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Draft Assessment

Manganese and its Compounds

Environment and Climate Change Canada
Health Canada

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Canada

Synopsis

Pursuant to section 68 of the *Canadian Environmental Protection Act, 1999* (CEPA), the Minister of the Environment and the Minister of Health have conducted a draft assessment of manganese and its compounds. This draft assessment focuses on the manganese moiety and therefore considers manganese in its elemental form, manganese substances, and manganese released in dissolved or particulate form. As such, this draft assessment considers all manganese-containing substances beyond those identified as priorities for assessment.

There are both natural and anthropogenic sources of manganese to the environment. Natural sources of manganese include weathering of rock, ocean spray, forest fires, vegetation, and volcanic activity. Manganese is found in more than 100 minerals, including oxides, sulfides, carbonates, silicates, phosphates, and borates. Manganese is also present in coal and crude oil. The potential for cumulative effects was considered in this assessment by examining cumulative exposures to the manganese moiety. This draft assessment considers the combined exposure of humans and other living organisms to the manganese moiety from natural or anthropogenic sources, and whether it is present in environmental compartments (for example, water, sediment, soil, or air), food, or consumer products. All substances that have the potential to dissolve, dissociate, or degrade to release manganese through various transformation pathways can potentially contribute to the exposure of living organisms and the environment to bioavailable forms of manganese.

Anthropogenic sources of manganese include the incidental production of manganese (that is, as a by-product) and the manufacture, import, and use of manganese and its compounds in products and manufactured items. 6 substances in this draft assessment were included in a survey issued pursuant to section 71 of CEPA. According to information received in response to the survey, 3 manganese substances were reported to be manufactured in Canada in quantities ranging from 1 tonne to greater than 10,000 tonnes, and 4 substances were imported into Canada in quantities ranging from 1 tonne to 10,000 tonnes. In addition, information from the Canadian International Merchandise Trade Web Application indicates that an average of 14,000 tonnes of manganese-containing commodities were imported per year from 2017 to 2021.

The primary use of manganese is as an additive and a component in alloys for steel production. Other metallurgical uses of manganese include use in alloys with aluminium, copper, zinc, titanium, gold, silver, and bismuth for a variety of specific applications. Non-metallurgical uses of manganese include use in adhesives and sealants; animal feed; non-pesticidal agricultural products (for example, soil amendments, plant fertilizers); automotive, aircraft and transportation manufacturing and uses; batteries; building and construction materials; catalysts; cleaning and furnishing care (for example, cleaning products and odour control products); electronics; food additives; food packaging and other food uses; fuels and related products (for example, fuel additives); intermediates in the chemical industry; lubricants and greases; medical devices; metal materials; paints and coatings; pest control products; self-care

products (that is, cosmetics, natural health products and non-prescription drugs); textiles; children's toys; playground and sporting equipment; and water treatment.

Manganese is considered to be persistent in the environment, though it can transform into different chemical species and partition among different phases within an environmental compartment.

Manganese is an essential element that is actively assimilated and utilized by organisms. The bioavailability and toxicity of manganese is largely dependent on environmental characteristics (for example, pH and water hardness). Manganous Mn(II) and manganic Mn(IV) are the 2 primary oxidation states of manganese in the environment. The former is the more soluble and therefore more bioavailable form. It has been shown that lower trophic level organisms may actively assimilate manganese as an essential element for their biological functions, while organisms at higher trophic levels are able to at least partially maintain manganese homeostasis. Currently, there is no evidence to suggest that manganese may biomagnify via aquatic food chains.

At moderate to high concentrations, manganese causes mortality as well as effects on growth and reproduction in freshwater aquatic and soil-dwelling organisms. Chronic predicted no-effect concentrations (PNECs) for manganese for freshwater organisms were derived using the long-term Canadian Water Quality Guidelines developed by the Canadian Council of Ministers of the Environment. Toxicity modifying factors that influence the bioavailability and toxicity of manganese, including water hardness and pH, were incorporated to derive site-specific freshwater PNECs. The PNEC for soil-dwelling organisms was derived using a species sensitivity distribution approach.

