PA DEPARTMENT OF ENVIRONMENTAL PROTECTION

BUREAU OF CLEAN WATER

Rationale

Development of the Human Health Criterion for Manganese

Executive Summary

In October 2017, a law was passed in the Commonwealth ("Act 40") that directed the Environmental Quality Board (Board) to promulgate proposed regulations related to manganese. Act 40 has directed a modification to Pennsylvania's water quality standards (WQSs). As the existing Potable Water Supply (PWS) criterion for manganese has not been reevaluated in many years and as states have an obligation under Section 303(c)(1) of the federal Clean Water Act (CWA) to periodically review and update, as appropriate, their WQSs to reflect current scientific knowledge and recommendations, the Department of Environmental Protection (DEP) evaluated the existing scientific data and information to ensure adequate criteria for manganese exist to protect all of PA's water uses. On January 27, 2018, DEP published an advance notice of proposed rulemaking soliciting information necessary to prepare the rulemaking documents required by law and support the Board's adoption of proposed regulations. The information received in response to the advance notice and recent scientific information relating to manganese were used to evaluate manganese water quality criteria with respect to the protected water uses identified in PA's water quality standards regulation.

Following an evaluation of the available scientific data, in accordance with its regulations and policies, DEP developed a human-health based water quality criterion for manganese of 0.3 mg/L. DEP recommends that this criterion should apply in all surface waters (i.e., at the point of discharge) in accordance with DEP's Water Quality Toxics Management Strategy (25 Pa. Code Chapter 16) and regulations found at 25 Pa. Code Chapters 93 (relating to water quality standards) and 96 (relating to water quality standards implementation).

History of Regulation

Prior to 1971, the Sanitary Water Board (SWB) in the Department of Health had primary responsibility for maintaining the rules and regulations related to water quality criteria and standards in Pennsylvania. Pennsylvania has had a water quality criterion for manganese since Article 301 Water Quality Criteria was added to the SWB Rules and Regulations on June 28, 1967. The criterion contained in Article 301 of the SWB Rules and Regulations appeared as "k –Total Manganese – Not to exceed 1.0 mg/L". This criterion was originally applied as Specific Criteria in Section 7 of Article 301 for selected waterbodies, or segments, in the North Branch Susquehanna, Monongahela, Allegheny, and Ohio River basins. In 1971, the SWB was abolished, and the authority and responsibilities of the SWB were transferred to the Pennsylvania Department of Environmental Resources (DER). Also, in 1971, the SWB Rules and Regulations, Article 301 Water Quality Criteria were replaced by the creation of 25 Pa. Code Chapter 93 Water Quality Standards, effective September 11, 1971 (1 Pa.B. 1804). In 1979, manganese was adopted as a statewide PWS criterion, implemented at the point of discharge by being added to 25 Pa.

Code § 93.7(d), Table 4, as part of DER's first triennial review of water quality standards (adopted by the Board on August 21, 1979, published in the *Pa. Bulletin* on September 8, 1979 (9 Pa.B. 3051), effective October 8, 1979). PWS is identified in §93.7 Table 3 as the *critical use*. As stated in §93.7, the critical use is the designated or existing use the criteria are designed to protect, and more stringent site-specific criteria may be developed to protect other more sensitive, intervening uses. When the critical use is identified and the statewide criterion is developed, it should provide protection of all water uses, unless new information shows additional protection is needed. In accordance with the current regulations found at Chapter 93, the purpose of PWS water quality criteria is to ensure that public water systems receive raw water at their intake structures that can achieve compliance with 25 Pa. Code Chapter 109 Safe Drinking Water (SDW) standards utilizing only conventional treatment. The only known rationale document for the existing PWS criterion was prepared by Kenneth Schoener, a DER water supply engineer. The rationale document explains the criterion was partially based on testimony from Mr. Reginald Adams, an experienced water supply manager from the Wilkinsburg Joint Water Authority. Mr. Adams stated that an "average up-to-date water plant can probably handle soluble manganese concentrations without too much difficulty. A well-designed plant can handle 1.5 to 2 parts per million…". He further indicated that if the manganese content of the raw water is 1.0 mg/L, or less, addition of potassium permanganate ($KMnO_4$) to the coagulation-sedimentation area at a rate of 2 parts of $KMnO_4$ to 1 part of manganese will remove the manganese. Operators can simply add $KMnO_4$ until a "slight pink residual color appears in the sedimentation unit". This process was commonly used in western PA, but it is considered a treatment process beyond "conventional treatment[1]".

DEP provided clarification to the manganese criterion in the 2000 Regulatory Basics Initiative (RBI) triennial review (30 Pa.B. 6059 on November 18, 2000) by adding a reference that the criterion is to be measured as total recoverable and based on potable water supply (PWS[2]) critical use protection. Manganese characteristics do not align with those of the other PWS substances included in § 93.7 (relating to specific water quality criteria), which are: total dissolved solids (TDS), bacteria (Bac_2), color (col), phenolics (Phen), iron (Fe_2), fluoride (F), chloride (Ch), sulfate (Sul) and nitrite plus nitrate (N). Through implementation requirements, compliance points differ for these substances. Compliance with total dissolved solids, fluoride, phenolics and nitrite plus nitrate criteria was moved from the point of discharge to the point of an existing or planned surface PWS withdrawal when § 93.5(e)[3] (relating to application of potable water supply use criteria) was added in the 1985 triennial review (adopted by the Board on December 18, 1984, effective on February 16, 1985 as published in the *Pa. Bulletin* (15 Pa.B. 544). The creation of 25 Pa Code, Chapter 96 Water Quality Standards Implementation occurred during the RBI Triennial Review in 2000. Language originally found in § 93.5(e) was relocated to § 96.3(d) during this RBI Triennial. Subsequently, chloride (Ch) and sulfate (Sul) were added to the § 96.3(d) provision in 2002, as adopted by the Board on September 17, 2002, and published in the *Pa. Bulletin* on December 14, 2002 (32 Pa.B. 6101). See Figure 1 for a summary of the regulatory changes.

