide (CAS No. 13463-67-7)

From: Michael Depa, Air Quality Division, Toxics Unit

Subject: Screening Level Updates

The Initial Threshold Screening Level (ITSL) for titanium dioxide is 24 µg/m³ with an 8-hour averaging time.

The following information sources were searched in order to support the development of screening levels for titanium dioxide ($TiO_2$): United States Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS), the Registry of Toxic Effects of Chemical Substances (RTECS, 2015), the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV), National Institute of Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, Environmental Protection Bureau Library, International Agency for Research on Cancer Monographs, National Library of Medicine, Health Effects Assessment Summary Tables, and National Toxicology Program Status Report. The EPA has not established a reference concentration (RfC) for titanium dioxide. California Office of Environmental Health Hazard Assessment (Cal-OEHHA) has not established reference exposure levels for $TiO_2$. The U.S. Agency for Toxic Substances and Disease Registry (ATSDR) has not established a chronic minimal risk level for $TiO_2$. Provisional Peer Reviewed Toxicity Values (PPRTV) for $TiO_2$ are not available.

**Occupational Exposure Limits**

The ACGIH has established a Threshold Limit Value (TLV) for $TiO_2$ at 10 mg/m³. NIOSH developed 2 recommended exposure limits (RELs) for $TiO_2$, each based on a specific size fraction of particles. NIOSH recommends airborne exposure limits of 2.4 mg/m³ for fine (respirable) $TiO_2$ and 0.3 mg/m³ for ultrafine (<0.1 µm) $TiO_2$.

**Evidence for Carcinogenicity**

The International Agency for Research on Cancer (IARC, 2010) evaluated the available evidence that $TiO_2$ causes cancer and concluded that there is inadequate evidence in humans, but that there is sufficient evidence in experimental animals for the carcinogenicity of $TiO_2$. IARC designated $TiO_2$ as a group 2B carcinogen: "possibly carcinogenic to humans".

NIOSH also evaluated the relevance of the human and animal data available to determine the potential carcinogenicity of $TiO_2$. NIOSH concluded that the fine fraction of $TiO_2$ (respirable) is not carcinogenic to humans based on the animal studies. The only chronic

animal inhalation study (Lee et al. 1985), which demonstrated the development of lung tumors (bronchioalveolar adenomas) in response to inhalation exposure of rats to fine sized $TiO_2$ did so at a dose of 250 mg/m³ but not at 10 or 50 mg/m³. NIOSH states that:

> [E]xposure concentrations greater than 100 mg/m³ are generally not considered acceptable inhalation toxicology practice today. Consequently, in a weight-of-evidence analysis, NIOSH questions the relevance of the 250 mg/m³ dose for classifying exposure to $TiO_2$ as a carcinogenic hazard to workers and therefore, concludes that there are insufficient data at this time to classify fine $TiO_2$ as a potential occupational carcinogen.

Concerning the ultrafine fraction (<0.1 µm) of $TiO_2$, NIOSH states:

> [T]he responses observed in animal studies exposed to ultrafine and fine $TiO_2$ are consistent with a continuum of biological response to $TiO_2$ that is based on particle surface area. In other words, all the rat tumor response data on inhalation of $TiO_2$ (ultrafine and fine) fit on the same dose-response curve when dose is expressed as total particle surface area in the lungs.
>
> NIOSH has concluded that $TiO_2$ is not a direct-acting carcinogen, but acts through a secondary genotoxicity mechanism that is not specific to $TiO_2$ but primarily related to particle size and surface area.

**Derivation of the ITSL**

The RELs of 2.4 mg/m³ for fine (respirable) $TiO_2$ and 0.3 mg/m³ for ultrafine (<0.1 µm) $TiO_2$.are designed to prevent pulmonary inflammation, and thus prevent the development of secondary toxicity (including lung tumors). The RELs are preferred over the ACGIH TLV because they have been recently reviewed (NIOSH in 2010 vs ACGIH in 2001), and the derivation of which is more appropriate than the ACGIH TLV. The TLV was based on prevention of particle overload of the clearance mechanism in the lung, whereas the REL is based on the prevention of inflammation in the lung.

An ITSL based on the fine fraction will be established as follows:

ITSL = (OEL/100).

> Where the OEL is the occupational exposure limit, in this case the recommended exposure limit (REL) of 2.4 mg/m³.

ITSL = (2.4 mg/m³)/100 x (1000µg/mg)

ITSL = 24 ug/m³

An 8-hr averaging time was applied to the screening level pursuant to Rule 232(2)(a). The ITLS is to be applied to the respirable fraction of $TiO_2$ particles (i.e., PM10).

An ITSL for the ultrafine fraction will not be developed at this time because the ultrafine fraction is not likely to be an air contaminant from industrial processes. If it is found to be emitted and subject to the air permit process, an ITSL based on 1% of the REL for ultrafine fraction may be appropriate; i.e., 1% of 0.3 mg/m³ or 3 µg/m³, (8-hr averaging time).

**References**

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NIOSH, 2011. Occupational Exposure to Titanium Dioxide. Current Intelligence Bulletin 63. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health (NIOSH). DHHS (NIOSH) Publication No. 2011–160, April 2011. http://www.cdc.gov/niosh/docs/2011-160/pdfs/2011-160.pdf3