A weight-of-evidence approach was used to determine the potential for ecological harm in Canada. Risk quotient analyses were performed for manganese by comparing predicted environmental concentrations (PECs) with freshwater and soil PNECs to determine the potential for ecological harm in Canada.

Facilities in 3 industrial sectors (that is, pulp and paper, metal ore mining, and wastewater systems), as well as a group of steel-related sectors, were examined. PECs derived from facilities in the pulp and paper, wastewater, and steel-related sectors resulted in few or no PNEC exceedances from the release of manganese in effluent. Furthermore, PECs that were derived from the application of biosolids from wastewater treatment resulted in no PNEC exceedances on agricultural lands in Canada. The analysis of effluent releases of manganese to water from metal ore mining facilities indicates that, while releases from most facilities are limited, there is a potential for harm to the aquatic environment as a result of manganese release from a small number of facilities across Canada.

Considering all available lines of evidence presented in this draft assessment, there is risk of harm to the environment from manganese and its compounds. It is proposed to conclude that manganese and its compounds meet the criteria under paragraph 64(*a*) of CEPA as they are entering or may enter the environment in a quantity or concentration

or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity. However, it is proposed to conclude that manganese and its compounds do not meet the criteria under paragraph 64(*b*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger to the environment on which life depends.

Manganese is an essential nutrient for human health, but elevated intake may result in adverse health effects. The central nervous system appears to be the most sensitive target of manganese toxicity in mammals. The developing fetus, infants, and children under 3 years of age are considered to be the most susceptible subpopulations for manganese toxicity as excessive manganese exposure can adversely affect brain development. Time of exposure is crucial, because susceptibility varies in different stages of brain development, and prenatal and early postnatal periods are considered the most sensitive developmental windows for manganese-induced neurotoxicity.

Subclinical neurological effects, including disturbances to fine motor control, memory, cognitive function, hyperactivity, and tremor are some of the earliest effects noted in humans and experimental animals following excess oral or inhalation exposure. Neurotoxic effects were used to characterize the risk for all routes of exposure. Neurobehavioural effects, which may have lasting impacts into later life, observed at low doses in neonatal rats were used to characterize risk via the oral and dermal routes of exposure. Alterations in fine motor control (including hand dexterity) from an occupational study were used to assess the risk associated with inhalation.

Manganese is ubiquitous in air, drinking water, food, soil, and house dust and is present in thousands of products available to consumers. Food is the primary source of exposure for the general public, followed by drinking water. Formula-fed infants have the highest background exposure from environmental media, food (formula), and drinking water, when normalized by body weight. Concerns to human health were identified in association with drinking water, air, and products available to consumers.

To characterize risk from drinking water, manganese concentrations in drinking water from provinces and territories and some First Nation communities were compared to the maximum acceptable concentration (MAC) for drinking water (120 µg/L). Exceedances were observed in British Columbia, Saskatchewan, Manitoba, Quebec, New Brunswick, and Newfoundland and Labrador, as well as in some First Nations communities in Manitoba and in the Atlantic region.

To characterize risk from oral and dermal exposures from products available to consumers, exposure estimates were derived for the general population, including susceptible subpopulations, and compared to the lowest observed adverse effect level from neurodevelopmental studies in neonatal rats. Margins of exposure from the use of automotive products, household products, and textiles are considered adequate to address uncertainties in the health effects and exposure data used to characterize risk. Margins of exposure from the use of some children’s paint products, paint products, and

self-care products (that is, cosmetics and natural health products) are considered potentially inadequate to address uncertainties in the health effects and exposure data used to characterize risk.