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[1] The term "conventional treatment" is defined in § 93.1 as follows: "For the purpose of surface water protection of the Potable Water Supply (PWS) use, coagulation, followed by filtration for the removal of solids, and disinfection for the control of pathogens to produce water for drinking and other human consumption."

[2] PWS is described in 25 Pa. Code § 93.3 as "used by the public as defined by the Federal Safe Drinking Water Act, 42 U.S.C.A. § 300F, or by other water users that require a permit from the Department under the Pennsylvania Safe Drinking Water Act (35 P.S. §§ 721.1—721.18), or the act of June 24, 1939 (P.L. 842, No. 365) (32 P.S. §§ 631—641), after conventional treatment, for drinking, culinary and other domestic purposes, such as inclusion into foods, either directly or indirectly."

[3] The language in § 96.3(d) was relocated from an earlier regulation, § 93.5(e), that is now a reserved section.

Figure 1. Summary Table for § 96.3(d) PWS exceptions.

PWS Criteria including Manganese(Mn) & those listed in 96.3(d)	Year that the point of application was moved from the point of discharge to the point of PWS withdrawal	Consistent with Primary MCL values?	Primary MCL (Value in mg/L)	Consistent with Secondary MCL values?	Secondary MCL (Value in mg/L)	Not based on either primary or secondary MCL values
Ch	2002	--	--	yes	250	
F	1985	no	4	yes	2	
Mn	--	--	--	no	0.05	yes
N - Nitrate	1985	yes	10	--	--	
N - Nitrite	1985	yes	1	--	--	
Phen	1985	--	--	--	--	yes
Sul	2002	--	--	yes	250	
TDS	1985	--	--	yes	500	

Implementation of water quality standards is discussed in 25 Pa. Code Chapter 96. Section 96.3(c) (relating to water quality protection requirements) states that the water quality criteria described in Chapter 93, including the criteria in §§ 93.7 and 93.8(b) (relating to specific water quality criteria; and toxic substances) shall be achieved *in all surface waters* at least 99% of the time, unless otherwise specified in this title. Section 96.3(d) states "as an exception to subsection (c), the water quality criteria for total dissolved solids, nitrite-nitrate nitrogen, phenolics, chloride, sulfate and fluoride established for the protection of potable water supply shall be met at least 99% of the time *at the point of all existing or planned surface potable water supply withdrawals* unless otherwise specified in this title."[4] PWS parameters that are currently met in all surface waters are manganese, color, coliform bacteria and dissolved iron.

Manganese Background

Natural and Anthropogenic Sources

Manganese (Mn) is a ubiquitous element that exists naturally at low levels in many types of rocks, soils, waterbodies and plants. Pure manganese is a silver-colored metal, but manganese does not exist as a free element in nature. It is typically found in a variety of salts and minerals often combined with iron (Fe).

While manganese can exist in multiple oxidation states, it is generally present in surface waters in only two oxidation states, Mn^{+2} and Mn^{+4}. The Mn^{+4} state is the insoluble manganese dioxide (MnO_2) and would be present in a suspended state. The Mn^{+2} state is dissolved. It is very soluble in acid waters and is sparingly soluble in alkaline waters. Mn^{+2} slowly oxidizes to MnO_2 under most natural water conditions.

[4] The language in § 96.3(d) was relocated from an earlier regulation, § 93.5(e), that is now a reserved section.

Surface water levels of manganese may increase either as a result of direct discharges of manganese to the waterbody or due to an alteration of the chemical composition of the surface waters through mobilization of existing manganese sinks (Kaushal, et. al. 2018). Manganese appears to primarily enter PA waters as a result of anthropogenic activities including, but not limited to, DEP permitted discharges of sewage, various types of discharges categorized as industrial waste, stormwater, other permitted discharges and non-permitted discharges such as abandoned mine drainage. Manganese also finds its way into surface waterbodies through the natural weathering of rocks and minerals present in the earth's crust which then enter the waterbody either via stormwater runoff or through groundwater base flow containing manganese. Groundwater in certain areas of PA is known to contain high levels of iron and manganese due to the underlying geology of the region.

In addition to direct discharges to surface waters and mobilization of manganese sinks, manganese can enter the air from power plants, iron and steel manufacturing, coke ovens, automobile emissions, and dust from mining operations. It is usually found in the subsoil layers and not in any significant level at the surface. Thus, high surface soil levels may indicate contamination from vehicle exhaust associated with the fuel additive, methylcyclopentadienyl manganese tricarbonyl (MMT) (Lytle 1994).

Unless otherwise impacted by anthropogenic activities, dissolved manganese concentrations in surface waters rarely exceed 1 mg/L and are usually less than 0.20 mg/L (WHO 2004). An analysis of surface water samples collected in Pennsylvania between 2008 and 2018 revealed that 4% of 775 sample sites exceeded the current PWS manganese criterion of 1.0 mg/L, and 48% of the sites exceeded the secondary drinking water MCL of 0.05 mg/L. The natural quality of PA's surface waters can be characterized by the median and mean values of the 2008-2018 comprehensive statewide dataset, which are 0.026 mg/L and 0.037 mg/L, respectively. Sample sites were assessed for land use type and graded for land disturbance, which is a strong indicator of the presence of anthropogenic activity. The analyses showed a very strong positive correlation between land disturbance (e.g., mining regions of Pennsylvania) and average manganese concentrations in surface waters, such that sites in areas with higher land disturbance measured higher average manganese concentrations in surface waters within the same areas. In accordance with §93.1, *natural quality* is defined as "the water quality conditions that exist or that would reasonably be expected to exist in the absence of human related activity." Thus, the available statewide data suggest that where anthropogenic activity is absent or limited, natural manganese concentrations in Pennsylvania's surface waters are low.

