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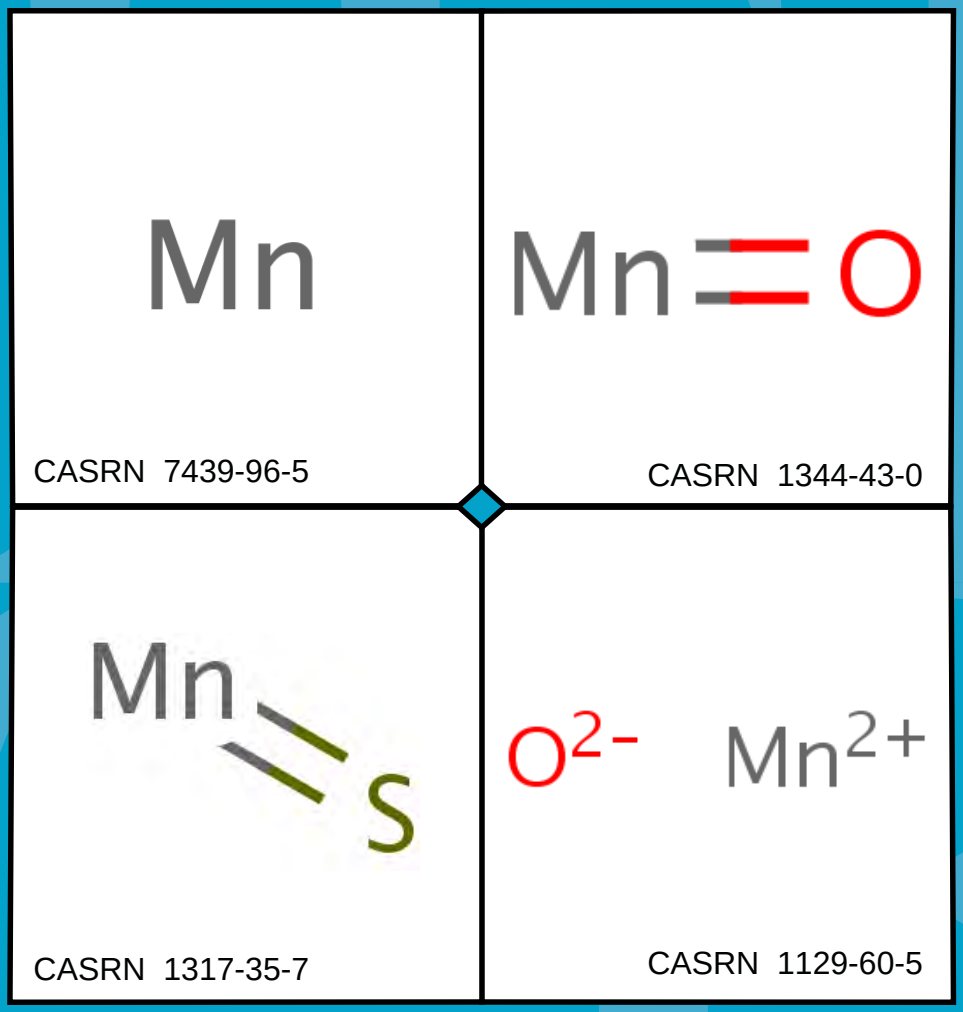
Agency

Inhalation Health Effect Reference Values for Manganese

(CASRN 7439-96-5 – Manganese)
and Compounds (CASRN 1344-43-0;
1317-35-7; and 1129-60-5)



National Center for Environmental Assessment
Office of Research and Development

U.S. Environmental Protection Agency
Research Triangle Park, NC

Inhalation Health Effect Reference Values for Manganese and Compounds (CASRN 7439-96-5 – Manganese)

Overview

The reader is strongly encouraged to read Section 1 of the following report for critical background information regarding the health effect reference values discussed in this summary: *Graphical Arrays of Chemical-Specific Health Effect Reference Values for Inhalation Exposures [Final Report]* (U.S. EPA, 2009a). This report is available on-line at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=211003.

This summary presents noncancer health effect reference values for inhalation exposures to manganese (Mn) across all durations for both the general public and workers. The physical size of Mn-containing particles has a bearing on the toxicity and some organizations have created different reference values based on size fraction, therefore some definitions of terms regarding particle size are provided below.