Hazard quotients (HQs) derived to characterize risk from inhalation exposure via outdoor air (ambient and with transit influence) and airborne manganese concentrations in the vicinity of the electric power generation, transmission, and distribution sector and the pulp, paper, and paperboard mills sector are considered adequate to address the uncertainties in the health effects and exposure data used to characterize risk. The HQs calculated for airborne manganese concentrations in the vicinity of the metal ore mining sector; the iron and steel mills and ferroalloy manufacturing sector; the agricultural, construction, and mining machinery manufacturing sector; the motor vehicle parts manufacturing sector; and the steel product manufacturing from purchased steel sector are considered potentially inadequate to address uncertainties in the health effects and exposure data used to characterize inhalation risk.

HQs calculated for air concentrations generated from the use of spray household products and some self-care products are considered adequate to address the uncertainties in the health effects and exposure data used to characterize inhalation risk. The HQs calculated for air concentrations generated from the use of aerosol spray paint (can), paint applied using an airless sprayer, and some loose face powders are considered potentially inadequate to address uncertainties in the health effects and exposure data used to characterize inhalation risk.

The human health assessment took into consideration those groups of individuals within the Canadian population who, due to greater susceptibility or greater exposure, may be more vulnerable to experiencing adverse health effects. Prenatal and postnatal life stages were identified as the life stage most susceptible to adverse health effects. The potential for elevated exposure among the Canadian population was examined in infants, young children, First Nations communities, and people living in the vicinity of industrial facilities. Young children and formula-fed infants were found to have higher exposure to manganese than adults. Compared to the general population, people living in the vicinity of industrial facilities have a potentially higher exposure to manganese in outdoor air.

Considering all of the information presented in this draft assessment, it is proposed to conclude that manganese and its compounds meet the criteria under paragraph 64(*c*) of CEPA as they are entering or may enter the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore proposed to conclude that manganese and its compounds meet one or more of the criteria set out in section 64 of CEPA.

It is also proposed that manganese and its compounds meet the persistence criteria but not the bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations* of CEPA.

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List of Tables and Figures

1. Introduction

Pursuant to section 68 of the *Canadian Environmental Protection Act, 1999* (CEPA) (Canada 1999), the Minister of the Environment and the Minister of Health have conducted an assessment of manganese and its compounds to determine whether these substances present or may present a risk to the environment or to human health. Eight manganese-containing substances were identified as priorities for assessment as they met categorization criteria or were prioritized through other mechanisms (ECCC, HC [modified 2017]). Three additional substances identified for further consideration following the prioritization of substances on the Revised In Commerce List (R-ICL[1]) were included in this draft assessment (Health Canada [modified 2023]).

This draft assessment focuses on the manganese moiety[2] and therefore considers manganese in its elemental form, manganese compounds, and manganese released in dissolved, solid, or particulate form. It includes all substances that have the potential to dissolve, dissociate, or degrade to release manganese through various transformation pathways and that can potentially contribute to the combined exposure of living organisms to manganese. Consequently, this draft assessment considers all manganese-containing substances and is not limited to the 11 substances identified as priorities for assessment. For simplicity, the manganese moiety is referred to as "manganese" in this draft assessment. Specific manganese compounds will be identified by chemical name or by their Chemical Abstracts Service Registry Number (CAS RN[3]), where relevant.

This draft assessment addresses key pathways and sources of manganese exposure relevant to ecological receptors and human health and therefore considers manganese in environmental compartments (for example, water, sediments, soil, and air), food, or products that may result from natural or anthropogenic sources. Anthropogenic sources include the incidental production of manganese (that is, as a by-product) and the manufacture, import, and use of manganese compounds, products, or manufactured items.

This draft assessment only considers the effects associated with manganese and does not address other elements or moieties that may be present in certain manganese

[1] The R-ICL is an administrative list of substances that were used in products regulated under the *Foods and Drugs Act* and in commerce in Canada between January 1, 1987, and September 13, 2001. The Government of Canada has prioritized these substances and is addressing them for their potential impact on human health and the environment in order to risk-manage them, if required.

[2] For the purpose of this document, "moiety" signifies a part of a molecule. A moiety is a discrete chemical entity, identified from a parent compound or its transformation products, that is expected to have toxicological significance.