Manganese is commonly used in the manufacture of metal alloys (aluminum and stainless steels), dry cell batteries, U.S. coins, glass, matches, fireworks, micro-nutrient fertilizer additives, organic compounds used in paint driers, textile bleaching, and leather tanning (EPA criteria 1979; Santamaria, 2008). It is also used in the manufacture of fungicides, such as Maneb and Mancozeb (Mora 2014, Bouabid, et. al 2016). Wastewater discharges resulting from these industrial manufacturing processes may be more likely to contain measurable, or significant, quantities of manganese. In addition, land application of manganese-containing pesticides could potentially result in the mobilization and discharge of manganese to waterbodies through discharges of stormwater runoff.

Discharges and Sources of Manganese in Pennsylvania

In Pennsylvania, coal mining activity has been and continues to be a significant contributor of manganese to waters of the Commonwealth. DEP's mining program has identified approximately 650 active NPDES mining permits containing numeric manganese limits. It is unknown how many abandoned mine discharges, which do not require permits, may exist across the Commonwealth.

In addition to mining, a recent review of Pennsylvania's sewage and industrial waste NPDES discharge permits revealed that manganese is also a potential issue for several non-mining sectors of the regulated community. These sectors include landfills, wastewater treatment plants (sewage and drinking water filter backwash plants) and power plants. Approximately 560 non-mining individual NPDES permits contain at least "monitor & report" conditions for manganese, and roughly 90 of those permits contain actual numeric effluent limits for manganese based on the existing PWS water quality criterion for manganese of 1.0 mg/L. Permits were identified across the state in each of the six DEP regions.

Human Health and Manganese

Physiological Need - Adequate Intake and Deficiency

Manganese is an essential micronutrient for plants and animals with Mn^{+2} and Mn^{+3} as the predominant oxidation states found in biological systems (Smith 2017). The highest concentrations in the human body are found in the bone, liver, kidney, pancreas, adrenal glands and pituitary gland (O'Neal 2015). Within the body's cells, it is found primarily in mitochondrial superoxide dismutase (MnSOD). MnSOD is a vital enzyme that maintains the overall health of the body's cells through its potent antioxidant capacity. Rodent studies have demonstrated that complete knockout of this enzyme results in death shortly after birth (Holley 2011). Beyond MnSOD, manganese is found in various metalloproteins especially glutamine synthetase in astrocytes, but it is also a cofactor for various enzymes that include hydrolases, kinases, decarboxylases and transferases (EPA IRIS). These manganese-based metalloproteins and enzymes play a critical role in the regulation of development, reproductive function, metabolism, blood clotting, digestion, bone growth, cell death and brain function (ATSDR 2012, Chen 2015, Chung 2015, Erikson 2007, Smith 2017, Yoon 2011).

Manganese deficiency can lead to bone malformation, skin lesions, hypocholesterolemia and seizures, but given the ubiquitous nature of manganese in the diet, deficiency is rarely observed except in susceptible individuals such as those with severely restricted diets or receiving total parenteral nutrition (TPN) formulated without manganese. Adequate intake (AI) levels recommended by the National Academy of Medicine vary by age group, gender and reproductive state (for women). The AI levels for adult males and non-pregnant, non-lactating females are 2.3 mg and 1.8 mg, respectively (Institute of Medicine 2001). Low manganese levels have also been associated with specific disorders including Alzheimer's disease, amyotrophic lateral sclerosis (ALS), epilepsy, phenylketonuria, maple syrup urine disease and Perthes' disease (Cordova 2013, Crossgrove 2004, Finley 1999). However, more research is needed to understand whether the observed low levels of manganese are present before (i.e., causal) or after the disease manifests.

Excessive Intake of Manganese - Effects of Elevated Manganese in the Human Body

As a micronutrient, only small quantities of manganese are necessary to achieve adequate health. As with many other heavy metals (i.e., lead, mercury), chronic exposure to elevated levels of manganese may lead to adverse health effects including various irreversible neurological deficits in adults, children, infants, and the developing fetus. Manganese is preferentially deposited in mitochondria-rich tissues such as the liver, pancreas and brain and has been shown to cross the placenta and the blood-brain barrier (BBB) (Lidsky 2007). Exposures to levels of manganese beyond those necessary for maintaining adequate health can lead to excess manganese in brain tissue resulting in a parkinsonian-like condition known as manganism. In 1837, James Couper became the first to describe this condition in a group of Scottish laborers working in the chemical industry (Menezes-Filho 2009, Santamaria 2008). Manganism is a neurodegenerative condition that results in extrapyramidal motor system dysfunction. It usually begins with neuropsychological symptoms that include aggressiveness, anxiety, headache, and decreased cognitive function. Upon very acute exposure or continued chronic exposure to lower levels of manganese, the condition will progress to changes in motor function which are characterized by a signature "cock-like" walk, dystonia, upright stance, difficulty walking backward and mild tremors (Aschner 2000, Chen et al. 2015, Crossgrove 2004). Depending upon the length and severity of the exposure, these neurological effects may result in permanent, irreversible damage to the brain. While the symptoms of manganism closely resemble Parkinson's Disease, it is a distinctly different condition (Bouabid 2016).