A detailed description of the reference values compared in this summary and the categories of reference values can be found in Section 1 of the EPA report (U.S. EPA, 2009a). In general, inhalation health effect reference values have been included which have been developed and formally reviewed by an authoritative governing body (government agency or professional association) for use in assessments of risk to support regulatory decision-making. The main exception to this inclusion criteria are the Provisional Advisory Concentration (PAC) and Temporary Emergency Exposure Level (TEEL) values for emergency response, which are the only emergency response values available for manganese compounds. Another exception is the discussion of a proposed reference value developed by Bailey et al. (2009) and reviewed by a panel convened by Toxicology Excellence for Risk Assessment (TERA, 2011); this value was not developed or endorsed by an agency or professional association which typically develops such reference values.

General Properties

Manganese (Mn) occurs naturally in many types of rocks and soil, usually as a salt or other compound in combination with other elements such as oxygen, sulfur, and chlorine (ATSDR, 2012). The average concentration of manganese in urban air (as a component of PM_{10}) is approximately 0.04 µg/m^3, ranging from < 0.01 µg/m^3 for remote areas and up to 0.089 µg/m^3 in areas near industrial sources of manganese emissions (ATSDR, 2012). Manganese is a necessary trace nutrient, but is toxic at high levels of exposure.

Production and Uses

Manganese is used to improve hardness, stiffness, and strength in the production of various varieties of steel (carbon steel, stainless steel, high-temperature steel, and tool steel) (ATSDR, 2012). Manganese also occurs naturally in most foods and is often a component of nutritional supplements. Manganese is used in a wide variety of other products, including: fireworks; dry-cell batteries; fertilizer; paints; a medical imaging agent; in cosmetics; and as an octane boosting additive to gasoline.

Exposure Potential

The Toxics Release Inventory for 2010 (U.S. EPA, 2010) reported 1,641,992 pounds of manganese were emitted to air from all industrial sources in the United States, with 111,391 pounds emitted from point sources (stacks, vents, ducts, or pipes) and 1,530,600 pounds coming from fugitive sources (equipment leaks, losses from surface impoundments and spills, and releases from building ventilation systems).

Potential Health Effects

The adverse effect most commonly associated with inhalation exposure to Mn is neurological (ATSDR, 2012; U.S. EPA, 1993). Mn and compounds have not been associated with cancer. Developmental and reproductive effects have not been investigated adequately for characterizing those potential risks.

Most health effect reference values for inhalation exposure to manganese-containing compounds are based on the Mn concentration, with no distinction made based on the valence state of the Mn ion, with Mn(II), Mn(III), and Mn(IV) most commonly encountered. However, more soluble Mn salts have been associated with greater bioavailability.

Cancer Potential

The US EPA (U.S. EPA, 1993) has stated that manganese is "*not classifiable as to human carcinogenicity*." This conclusion was based on the assessment that "*existing studies are inadequate to assess the carcinogenicity of manganese*."

Particle Size Definitions

The location in the respiratory tract (extrathoracic, tracheobronchial, alveolar) where Mn-containing particles may be deposited is a determinant of toxicity. Many organizations refer to various particle size fractions (respirable, thoracic, and inhalable), with some slight variations in size cut-offs and in terminology, often with overlapping categories. The following definitions come from the Integrated Science Assessment for Particulate Matter (U.S. EPA, 2009b), and are generally applicable to the remainder of this discussion:

- *Particulate Matter (PM)* - PM is the generic term for a broad class of chemically and physically diverse substances that exist as discrete particles (liquid droplets or solids) over a wide range of sizes.
- *Total Suspended Particulates (TSP)* – Particulate matter up to a nominal size of 25-45 micrometers (μm).
- PM_{10} –Particulate matter with a nominal aerodynamic diameter[1] less than or equal to 10 μm (50% cut point of the sampler). PM_{10}delineates the subset of inhalable particles, referred to as thoracic particles, that are small enough to penetrate to the thoracic region (including the tracheobronchial and alveolar regions) of the respiratory tract.

[1] The more precise term is 50% cut point or 50% diameter (d50). This is the aerodynamic particle diameter for which the efficiency of particle collection is 50%. Larger particles are not excluded altogether, but are collected with decreasing efficiency which approaches zero for 20 μm particles. Smaller particles are collected with increasing efficiency (up to around 100%) for less than 3 μm particles.

- $PM_{2.5}$ – Particulate matter with a nominal aerodynamic diameter less than or equal to 2.5 µm (50% cut point of the sampler), an indicator for fine particles.