[3] The Chemical Abstracts Service Registry Number (CAS RN) is the property of the American Chemical Society, and any use or redistribution, except as required in supporting regulatory requirements and/or for reports to the Government of Canada when the information and the reports are required by law or administrative policy, is not permitted without the prior written permission of the American Chemical Society.

compounds (for example, aluminium or iron). Some of these other elements or moieties have been addressed through previous assessments conducted as part of the Priority Substances List program under CEPA or are being addressed via other initiatives under the Chemicals Management Plan (CMP). Engineered nanomaterials containing manganese (1 to 100 nm) and that may be present in environmental media or in products are not explicitly considered in the exposure scenarios of this draft assessment, but measured concentrations of manganese in the environment could include manganese from these sources. Similarly, this draft assessment does not explicitly consider ecological or health effects associated with nanomaterials containing manganese. The Government of Canada's Proposed Approach to Address Existing Nanomaterials will consider nanoscale forms of substances that are currently on the *Domestic Substances List* (DSL) (Health Canada [modified 2022a]).

Manganese is an essential element for human and organism health. This draft assessment evaluates the potential for harm from elevated manganese exposure rather than deficiency or essentiality.

This draft assessment includes consideration of information on chemical properties, environmental fate, hazards, uses, and exposures, including additional information submitted by stakeholders. Relevant data were identified up to September 2021. Targeted literature searches were conducted up to June 2022. Empirical data from key studies and results from models were used to reach the proposed conclusions. When available and relevant, information presented in assessments from other jurisdictions was also considered.

This draft assessment was prepared by staff in the CEPA Risk Assessment Program at Health Canada and Environment and Climate Change Canada and incorporates input from other programs within these departments. The ecological and human health portions of this draft assessment have undergone external review and/or consultation. Comments on the technical portions relevant to the environment were received from Mr. Geoff Granville (GCGranville Consulting Corp.), Dr. Beverley Hale (University of Guelph), Dr. Gregory Pyle (University of Lethbridge), and Dr. William Stubblefield (Oregon State University). Comments on the technical portions relevant to human health were received from Dr. Lisa Bailey (Gradient), Dr. Sandra Sulsky (Ramboll; Environ International Corporation), and Dr. Nataliya Karyakina (Risk Sciences International Inc.). While external comments were taken into consideration, the final content and outcome of this draft assessment remain the responsibility of Health Canada and Environment and Climate Change Canada.

Assessments focus on information critical to determining whether substances meet the criteria as set out in section 64 of CEPA by considering scientific information, including information (if available) on subpopulations who may have greater susceptibility or

greater exposure, vulnerable environments, and cumulative effects,[4] and by incorporating a weight-of-evidence approach and precaution.[5] This draft assessment presents the critical information and considerations on which the proposed conclusions are based.

2. Identity of substances

Manganese and manganese compounds in commerce or that are incidentally produced belong to various categories, including elemental manganese; inorganic compounds; organic-metal salts; organometallic compounds; and substances of unknown or variable composition, complex reaction products, or biological materials (UVCBs).[6] Manganese compounds may dissolve, dissociate, or degrade to release manganese. The CAS RNs, DSL or R-ICL names, molecular formulas, molecular weights, and physical-chemical properties of the manganese and manganese compounds identified as priorities for assessment are presented in Appendix A.

3. Physical and chemical properties

Manganese is a transition metal belonging to group VII in the periodic table. It does not occur naturally as a base metal in its elemental form but occurs as a constituent in many compounds (UKTAG 2012). The physical and chemical properties of manganese compounds vary. The physical-chemical properties of the 11 manganese and manganese compounds that were prioritized for assessment are summarized in Appendix A. Most manganese salts are readily soluble in water, with the exception of phosphates and carbonates, which have low water solubility, and silicates, hydroxides, and oxides that are poorly soluble in water (Cotton and Wilkinson 1980; IPCS 2004; O'Neil 2006; Rayner-Canham and Overton 2010). The most common oxidation states for manganese are manganous Mn(II), manganic Mn(IV), and the environmentally unstable state of +7 (IPCS 2004). Manganese carboxylates are mainly in the +2 oxidation state, with solubilities varying from slightly soluble to soluble (ECHA c2007-2017a,b,c). Hypomanganate (MnO_4^{3-}), manganate (MnO_4^{2-}), and permanganate (MnO_4^-)

[4] The consideration of cumulative effects under CEPA may involve an analysis, characterization, and possible quantification of the combined risks to health or the environment from exposure to multiple chemicals.