Historically, public health policies were primarily concerned with addressing acute toxicities that resulted from occupational exposure of adults to various heavy metals and chemicals. History has also shown that identification of other toxic effects in sensitive subpopulations will slowly follow, and eventually, subclinical effects are considered and examined. Unfortunately, significant amounts of time generally pass between our understanding of the initial acutely toxic events and the subtle chronic impacts on children and development, which results in considerable delays in removing the exposure pathway. In fact, it took several decades of research and periodic reevaluation of the approved threshold level for lead to understand that there is no safe level of exposure for children (Lidsky 2007). The acute effects associated with high levels of manganese are widely known and well understood, but our understanding of the chronic, subclinical effects is lacking for manganese particularly with regards to children and brain development. Researchers have begun to examine the effects of chronic low-level exposures on children. Preliminary data suggests that the period of fetal development through early childhood represents a sensitive time period, but more research is needed to determine possible exposure-related effects and what levels are considered safe. Consequences of low-level exposure are often subtle for an individual child and thus easily dismissed, but at the population level, such shifts in intellectual ability or behaviors can have a substantial impact (Lanphear 2015). The available epidemiological data on children suggests that exposure to elevated manganese levels may result in a variety of neurological and developmental deficits including symptoms consistent with attention-deficit, hyperactivity disorder (ADHD), short-term memory impairments, visual identification impairments, impaired performance on manual dexterity and rapidity tests and a reduction in IQ scores (Bouchard 2007, Chung 2015, Henn 2011, Grandjean 2014, Haynes 2015, Khan 2011, Khan 2012, Kim 2009, Menezes-Filho 2009, Oulhote 2014, Wasserman 2006). In addition, Kim et. al. (2009) examined the possibility that co-exposure to neurotoxicants may have an additive effect on neurodevelopment. In this case, the researchers assessed the intellectual function of school-aged children in Korea exposed to environmentally relevant levels of lead and manganese (Kim 2009).

Exposure Pathways and Homeostatic Control Mechanisms

There are two primary human exposure pathways for manganese – inhalation and oral exposure. Intravenous injection of illegal narcotics and TPN represent other possible routes of exposure. We know that inhalation of manganese dusts poses greater immediate toxicity risks and often results in significant acute and chronic neurotoxic effects because inhaled manganese bypasses the body's homeostatic control mechanisms. The majority of manganese intoxication cases have been associated with occupational exposures (i.e., welders, miners, smelters, battery-manufacture workers, etc.) (Crossgrove 2009). The increased level of toxicity associated with this exposure pathway is not unexpected since inhaled manganese has a direct pathway to the brain via the olfactory nerve (O'Neal 2015). Manganese can also be absorbed through the lungs. The human body tightly regulates the amount of *ingested* manganese that enters the circulatory system via intestinal absorption and the amount that circulates through the body via biliary excretion (Chen, 2015, Crossgrove 2004, Erikson 2007, O'Neal 2015, Schroeter 2012, Yoon 2011). The intestines and liver, which regulate manganese blood levels by reducing absorption from the digestive tract and by increasing excretion through the production of bile, are effectively bypassed when manganese is inhaled. Thus, the body will typically absorb 100% of the inhaled manganese. Other possible environmental sources of inhalable manganese include power plant and automobile (MMT) emissions.

By far, the major route of exposure for most individuals is through the oral pathway (i.e., dietary sources). In addition to food, individuals may also consume manganese via surface water and groundwater sources. Dietary sources and amounts vary greatly with average intake for adults ranging between 2 and 9 mg/day. Significant sources of manganese include nuts, whole grains, legumes and rice. Moderate to high amounts can also be found in tea, green leafy vegetables, egg yolks, chocolate, seeds, and some fruits (Aschner 2000, Chen 2015, Finley 1999). Therefore, manganese levels at the higher range are more likely to be encountered with vegetarian (plant-based) diets. According to the EPA's Integrated Risk Information System (IRIS) database, studies have suggested that absorption rates may differ between drinking water and food sources due to differences in bioavailability and fasting state of the individual. For example, a vegetarian diet can provide in excess of 9 mg/day of manganese. However, it is important to note that the plant-based diet also contains many substances that bind and inhibit the absorption of manganese including tannins, oxalates, phytates and fiber which significantly reduces bioavailability (EPA IRIS). In addition, many manganese-rich foods are likely to contain a wide variety of minerals in addition to manganese, and the transport protein mechanisms of intestinal cell membranes may have a greater affinity for those other minerals, such as iron, thus limiting the absorption of manganese. Unlike for other heavy metals, the oral exposure pathway is generally not expected to result in toxic levels of manganese within the body due to the tight homeostatic control mechanisms mentioned above. Proper functioning of these homeostatic control mechanisms generally ensures that manganese levels remain within the appropriate range necessary for good health. Compared to the inhalation route which results in nearly 100% absorption, absorption of manganese from the diet averages only 3-5% (ATSDR 2012, Smith 2017).

Factors influencing Manganese levels in the body

Although diet is not generally expected to lead to elevated manganese levels, the blood and tissue manganese levels within specific individuals of the population are highly influenced by a variety of factors including manganese oxidation state, liver function, gender/mineral status, fasting state and age. Furthermore, with a narrow dose range between inadequate and excess intake and such low oral

absorption rates (typically less than 5%), a small variation in absorption of manganese could substantially change the overall body burden of manganese (Smith 2017).

Different oxidation states of manganese are absorbed by different cell membrane transport proteins and pathways. The divalent metals transporter 1 (DMT-1) shuttles primarily divalent manganese while the transferrin (Tf)/transferrin receptor (TfR) system is responsible for transporting trivalent manganese (Chen 2015). Mn^{+3} has a high affinity for the Tf system. On the other hand, Mn^{+2} may be transported into cells through a variety of transporters other than DMT-1 including the zinc transporters (ZIP8 and ZIP14), the citrate transporter, the choline transporter, the dopamine transporter (DAT), and calcium (Ca) channels (Chen 2015). The divalent oxidation state is one of two oxidation states typically found in surface waters.

As already discussed, the liver plays an important role in maintaining manganese homeostasis within the body. Liver impairment has a profound effect on manganese levels in the blood. If excess manganese has been absorbed, biliary excretion is the major pathway for elimination (Crossgrove 2004). Thus, any form of liver impairment (i.e., cirrhosis, hepatitis, fatty liver disease, etc.) may decrease manganese elimination and increase blood plasma levels leading to neurotoxicity.