The ISA for PM (U.S. EPA, 2009b) also notes the following regarding particle size and dosimetry:

> *"Particles of different sizes can penetrate different regions of the human respiratory tract. Thoracic particles refer to particles that travel past the larynx to reach the lung airways and the gas-exchange region of the lung, and respirable particles are those that reach the gas-exchange region. Respiratory tract dosimetry supports the choice of PM_{10} as an index of thoracic particles. However, dosimetric considerations do not provide insight into the selection of a size cut to characterize a fine particle mode. American Conference of Governmental Industrial Hygienists (ACGIH, 2005), the International Standards Organization (ISO), and the European Standardization Committee (CEN) have adopted a 50% cut point of 4 µm as an indicator of respirable particles."*

Airborne particles have been classified into different aerosol fractions based on the penetration of these particles in the various regions of the respiratory tract by the American Conference of Governmental Industrial Hygienists (ACGIH) and European Committee for Standardization (CEN). The definitions adopted from the European Committee for Standardization (CEN, 1993), are shown below:

- *Inhalable fraction* – the mass fraction of total airborne particles which is inhaled through the nose and mouth.
- *Thoracic fraction* – the mass fraction of inhaled particles penetrating beyond the larynx, which is inclusive of the trachea and bronchi.
- *Respirable fraction* – the mass fraction of inhaled particles penetrating to the unciliated airways. More typically, the literature have defined this term in relation to the fraction of particles entering the gas-exchange region or the fraction penetrating through the tracheobronchial region, the ciliated airways, or conducting airways.

The above definitions are stated in terms of a mass fraction. Relative to total airborne particles, the particle size having 50% penetration for the thoracic and respirable fractions are 10 µm and 4.0 µm, respectively (ACGIH, 2005; CEN, 1993).

Many of the values developed for application to the general public assume exposure to the respirable fraction as being protective for exposure to larger particle fractions and are applicable to that fraction, unless specifically noted in the following text and table.

Emergency Response Values

No peer-reviewed emergency response values (Acute Exposure Guideline Levels – AEGLs, or Emergency Response Planning Guidelines – ERPGs) have been developed for Mn. The Provisional Advisory Concentrations (PACs) include an AEGL or ERPG value when available, and Temporary Emergency Exposure Levels (TEELs) values when they are not, using a methodology developed by the Department of Energy (DOE, 2008). Both the TEEL-1 and -2 values for Mn draw largely from the occupational values (See Figure 1 and Table 1), in keeping with the DOE methodology, and were not independently developed. There were major changes

in the PAC values for manganese going from Revision 26 (DOE, 2010) to Revision 27 (DOE, 2012); all TEEL-0 values were dropped from the tables in the later version (including the value of 0.2 mg/m^3 for Mn) and the PAC-3 value increased from 500 mg/m^3 in Revision 26 up to 1,800 mg/m^3 in Revision 27. The PAC-3 was equivalent to the NIOSH IDLH (see below) in Revision 26. Although no documentation is currently available to the public documenting the basis for the revised PAC-3, it was based on a TEEL-3 value calculation[2]. The TEEL-3 for manganese is based on a rat oral LD50 of 9 g/kg obtained from the Registry of the Toxic Effects of Chemical Substances (RTECS) database, and derived using the DOE TEEL methodology (DOE, 2008).

Occupational Values

Typically, there is less publically available information regarding the derivation of occupational values which are formulated based on a weight-of-evidence (WOE) approach and judgement by a panel of experts; therefore, fewer details are provided here on the derivation of occupational values. The National Institute for Occupational Safety and Health (NIOSH) and the American Conference of Governmental and Industrial Hygienists (ACGIH) have established Time-Weighted Average (TWA) values for exposure levels during the course of a working day, with assumptions of exposures repeated 5 days per week, for up to a 40-year career. See Figure 1 and Table 1 for additional comparison of the occupational values described below. The NIOSH Recommended Exposure Level (REL) is 1 mg/m^3 (NIOSH, 2007) and the ACGIH Threshold Limit Value (TLV®) is 0.2 mg/m^3 (200 µg/m^3) (ACGIH, 1996). Additional assumptions of a healthy adult worker population are included in the derivation of these occupational values. The Occupational Safety and Health Administration (OSHA) Ceiling value and NIOSH Short-Term Exposure Level (STEL), for exposure durations of 15 minutes or less, have been established at 5 mg/m^3 and 3 mg/m^3, respectively, to protect workers from spikes in exposure that may not be reflected on a TWA basis (NIOSH, 2007). All of these occupational values are for the respirable fraction with nominal particle aerodynamic diameter of 4 µm (see definitions above) and are based on neurological effects observed in studies on occupationally exposed adults.