[5] A determination of whether one or more of the criteria of section 64 of CEPA are met is based on an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and products available to consumers. A conclusion under CEPA is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the *Hazardous Products Regulations*, which are part of the regulatory framework for the Workplace Hazardous Materials Information System for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA does not preclude actions being taken under other sections of CEPA or other acts.

[6] These materials are derived from natural sources or complex reactions. A UVCB is not an intentional mixture of discrete substances and is considered a single substance. The complexity and variability of UVCB compositions can make them difficult to fully and consistently characterize.

form soluble salts with other metal cations (Cotton and Wilkinson 1980). Manganous Mn(II) is the most soluble and bioavailable form.

Elemental manganese and inorganic manganese compounds typically have high boiling points and negligible vapour pressures (US EPA 2003).

4. Sources and uses

4.1 Natural sources

Manganese is naturally occurring and abundant in the environment. It is the 12th most common element in the Earth's crust (Webb 2008). Manganese is estimated to comprise between 0.085% and 0.1% of the Earth's crust (NAS 1973 as cited in IPCS 1981; Graedel 1978 as cited in ATSDR 2012; HSDB 1983-), with an average concentration of approximately 950 mg/kg (Matrone 1977). Manganese is found in more than 100 minerals, including oxides, sulfides, carbonates, silicates, phosphates, and borates (NAS 1973 as cited in IPCS 1981). The primary ores of manganese include manganite ($Mn_2O_3H_2O$), hausmannite (Mn_3O_4), pyrolusite (MnO_2), and rhodochrosite ($MnCO_3$). Ferromanganese minerals, including biotite mica ($K(Mg,Fe)_3(AlSi_3O_{10})(OH)_2$) and amphibole ($(Mg,Fe)Si_8O_{22}(OH)_2$), also contain large amounts of manganese (Nagpal 2001). Manganese is also found in coal and crude oil in concentrations ranging from 6 to 100 mg/kg and from 0.001 to 0.15 mg/kg, respectively (Bryan et al. 1970; Ruch et al. 1973). Bog manganese, consisting mainly of hydrated manganese oxides, is also an important ore of manganese (Hanson 1932).

Manganese is released into the environment primarily through weathering. Atmospheric manganese originates from crustal rock, as well as from ocean spray, forest fires, vegetation, and volcanic activity (Stokes et al. 1988). In soil, manganese originates mostly from crustal weathering and from atmospheric deposition, wash-off, leaching from plants, animal excretion, and decomposition of biological material (Stokes et al. 1988). In water, sources of dissolved manganese include weathering of manganese-containing minerals, the reduction of particulate manganese oxides in anaerobic environments, the biotic or abiotic reduction of manganese oxides in aerobic environments, and manganese liberated from soils and sediments in acidic environments (Stokes et al. 1988).

4.2 Anthropogenic sources

4.2.1 Manganese production

Manganese is the fourth most widely used metal in the world behind iron, aluminium, and copper (Webb 2008). Manganese compounds can be produced from naturally occurring ores or from elemental manganese. The main suppliers of manganese, in decreasing order of mining production in 2019 and 2020, are South Africa, Australia, Gabon, Brazil, and China, which collectively supply 80% of the global market (USGS 2021). In 2018, global production of manganese ore was 21 million tonnes, and global

production of elemental manganese was 1.59 million tonnes (IMnI 2018a). In 2018, global production of silico-manganese, high-carbon ferromanganese, and refined ferromanganese was 17 million tonnes, 4.1 million tonnes, and 1.6 million tonnes, respectively (IMnI 2018a). Global demand for manganese is increasing, primarily due to increasing demand for steel production (IMnI 2018a). As efforts to reduce greenhouse gas emissions progress, demand for manganese is expected to increase further due to its potential uses in wind electricity generation, carbon capture, and energy storage technologies (World Bank 2017).