Individuals with iron-deficiency anemia are at risk for increased manganese levels in the body because both minerals use common transporters for uptake, and iron-deficiency increases the expression of these transport systems (Chen 2015). Manganese is structurally and biochemically similar to iron in numerous ways (Smith 2017). Both metals are transition elements, carry similar valence charge under physiological conditions (2+ and 3+), strongly bind Tf and preferentially accumulate in mitochondria (Aschner 2008). Not surprisingly, females of childbearing age have been shown to absorb more manganese than males. Iron-deficiency anemia is prevalent among this group (Bouchard 2007, O'Neal 2015).

Fetuses, neonates and infants are known to absorb greater amounts of manganese than adults due to several unique features of these life stages (Brown 2008, O'Neal 2015, Yoon 2011). First, this age group appears to lack a fully-developed excretory pathway via the liver. Second, there is evidence that neonate and infant digestive systems may absorb more manganese than adults. The increased absorption may be related to increased expression of the DMT-1 protein at the cell surface due to the need for large amounts of iron during early development. Third, formula-fed infants consume more water per unit of body weight. This difference is at a maximum in the first month and decreases with increasing age. Infants consuming at the 95^{th} percentile of intake ingest 8 times more water on a ml/kg basis than a 70 kg adult (Brown 2008). Fourth, there is increased permeability across the BBB and retention of manganese in infant tissues. To date, this tendency has been attributed to an immaturity of the BBB mechanisms. However, research has suggested that the uptake of manganese may be controlled by active transport mechanisms distinct from adults allowing for greater uptake of compounds required for normal development (Yoon 2011).

Guidelines for Manganese

Health-based and Aesthetic Guidelines

EPA first mentions manganese in the Water Quality Criteria 1972 book, also known as the "Blue Book". At that time, EPA established a recommendation that soluble manganese not exceed 0.05 mg/L in public water sources. In the 1976 Quality Criteria for Water book, known as the "Red Book", EPA retained the 0.05 mg/L criterion to protect domestic water supply and added a 0.1 mg/L "organism only" criterion for protection of consumers of marine mollusks. These criteria remained unchanged in EPA's Quality Criteria for Water 1986, known as the "Gold Book". According to these EPA documents, public water systems with conventional treatment should be able to partially sequester manganese with special treatment, but manganese is not removed by conventional filtration. Complaints of laundry staining and objectionable tastes are common when manganese levels exceed 0.150 mg/L and low concentrations of Fe may increase these effects. In 1963, McKee and Wolf summarized the available toxicity data on freshwater aquatic life. Tolerance values ranged from 1.5 mg/L to over 1,000 mg/L. According to the EPA Red Book, background surface water levels of manganese were not expected to exceed 1 mg/L. As background levels were not expected to exceed 1.0 mg/L, manganese was not considered to be a problem in freshwater waterbodies. It is unclear whether this data included consideration of impacts of manganese on freshwater mollusks. With respect to marine mollusks, manganese was found to bioaccumulate in the edible portions with bioaccumulation factors (BAFs) as high as 12,000. As such, EPA established the 0.1 mg/L "organism only" criterion. At concentrations of slightly less than 1.0 mg/L to a few milligrams per liter, manganese may be toxic to plants from irrigation water applied to soils with pH values lower than 6.0 (EPA Red Book). As elevated manganese levels in groundwater and surface water tend to be limited to specific regions within the country, EPA does not have a national water quality standard recommendation for manganese for the protection of human health or aquatic life.

EPA's IRIS database provides human health assessment information on chemical substances following a comprehensive review of toxicity data as outlined in the *IRIS assessment development process*. The oral reference dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The RfD for manganese is for the total oral (dietary) intake of manganese and was last revised in November 1995. EPA recommended that a modifying factor of 3 be applied if this RfD is used for assessments involving nondietary exposures (soils or water). There are four primary reasons for the recommendation. First, fasting individuals have been shown to absorb more manganese from drinking water than non-fasting individuals. Second, a study by Kondakis et. al. (1989) raised concerns about possible adverse health effects associated with a lifetime consumption of drinking water containing approximately 2 mg/L of manganese. Third, formula fed infants have been found to have a much higher concentration of manganese in hair samples versus breast fed infants. Not only does infant formula contain higher amounts of manganese than breast milk, the valence form of the manganese in formula appears to increase the absorption rate. Studies have shown that the levels of manganese in learning-disabled children were significantly increased in comparison with that of non-disabled children. Although no causal relationship has been determined, further research is needed. There is evidence that the infant digestive tract absorbs more manganese than adults and that infants are less able to excrete it. Furthermore, it has been shown to readily cross the blood-brain barrier in infants. A study by Mena et.

al. (1974) found the rate of penetration in animal experiments to be 4 times higher in infants than in adults. These considerations, in addition to the likelihood that any adverse neurological effects of manganese associated with early exposure are likely to be irreversible and not manifested for many years after exposure, warrant caution when establishing safe levels of manganese in water until more definitive data are available (EPA IRIS 2017).

EPA's Drinking Water Health Advisory Program, sponsored by the Health and Ecological Criteria Division of the Office of Science and Technology (OST), Office of Water (OW), provides information on the health and organoleptic (e.g., taste, odor, color) effects of contaminants in drinking water. A health advisory (HA) is not an enforceable standard, but rather provides technical guidance to assist Federal, State and local officials when emergency spills or contamination situations occur. The current HA for manganese was issued in 2004 and was based partly on the Agency for Toxic Substances and Disease Registry's final Toxicological Profile for Manganese (ATSDR 2000) and the Institute of Medicine's Dietary Reference Intakes for Manganese (IOM 2001). HAs are generally determined for one-day, ten-day and lifetime exposure if adequate data are available that identify a sensitive noncarcinogenic end point of toxicity. There was no suitable information to develop a one-day HA for manganese. The ten-day HA of 1 mg/L for a child is recommended as a conservative estimate for a 1-day exposure for both children and adults. The ten-day HA for a 10-kg child is 1 mg/L. The lifetime HA for adults and children is 0.3 mg/L and was calculated using the RfD in IRIS. For infants younger than 6 months, the lifetime HA of 0.3 mg/L is also recommended for acute exposures (ten-day, one-day) due to similar concerns identified by EPA in establishing the oral RfD for manganese (EPA manganese HAL). Currently, the federal Safe Drinking Water regulations only regulate manganese as a secondary contaminant. Under Federal regulations, SMCLs are considered non-enforceable federal guidelines for contaminants that may cause cosmetic or aesthetic effects. However, as mentioned previously, SMCLs are enforceable standards in the Commonwealth of Pennsylvania, and they are regulated under 25 Pa. Code Chapter 109. The SMCL for manganese in potable water is 0.05 mg/L.