ACGIH has proposed changes (ACGIH, 2012) – Notice of Intended Change (NIC) – to the TLV® TWA from the current 0.2 mg/m^3 to a value of 0.02 mg/m^3 (20 µg/m^3) for the respirable fraction, and the addition of a separate value of 0.1 mg/m^3 (100 µg/m^3) for the larger inhalable Mn-containing particles (see particle size definitions above). These proposed changes indicate concerns raised by the studies of Bast-Pettersen et al. (2004), Lucchini et al. (1999), Mergler et al. (1994), and Roels et al. (1992), which indicated neurological effects in workers at levels between 0.03 and 0.04 mg/m^3, which is below the current TLV® TWA of 0.2 mg/m^3 (i.e., the current value may not be protective enough). The inclusion of a separate value for the inhalable fraction is in recognition of the potential for toxicity from these larger sized particles due in part to intestinal absorption subsequent to inhalation exposure (swallowing of mucus with entrained larger particles) and possible absorption of soluble particles deposited in the nasopharynx, and due to the smaller particles (e.g., PM_5) being included as a component of the larger particle definition (e.g., TSP). It should be emphasized that the ACGIH is an independent professional organization and not a governmental agency.

[2] Correspondence between George Woodall (US EPA) and David Freshwater (US DOE), August 23, 2012.

General Public Values (Routine Non-emergency Exposures)

IRIS RfC

The current Reference Concentration (RfC) on IRIS (U.S. EPA, 1993) was derived using the Lowest Observed Adverse Effect Level (LOAEL) of 0.15 mg/m^3 (150 µg/m^3) from a study of occupationally exposed workers (Roels et al., 1992) exhibiting neurological effects (visual reaction time, eye-hand coordination, and hand steadiness). The LOAEL was duration adjusted to 0.05 mg/m^3 using a factor 2 to account for an assumption of 10 m^3 of air inhaled during active work versus 20 m^3 inhaled over the course of a full day, and a factor of 5/7 to adjust for work during 5-days/week. Following the duration adjustments, derivation of the final RfC (0.05 µg/m^3) included application of a total Uncertainty Factor (UF) of 1000, with factors of 10 for inter-individual variability, 10 for going from a LOAEL to a No Observed Adverse Effect Level (NOAEL), and 10 to account for database uncertainty (including the lack of data for developmental and reproductive effects, as well as potential but unquantified differences in the toxicity of different forms of Mn). The median cut point of 5 µm aerodynamic diameter for the respirable fraction in the study of Roels et al. (1992) was used in the derivation of the RfC (U.S. EPA, 1993).

California REL

The Office of Environmental Health and Hazard Assessment (OEHHA) of the State of California developed Mn Reference Exposure Level (REL) values for both the 8-hour and chronic durations (OEHHA, 2008) using their most up-to-date methodologies. The point of departure (POD) was derived using benchmark analysis (U.S. EPA, 2008) on data from the same study as used for the current RfC (Roels et al., 1992) to arrive at a $BMCL_{05}$ (the 95% lower confidence limit of the benchmark concentration for a 5% effect level). REL values for both durations were based on the same study, health endpoint, POD, and total UF (300); the main difference between the two REL values was in the adjustments for duration, with the 8-hour value only adjusted from 5-days/week to 7-days/week and the chronic value also adjusted to account for a breathing rate of 10 m^3 during the average 8-hour work day to an average 20 m^3 in a 24-hour day. The final chronic REL is 0.09 µg/m^3 and the final 8-hour REL value is 0.17 µg/m^3. OEHHA based their REL on inhalable particles with an assumption of a 3-4-fold greater deposition of inhaled particulates in the 1-10 µm range in the lungs of neonates relative to adults exposed to similar particulate levels in ambient air (OEHHA, 2008).