Canada has manganese deposits in the Maritime Provinces and British Columbia, with only a few small bog deposits located in other parts of the country (Hanson 1932; Johnston and McCartney 1965). Canada imports the vast majority of its manganese requirements due to the economic viability of the extraction and processing of ore (Webb 2008). However, small mines have been functional in the past for low- to medium-grade manganese ore, and, in 2021, a drill program was commenced in New Brunswick by a company that aims to become a supplier of high-purity manganese metal products (CMC 2022).

4.2.2 Manufacture and imports

Information on the manufacture and import of manganese and its compounds in Canada was acquired through a survey issued pursuant to section 71 of CEPA, from the Canadian International Merchandise Trade Web Application (CIMTWA), and from voluntary data submissions received from stakeholders. Six of the manganese compounds identified as priorities for assessment were included in a survey issued pursuant to section 71 of CEPA (Canada 2012). Table 4-1 presents a summary of the information reported on the total manufacture and total import quantities for 5 of the substances in 2011 (Environment Canada 2013). No information was received for CAS RN 68551-42-8 for the reporting year 2011.

Table 4-1. Summary of information for the year 2011: Canadian manufacturing and imports of 5 manganese compounds submitted in response to a CEPA section 71 survey

CAS RN	Common or simplified name	Total manufacture[a] (tonnes)	Total imports[a] (tonnes)
7439-96-5	Elemental manganese	Greater than 10,000	1,000 to 10,000
10101-66-3	Manganese violet	0	1 to 10
12108-13-3	MMT	0	1 to 10
18820-29-6	Manganese sulfide	10 to 100	10 to 100
35355-77-2	C.I. Pigment Red 63:2	1 to 10	0

Abbreviations: MMT, Manganese, tricarbonyl[(1,2,3,4,5-<C)-1-methyl-2,4-cyclopentadien-1-yl]-(Methylcyclopentadienyl manganese tricarbonyl).
[a] Values reflect quantities of manganese compounds reported in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (Schedules 2 and 3).

Average annual import quantities from 2013 to 2017 were 46,452 tonnes silico-manganese, 40,696 tonnes refined ferromanganese, 33,726 tonnes high-carbon ferromanganese, 5,026 tonnes electrolytic manganese metal, and 3,652 tonnes electrolytic manganese dioxide (IMnI 2018b). During this time period, the top suppliers of manganese to Canada were Norway, South Africa, Georgia, and the United States (IMnI 2018b).

Import quantities from the CIMTWA were considered to identify quantities of manganese imported into Canada in recent years. Import quantities of 6 manganese-containing harmonized system (HS) 6 codes (listed in Table 4-2) from 2017 to 2021 were considered (CIMTWA [modified 2022]). From 2017 to 2021, Canada imported an average of approximately 14,000 tonnes of manganese-containing commodities per year (Table 4-2) (CIMTWA [modified 2022]).

Table 4-2. Summary of annual manganese-containing commodities imported into Canada from 2017 to 2021 (CIMTWA [modified 2022])

HS code name[a]	HS code	Average quantity imported per year (tonnes)[b]
Manganese ores and concentrates, including ferruginous manganese ores ≥20% manganese	2602.00	480
Manganese dioxide	2820.10	4,200
Manganese oxides, nes	2820.90	2,400
Potassium permanganate	2841.61	400
Manganites, manganates & permanganates of metals, o/t potassium permanganate	2841.69	150
Manganese and articles thereof, including waste and scrap	8111.00	6,100
Total	N/A	14,000

Abbreviations: HS, harmonized system; N/A, not applicable; nes, not elsewhere specified; o/t, other than.
[a] HS code is an international goods classification system developed by the Customs Co-operation Council (now the World Customs Organization) and used by Canada to classify imported and exported goods.
[b] The quantities reported originate from multiple substances that may contain variable amounts of manganese according to their chemical formula.