Technology-based Guidelines

Effluent Limitation Guidelines (ELGs) are national, technology-based wastewater discharge regulations that are developed by EPA on an industry-by-industry basis. DEP received comments from the mining industry during the public comment period of the ANPR regarding ELGs. The mining sector has pointed to the federal ELGs found at 40 CFR 434, which place limitations on the amount of manganese that can be legally discharged in mining effluent. Pennsylvania's mining regulations found at 25 Pa. Code §§ 87.102, 88.92, and 89.52 mirror these federal limitations. Both the state and federal regulations effectively limit discharges of manganese to 2.0 mg/L as a 30-day average, 4.0 mg/L as a daily maximum and 5.0 mg/L as an instantaneous maximum. The mining sector contends that moving the application of the PWS criterion to the point of PWS withdrawal would not result in harmful levels of manganese in waters of the Commonwealth at the point of discharge because the federal ELGs effectively prevent mining companies from discharging at such levels. DEP recognizes that this industry has additional regulations that would limit the amount of manganese in their discharges if the Commonwealth's PWS manganese criterion would be applied at the point of PWS withdrawal. However, the other industrial sectors identified earlier in this rationale document do not have federal ELGs in place to restrict the discharge of manganese to waters of this Commonwealth. Therefore, the mining ELGs and regulations do not adequately address control of manganese at the point of discharge for any industrial sector other than mining. Conversely, water quality criteria are applicable to, and are

necessary to prevent pollution from, all types of activities associated with and discharges to surface waters of the Commonwealth. Criteria are also used by DEP in the assessment of waterbodies and for other permit and non-permit related activities.

Water quality criteria are developed by DEP to protect all existing and designated water uses, and their application is not restricted to any one particular group or activity. DEP must follow appropriate Federal and State regulations when developing water quality criteria. Under section 303(c)(1) of the federal CWA, DEP is also required to review and update its WQSs periodically, but at least once every 3 years. Therefore, DEP must develop the necessary water quality criteria to protect Pennsylvania's water uses as defined in 25 Pa. Code §93.3 based on the best available scientific information and recommended guidelines, as appropriate.

Scientific Literature and Data Related to the Human Health Effects of Manganese

DEP has reviewed, and will continue to review, the scientific literature on the human health effects of manganese, a metal that will behave similarly to other heavy metals at levels beyond those necessary to maintain adequate health. Such a narrow dose range exists between inadequate and excess intake that small variations in the body's absorption and handling of manganese could substantially change the body burden (Smith 2017). Epidemiological studies and research have begun to examine the effects of manganese exposure on the developing fetus, infants and children. The summary that follows highlights some of the current knowledge on the human health effects of manganese.

In 2006, Grandjean et. al. reviewed the scientific literature and identified five industrial chemicals as neurodevelopmental toxicants: lead (Pb), methylmercury, PCBs, arsenic (As) and toluene. Since that time, epidemiological studies have documented six additional neurotoxicants: manganese, fluoride, chlorpyrifos, dichlorodiphenyltrichloroethane, tetrachloroethylene, and polybrominated diphenyl ethers (PBDEs) (Grandjean 2014). Lidsky (2007) and Grandjean recognized that the risks of industrial chemicals to brain development has historically required decades of research to identify and understand the subclinical neurotoxic effects since the initial discovery of toxicity often begins with poisoning and episodes of high-dose exposure. In addition, the full effects of early damage may not become apparent until school age or beyond due to the normal sequence of developmental stages (Grandjean 2014). Efforts to control and restrict developmental neurotoxicity are hampered by the lack of data required by law on developmental neurotoxicity for chemicals. While our understanding of the effects of early manganese exposure is currently limited, the recent research on well-documented neurotoxicants such as lead and methylmercury has generated new insights into the consequences of early exposure to heavy metals.

Between 2007 and 2011, Chung et. al. (2015) recruited 232 mother-infant pairs from the Mothers and Children's Environmental Health study (MOCEH) in Korea to evaluate the relationship between neurodevelopment and maternal blood manganese level without a specific source of occupational or environmental exposure (Chung 2015). The results of the study suggest an association between maternal blood manganese at delivery and neurodevelopmental scores of infants at 6 months of age.

Manganese levels in infant formula have been shown to contain as much as 75 times more manganese per liter than human breastmilk not including any additional manganese from the water used in the mixture (Brown 2008, Ljung 2007). Breastmilk manganese content can range between 1.8 and 27.5

µg/L and has been shown to vary with the stage of lactation. Higher levels of manganese occur during the initial weeks of breastfeeding and gradually decrease over the first several months. Levels at this later time generally average around 3 µg/L (Erikson 2007). Concentrations in infant formula, however, can range dramatically from 33 µg/L to well over 300 µg/L (EPA IRIS 1995). Soy-based formulas have been shown to contain the highest levels of manganese with a typical level between 200-300 µg/L. Unlike the natural decline of manganese levels observed in breastmilk over time, infant exposure to the manganese levels in formula will remain fairly constant until weaned. It is notable that human breastmilk manganese is also in a different oxidation state than infant formula. Human milk manganese is in the trivalent oxidation state whereas infant formula manganese is in the divalent oxidation state (Erikson 2007). Differences in absorption have been observed and may be attributed to the transport mechanisms that allow for manganese uptake across the gastrointestinal tract. Studies have found that formula-fed infants consume, absorb, and retain more manganese per day than breastfed infants (Brown 2008). If manganese is present in the drinking water used to prepare the infant formula, the manganese content will be further increased.