Chronic[3] ATSDR MRL

ATSDR posted a revision to the chronic Minimal Risk Level (MRL) for Mn (respirable fraction) in December 2012 (ATSDR, 2012) of 0.3 µg/m^3. The MRL was derived using benchmark analysis giving a 10% effect ($BMCL_{10}$) of data from the same study as used in the current EPA RfC (Roels et al., 1992). The $BMCL_{10}$ of 142 µg/m^3 was adjusted from an occupational to continuous exposure (5/7 days per week and 8/24 hours per day), resulting in an adjusted value of 33 µg/m^3. Application of a total UF of 100 (10 for human variability; and 10 for database deficiencies and limitations) lead to the final MRL value of 0.3 µg/m^3. The previous MRL included an additional factor of 5 to account for potentially increased susceptibility in children based on differential kinetics in the young (ATSDR, 2010). However, ATSDR (2012) cited recent toxicokinetic studies in lactating rats and their offspring exposed to manganese by

[3] ATSDR defines chronic durations as being for periods of one year or longer.

the oral or inhalation routes which suggest that the human variability factor of 10 provides sufficient protection for differential kinetics in children and adults.

Health Canada RfC

The chronic reference value developed by Health Canada (2010a) used a study of Italian ferroalloy workers (Lucchini et al., 1999). Neurotoxic effects were noted and serum prolactin levels were also observed to be affected. The results from a benchmark concentration analysis for a $BMCL_{05}$ were duration adjusted from the occupational exposure of 8-h/day and 5-days/week, to 24-h/day and 7-days/week. Uncertainty factors of 10 for inter-individual variability in response and 10 to account for limitations to the database (potential for the general population to be exposed to more soluble forms of Mn; the lack of studies on prenatal effects; and the impact of Mn on serum prolactin). *"[The] … Health Canada reference concentration for inhaled manganese is 0.05 µg/m³ in $PM_{3.5}$. This value reflects the concentration to which the general population, including sensitive subgroups, can be exposed for a lifetime without appreciable harm* (Health Canada, 2010b)."

World Health Organization Health Guidelines

The WHO (2000) developed a Health Guideline value of 0.15 µg/m³ as an annual average for exposure to Mn based on a $BMCL_{05}$ from the data reported by Roels et al. (1992), with an adjustment factor of 4.2 to account for duration adjustments, and a total UF of 50 (10 for human variability and a modifying factor of 5 for the potential for increased susceptibility in children).

Ontario Ministry of the Environment (MOE) Ambient Air Quality Criteria and Standard

In 2011, the MOE updated their Ambient Air Quality Criteria (AAQC) and Standards for Mn-containing particulates from a single AAQC and Standard based on total suspended particulates (TSP) to one based on the smaller sized fraction of $PM_{2.5}$ (MOE, 2011). The MOE developed the AAQC for $PM_{2.5}$ in much the same way as an RfC or other similar reference value would be developed. Benchmark analysis was applied to the study data from Roels et al. (1992) to arrive at a POD ($BMCL_{05}$) of 84 µg/m^3. Duration adjustments were applied in the same manner as in the RfC and REL derivation arriving at an adjusted value of 30 µg/m^3. Application of a total UF of 300 (10 for human variability, 3 for database limitations, 3 for vulnerability to the developing nervous system, and 3 for subchronic to chronic extrapolation) led to final derivation of an AAQC value of 0.1 µg/m^3.

Health Canada (1998) noted from observations across multiple monitoring sites that, on average, approximately 50% of TSP consisted of PM_{10}, and similarly 50% of PM_{10} consisted of $PM_{2.5}$. Therefore, the MOE (2011) used the $PM_{2.5}$ AAQC of 0.1 µg/m³ and the previously mentioned ratios as the basis for deriving AAQCs for PM_{10} (0.2 µg/m³) and TSP (0.4 µg/m³). The revised 24-hour standard for Mn and Mn-containing compounds in TSP was set to equal the Mn AAQC for TSP (0.4 µg/m³). An additional half-hour monitoring standard of 1.2 µg/m³ was also set for Mn and Mn-containing compounds in TSP.

ITER "Proposed RfC" for Manganese Oxide (MnO)

The "proposed RfC" for MnO was neither developed nor endorsed by an agency or professional association which typically develops reference values. This value was based on a paper from a peer-reviewed journal (Bailey et al., 2009) which was further reviewed by a panel

convened by TERA (2011), and placed on the International Toxicity Estimates for Risk Assessment (ITER) database managed by TERA. Values from ITER are also available through the National Library of Medicine TOXNET web site (http://toxnet.nlm.nih.gov). Although the ITER values (chronic values of 2 µg/m³ based on a NOAEL and 7 µg/m³ based on a benchmark dose analysis) have received a second level of review by TERA for methodological considerations, the level of review was not deemed to be comparable to the reviews provided by the other sources developing reference values. Additionally, no authoritative body (government agency or professional association) has endorsed the use of these values for the purposes of risk assessment; TERA states in their posting on ITER, "*... the panel was not asked to explicitly endorse the value derived by Bailey et al. (2009).*" For these reasons, the ITER values for manganese oxide are not included in the array shown in Figure 1 or described in detail in Table 1.

Summary

The graphical array of the available health effect reference values for inhalation exposure to manganese in Figure 1 includes all of the values described here and in Table 1, unless otherwise noted. The Ontario Ministry of the Environment (MOE) 24-hour Standard for Mn is equal to the TSP AAQC, therefore it was not included in the accompanying graphic or in the table. Additionally, the Ontario MOE half-hour monitoring standard for Mn mentioned in the text above was not included in the array or table. The Health Canada RfC (Health Canada, 2010a, b) is identical to the EPA RfC (U.S. EPA, 1993) and may be difficult to discern on the graphic.

Some variability in the results from application of BMD analyses between organizations using the same base study can be noted, for example when comparing the derivations of $BMCL_{05}$ values based on the study of Roels et al. (1992) by OEHHA (0.072 mg/m^3) versus the value derived by MOE (0.084 mg/m^3). On the other hand, the $BMCL_{10}$ value derived by ATSDR (0.142 mg/m^3) is within the range of values described in Clewell et al. (2003) (0.09 – 0.27 mg/m^3). These apparent discrepancies are due in part to differences in application of the models (e.g., model choice) and differences in policy and guidance between the organizations for performing BMD analysis and interpretation of the results. These differences are noted here, but further analysis or commentary is beyond the scope of this document.

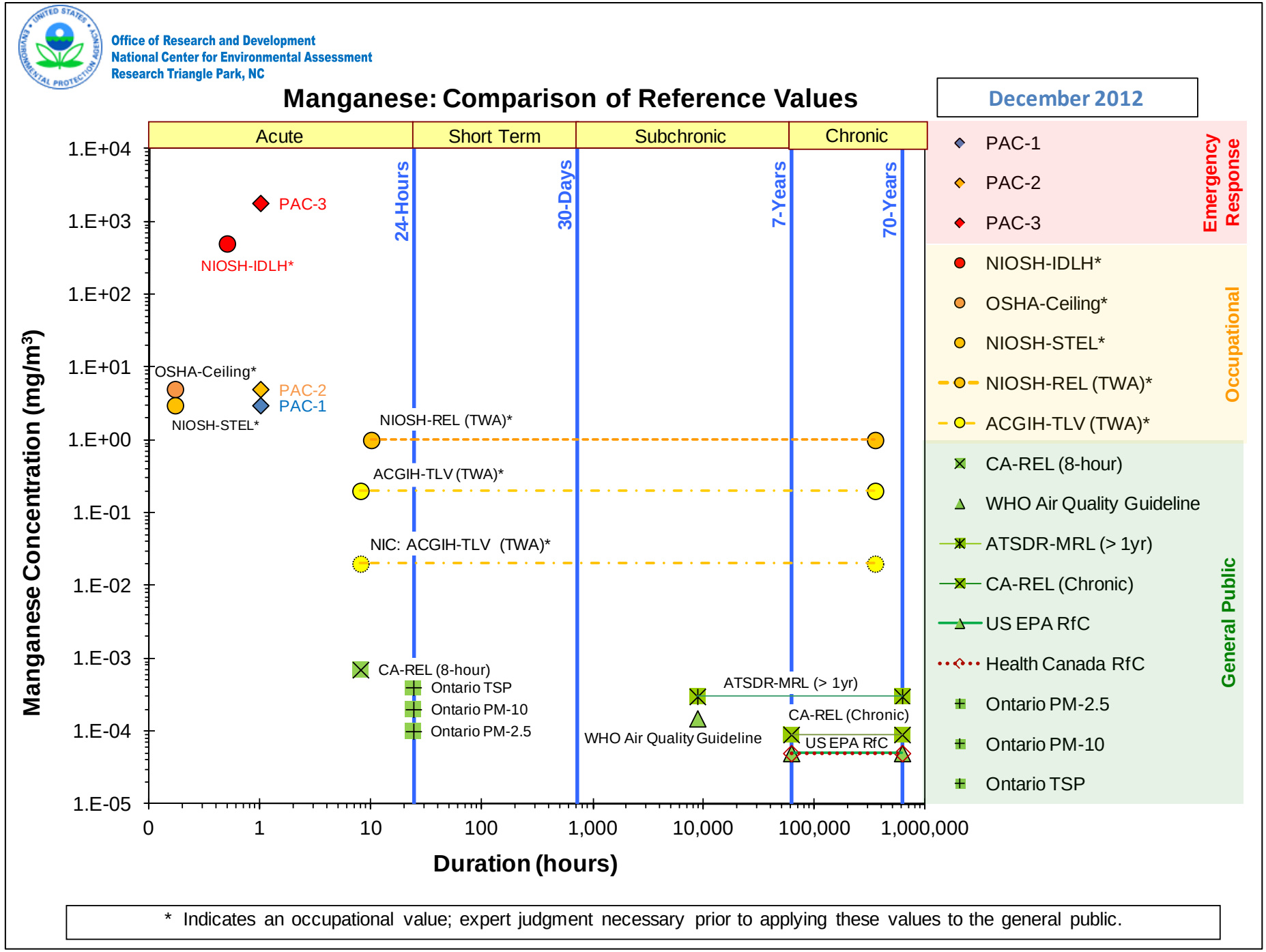


Figure 1. Graphic array of health effect reference values for inhalation exposure to manganese

Table 1. Summary information on the basis and derivation of the available reference values for inhalation exposure to manganese