Bouchard et. al. (2007) conducted a pilot study of 46 Canadian children (boys and girls ages 6-15 years) to assess differences in children's exposure to public well water from two wells with different manganese concentration. Manganese levels in Well 1 had increased from 230 to 610 µg/L over the period from 1996-2005 with a mean value of 500 $\pm$ 129 µg/L. Well 2 was drilled in 1999 and had stable manganese levels that averaged 160 µg/L. Most families drank bottled water due to the bad taste associated with elevated manganese, but well water was used in cooking and to prepare soups and concentrated fruit juices. Manganese body burden was determined by measuring the manganese content of hair samples. Elevated levels of manganese in hair was associated with increased hyperactivity and oppositional behaviors in the classroom after adjusting for income, age and sex. Girls had significantly higher hair manganese levels than boys. The group was ethnically homogeneous, had an economic level above provincial average and most had a biparental family structure.

Following the 2007 pilot study, Bouchard et. al. (2011) conducted a cross-sectional study on 362 children (ages 6-13) living in southern Quebec. Researchers examined the effects of manganese intake from diet and drinking water on intellectual impairment. The results showed that children exposed to higher concentrations of manganese in tap water had lower IQ scores after adjustment for socioeconomic status and other metals present in the water. The study also showed that manganese intake from water ingestion, but not from the diet, was significantly associated with elevated hair manganese. This finding suggests that the body's normal homeostatic control mechanisms may not respond to drinking water manganese in the same manner as dietary manganese and may not prevent increased body burden (Bouchard 2011).

Oulhote et. al. (2014) conducted an additional assessment of the Bouchard cohort to determine possible associations between manganese in water and behavioral impairments (i.e., issues with memory, attention, motor function and hyperactive behaviors.) The results suggest that higher levels of manganese exposure are associated with poorer performance of memory, attention and motor functions, but not hyperactivity, in children.

Haynes et. al. (2015) assessed the impact of manganese on neurocognition in a cohort of school-age children (age 7-9) residing in communities near Marietta, Ohio, which is home to the longest operating ferromanganese refinery in North America. Mothers of selected children must have resided in the area

during their pregnancies. Results showed that both high and low levels of manganese may affect neurodevelopment.

Kern et. al. (2010) conducted experiments on neonate Sprague-Dawley rats to better understand the relationship between early, pre-weaning manganese exposure and neurobehavioral deficits. The pre- and early post-weaning period coincides with the development of dopaminergic pathways in specific brain regions that are instrumental in the regulation of executive function behaviors involving learning, memory and attention (Kern 2010). Experimental exposure doses approximated the relative increases in manganese exposure experienced by infants and young children exposed to manganese contaminated water or soy-based infant formulas (or both) compared to manganese ingestion from human breastmilk. Pre-weaning oral manganese exposure led to significant learning deficits in the 8-arm radial maze. Since the rats were measured at a time (postnatal day 33-46) when brain manganese levels had declined to near-control levels, the deficits may reflect lasting effects of early exposure (Kern 2010).

Beaudin et. al. (2013) evaluated fine sensorimotor dysfunction in 55 adult Long-Evans rats following either pre-weaning or lifelong manganese exposure using objective measurements that are directly relevant to the types of motor outcomes studied in pediatric manganese research. The pre-weaning exposure group showed selective long-lasting impairment in reaching skills 3 months after the last oral dose of manganese, when blood and brain manganese levels had long since returned to background levels. These deficits suggest permanent or irreversible damage to the basal ganglia systems of the adult rat brain. Lifelong manganese exposure produced wider-spread deficits that included both reaching and grasping skills (Beaudin 2013).

Khan et. al. (2011) assessed the effects of manganese on a community in Bangladesh. Children (ages 8-11) were designated into one of four groups: a) high arsenic, high manganese; b) high arsenic, low manganese; c) low arsenic, high manganese; d) low arsenic, low manganese. Each group contained approximately 75 children. Significant associations were found between manganese (water) and test scores for both externalizing and internalizing behaviors. Manganese was significantly more strongly related to externalizing behavior problems. Interestingly, arsenic was not associated with either externalizing or internalizing behavior problems (Khan 2011).

Moreno et. al (2009) investigated whether exposure to manganese in early life alters susceptibility to manganese during aging. C57B1/6 mice were exposed to manganese by gavage as juveniles, adults or juveniles and again as adults. Moreno et. al. examined metal accumulation in multiple brain regions and serum as well as catecholamine and monoamine neurotransmitter levels and neurobehavioral parameters. Results indicated that developing mice are highly susceptible to changes in behavior and striatal neurochemistry and effects of exposure persist during aging that render specific brain regions more vulnerable to neurotoxic insults later in life (Moreno 2009).

Wasserman, et. al. (2006) examined associations between drinking water manganese (WMn) and intellectual function in 124 children (ages 9.5-10.5) from Araihazar, Bangladesh. The mean WMn concentration in the studied drinking water was 795 µg/L. After adjusting for sociodemographic factors, WMn was associated with significantly reduced Full-Scale, Performance, and Verbal raw scores in a dose-dependent fashion.