	Reference Value Name	Duration	Reference Value (mg/m^3)	Health Effect	Point of Departure	Qualifier	Principal Study	Uncertainty Factors[4]	Notes on Derivation	Review Status
Emergency Response	**PAC-3**	1 hour	1800 (Respirable)	NA	9000 mg/kg	Rat LD-50 in RTECS (NIOSH, 2009)	Marhold (1972)	NA	PAC and TEEL values derived via an approach developed by the Department of Energy (DOE, 2008)	Final Revision 27 (DOE, 2012)
	PAC-2	1 hour	5 (Respirable)	NA	OSHA Ceiling (see below)	NA		NA		
	PAC-1	1 hour	3 (Respirable)	NA	NIOSH STEL (see below)	NA		NA		
Occupational	**OSHA Ceiling**	< 15 minutes	5	Manganism; asthenia, insomnia, mental confusion; metal fume fever: dry throat, cough, chest tightness, dyspnea, rales, flu-like fever; low-back pain; vomiting; malaise; lassitude; kidney damage	NR	NR	NR	NR	Adoption of previous ACGIH TLV	Final (2006)
	NIOSH STEL	< 10 minutes	3		Various	NA		NA	WOE Approach	Final (NIOSH, 2007)
	NIOSH REL (TWA)	10 hour TWA	1		Various	NA				
	NIOSH IDLH	30 minutes	500		5,282 mg/m^3	Adjusted from Oral Lethal Dose in mice	Gupta et al. (1981)	Total UF = 10	Total UF and adjusted POD from the IDLH Documentation (NIOSH, 1994)	
	ACGIH TLV-TWA (NIC[5])	8 hour TWA	0.2 (0.02 – respirable; 0.1 - inhalable)	CNS (manganism); lung; reproduction	1 mg/m^3	LOEL	(Roels et al., 1992; 1987)	NR	WOE Approach	Final (ACGIH, 2001) (NIC is draft)

[4] Uncertainty Factor (UF) component definitions: UF_H – inter-human variability; UF_A – animal to human variability; UF_L – LOAEL to NOAEL adjustment; UF_S – subchronic to chronic adjustment; UF_{DB} – database uncertainty

[5] Notice of Intended Change – the values in parentheses are the proposed change in TLV-TWA, and include separate values for respirable and inhalable fractions.