Evaluation of Available Recommendations and Scientific Data

DEP has reviewed and considered the available scientific data and recommendations in accordance with 25 Pa. Code Chapter 16. Water Quality Toxics Management Strategy – Statement of Policy and 25 Pa. Code Chapter 93. Water Quality Standards. Human health criteria are based on one of two approaches – threshold level or non-threshold level toxic effects (carcinogens). DEP guidelines for the development of threshold level toxic effect human health-based criteria are found specifically at 25 Pa. Code §16.32. When no criteria have been developed by EPA for a substance identified or expected in a discharge, DEP will develop criteria following EPA's standard toxicological procedures outlined in the Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (EPA-822-B-00-004, October 2000) as amended and updated (25 Pa. Code §16.32(c)(2)). As further stated in §16.32(d), the sources DEP uses to obtain relevant risk assessment values for protection for threshold level toxic effects to human health as are follows:

(1) Verified references doses, listed in the EPA agency-wide supported data system known as IRIS (Integrated Risk Information System) and other EPA approved data sources referred through IRIS
(2) Maximum contaminant Level Goals (MCLGs)
(3) The EPA's CWA § 304(a) health criteria listed under the National Toxics Rule in 40 CFR 131.36 (57 FR 80848, December 22, 1992) (relating to toxics criteria for those States not complying with Clean Water Act section 303(c)(2)(B)), as amended and updated and other final criteria published by the EPA and the Great Lakes Initiative Clearinghouse.
(4) Teratology and other data that have been peer-reviewed may provide information for criteria development.

In accordance with policy, DEP would use the verified reference dose for manganese listed in EPA's IRIS database unless more recently published, peer-reviewed studies are available which provide sufficient information for DEP to develop an updated reference dose. At this time, DEP has reviewed the available scientific data and literature and is not proposing to develop an updated reference dose. However, the data broadly supports the need for an IRIS reference dose for manganese.

Development of Manganese Criteria

Criteria for the protection of Human Health (Toxics)

As described above, DEP develops human health-based criteria in accordance with the Water Quality Toxics Management Strategy. Human health criteria development considers various exposure pathways including exposures from drinking water and fish consumption and may include exposures from inhalation or dermal absorption. Inclusion of multiple exposure pathways and the toxicity risk of the substance make development of human-health based criteria different than PWS criteria. Many of PA's existing PWS criteria are based on SDW primary MCLs or SMCLs and are related to aesthetic qualities of the water (i.e., taste and odor). MCLs are not developed using the same risk assessment factors required by DEP's regulations for the development of WQS. SMCLs are not based on concerns related to toxicity.

Development of a Human Health Criterion based on IRIS

The EPA developed an oral reference dose (RfD) for manganese and published it in the IRIS database in 1995. Central nervous system effects were identified as the non-threshold critical health effect. As discussed throughout this rationale, the research on manganese is currently advancing and it continues to support the need for an RfD for manganese. At this time, DEP is not proposing to develop a new approach, or RfD, to develop human health-based manganese criteria. DEP is proposing to use EPA's existing IRIS RfD for manganese. This information represents the best available science and data for the purposes of criteria development and is in accordance with the DEP's Water Quality Toxics Management Strategy. As the science and knowledge on manganese toxicity progresses, DEP will review and evaluate new manganese exposure recommendations and will revise the manganese criterion, as appropriate, through DEP's required and ongoing WQSs review process.

To date, manganese has not been shown to be carcinogenic. Thus, the criterion has been developed following the threshold level approach. The applicable RfD in IRIS is for the total daily oral intake of manganese, which includes drinking water and dietary sources. However, the No Observed Adverse Effect Level (NOAEL) study data which informed the RfD value were obtained solely from dietary studies; therefore, EPA recommends that an assessment of drinking water exposure should include a modifying factor of 3. DEP agrees with this recommendation and has applied a modifying factor 3 to the current RfD in its calculation of a criterion. The published RfD assumes an uncertainty factor (UF) of 1 and a modifying factor (MF) of 1.

Calculation of the RfD in IRIS

RfD = (NOAEL)/ (UF) or (MF)

= 0.14 mg/kg-day ÷ 1

= 0.14 mg/kg-day

Calculation of the modified RfD

In order to assess manganese exposure from water consumption, DEP followed the EPA recommendation to apply an MF of 3 to the RfD.

RfD_{DW} = (0.14 mg/kg-day ÷ 3)

= 0.05 mg/kg-day

In accordance with the 2000 EPA Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health using the 2015 updated exposure input values (body weight, drinking water intake, and fish consumption) and PA Chapter 93 guidelines, DEP derived the following human health criterion for manganese. Manganese is currently not known to significantly bioaccumulate in fish; therefore, a bioaccumulation factor of 1 has been assumed. While it has been observed in marine mollusks (EPA Red Book), it is not known if significant bioaccumulation occurs in freshwater mussels.

Bioaccumulation factors (BAFs) for manganese may be adjusted in the future if peer-reviewed, published research shows that bioaccumulation is occurring in freshwater fish or mussels.

$AWQC_{Mn}$ = RfD x RSC x (BW ÷ [DWI + (FI x BAF)])

Where:

RfD = 0.05 mg/kg-day
Relative Source Contribution (RSC) = 0.2
Body Weight (BW) = 80 kg
Drinking Water Intake (DWI) = 2.4 L
Fish Intake (FI) = 0.022 kg/day
Bioaccumulation factor (BAF) = 1

$AWQC_{Mn}$ = 0.05 mg/kg-day x 0.2 x (80 ÷ [2.4 + (0.022 kg/day x 1)])

$AWQC_{Mn}$ = **0.3 mg/L**

Conclusion

DEP has calculated a threshold level toxic effect human health-based criterion for manganese of 0.3 mg/L. Since this criterion is not limited to the protection of the PWS use or to addressing aesthetic concerns, DEP recommends that it will apply in all surface water (i.e., at the point of discharge). Water quality based effluent limits (WQBELs) for manganese will be developed using the design flow conditions for threshold human health criteria contained in 25 Pa. Code §96.4, Table 1. In addition, DEP recommends that the human health water quality criterion for manganese shall be achieved in all surface waters at least 99% of the time as specified in 25 Pa. Code §96.3(c).

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