	Reference Value Name	Duration	Reference Value (mg/m^3)	Health Effect	Point of Departure	Qualifier	Principal Study	Uncertainty Factors[4]	Notes on Derivation	Review Status
General Public	**CA-REL**	8 hour	1.7×10^{-4} (Respirable; PM_5)	Impaired neurobehavior: visual reaction time, eye-hand coordination, hand steadiness (Human)	0.051 mg/m^3 0.072 mg/m^3	$BMCL_{05\text{-}ADJ}$ $BMCL_{05}$ (5-d/wk, mean of 5.3 yr)	Roels et al. (1992)	Total UF = 300 $UF_{H\text{-}k} = 10$ $UF_{H\text{-}d} = 10$ $UF_S = 3$	Duration adjusted from 5-d/week to 7-d/week.	Final (OEHHA, 2008)
		Chronic	9×10^{-5} (Respirable; PM_5)	Impaired neurobehavior: visual reaction time, eye-hand coordination, hand steadiness (Human)	0.026 mg/m^3 0.072 mg/m^3	$BMCL_{05\text{-}ADJ}$ $BMCL_{05}$ (5-d/wk, mean of 5.3 yr)	Roels et al. (1992)	Total UF = 300 $UF_{H\text{-}k} = 10$ $UF_{H\text{-}d} = 10$ $UF_S = 3$	Duration adjusted[6]	
	Chronic ATSDR MRL	Chronic (> 1 year)	3×10^{-4} (Respirable; PM_5)	Abnormal performance in tests of hand steadiness, eye-hand coordination, or reaction time. (Human)	0.033 mg/m^3 0.142 mg/m^3	$BMCL_{10\text{-}ADJ}$ $BMCL_{10}$	Roels et al. (1992)	Total UF = 100 $UF_H = 10$ $UF_{DB} = 10$	Duration adjusted from 5-d/week, 8-h/d to 7-d/week, 24-h/d	Final (ATSDR, 2012)
	Chronic RfC (IRIS)	Chronic	5×10^{-5} (Respirable; PM_5)	Impairment of neurobehavioral function	0.05 mg/m^3 0.15 mg/m^3	$LOAEL_{ADJ}$ LOAEL	Roels et al. (1992)	Total UF = 1000 $UF_H = 10$ $UF_L = 10$ $UF_{DB} = 10$	Duration adjusted[6]	Final (U.S. EPA, 1993)
	Health Canada RfC	Chronic	5×10^{-5} ($PM_{3.5}$)	Neurobehavioral end points from a study of manganese alloy workers	0.005 mg/m^3 0.019 mg/m^3	$BMCL_{05\text{-}ADJ}$ $BMCL_{05}$	Lucchini et al. (1999)	Total UF = 100 $UF_H = 10$ $UF_{DB} = 10$	Duration adjusted from 5-d/week, 8-h/d to 7-d/week, 24-h/d	Final (Health Canada, 2010a, b)

[6] Duration adjusted from 5-d/week to 7-d/week, and for 10 m^3 of air inhaled for an 8-hour work day compared to 20 m^3 inhaled over a full day.

	Reference Value Name	Duration	Reference Value (mg/m^3)	Health Effect	Point of Departure	Qualifier	Principal Study	Uncertainty Factors[4]	Notes on Derivation	Review Status
	Ontario MOE Ambient Air Quality Criteria	Chronic - based on a 24 hour sampling period	1.0×10^{-4} ($PM_{2.5}$) 2.0×10^{-4} (PM_{10}) 4.0×10^{-4} (TSP)	Neurological end-point from an occupational study, 5.3 year average exposure.	0.030 mg/m^3 0.084 mg/m^3	$BMCL_{05\text{-}ADJ}$ $BMCL_{05}$	Roels et al. (1992)	Total UF = 300 UF_H = 10 UF_{DB} = 3 UF_S = 3 MF[7] = 3	Duration adjusted[8] Values for larger size fractions were based on effects seen with $PM_{2.5}$	Final (MOE, 2011)
	WHO Health Guideline	Chronic (Annual average)	1.5×10^{-4} (PM_5)	Neurotoxicity in adult workers	0.007 mg/m^3 0.03 mg/m^3	$BMCL_{05\text{-}ADJ}$ $BMCL_{05}$	Roels et al. (1992)	Total UF = 50 UF_H = 10 MF[9] = 5	Factor of 4.2 used to convert to continuous exposure.	

[7] MOE termed this as an UF for "vulnerability of the Developing Nervous System;" it was termed a modifying factor in this document to be consistent with the application by other organizations.
[8] Duration adjusted from 5-d/week to 7-d/week, and for 10 m^3 of air inhaled for an 8-hour work day compared to 20 m^3 inhaled over a full day.
[9] Modifying factor based on developmental effects in younger children "by analogy with lead where neurobehavioural effects were found in younger children at blood lead levels five times lower than in adults and supported by evidence from studies of experimental animals."

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