4.3 Uses

Globally, 90% of all manganese consumed is used as an additive or as a component in alloys (that is, at up to 16%) for steel production (IMnI 2022). As an additive, manganese binds excess oxygen and sulfur, allowing them to be easily removed from products. As a component of steel alloys, manganese increases the strength of steel, rendering it less brittle and more resistant to shock, abrasion, and corrosion (Webb 2008; IMnI 2022).

Manganese is used in alloys with aluminium, copper, and zinc, and in a variety of specific applications with metals such as titanium, gold, silver, and bismuth. Manganese (that is, at up to 1.5%) is used in aluminum production to reduce corrosion in beverage cans, in kitchenware, and in roofing and transportation (IMnI 2022). Manganese is also used as a deoxidizing element (0.1% to 0.3% Mn) in copper alloys and is used in corrosion-resistant products such as pumps, valves, heat exchanger components, and propeller hubs (IMnI 2022).

Manganese dioxide is used as a depolarizer in dry-cell alkaline batteries, as a catalyst in the production of artificial flavours, as an oxidizing agent to treat uranium ore, as a dryer for paints, and as a pigment (IMnI 2022). As an effective oxidizer with bacterial and algicidal properties, potassium permanganate is used to treat both wastewater and drinking water, and to reduce odours in paint and fish factories (IMnI 2022). Manganese sulfate is used in fertilizers and animal feed, and as an intermediate product in the chemical industry (IMnI 2022). Manganese phosphating is used to produce surface films that are sealed with wax or oil to protect steel and improve lubrication for efficient moving parts (IMnI 2022).

In Canada, manganese and its compounds have a wide array of industrial and commercial applications. According to non-confidential use information submitted in response to a CEPA section 71 survey (Environment Canada 2013) and results from voluntary stakeholder engagement (ECCC, HC 2017, the substances surveyed have various commercial and industrial uses including in non-pesticidal agricultural products, cleaning and furnishing care, water treatment, paints and coatings, building or construction materials, metal materials, medical devices, toys, playground and sporting equipment, alloying materials used in steel making, batteries, electronics, deoxidizers, fuels and related products, automotive care, aircraft transportation, and vehicle manufacturing. Other uses identified in response to a CEPA section 71 survey beyond those identified here were notified as confidential business information (CBI).

Table 4-3 presents a summary of the major uses of 5 manganese substances in Canada, according to information submitted in response to a CEPA section 71 survey (Environment Canada 2013).

Table 4-3. Summary of the major Canadian uses of 5 manganese substances submitted in response to a CEPA section 71 survey

CAS RN	Common or simplified name	Use associated with largest quantity[a,b]	Use associated with second largest quantity[a,b]
7439-96-5	Elemental manganese	Process additive (U999)	Fillers (U009) / Deoxidizer and waste (U999)[c]
10101-66-3	Manganese violet	Pigments (U021)	Chemical additive (U999)
12108-13-3	MMT	Fuels and fuel additives (U012)	CBI
18820-29-6	Manganese sulfide	CBI	By-product (U999)
35355-77-2	C.I. Pigment Red 63:2	CBI	N/A

Abbreviations: CBI, confidential business information; N/A, not applicable.
[a] Highest uses by quantity were reported in response to the survey conducted under section 71 of CEPA (Environment Canada 2013). See survey for specific inclusions and exclusions (Schedules 2 and 3).
[b] Substance function codes are in brackets.
[c] Multiple substance function codes were reported for a single quantity.

According to non-confidential use information submitted in response to a CEPA section 71 survey (Environment Canada 2013) and results from voluntary stakeholder engagement (ECCC, HC 2017), publicly available websites (for example, CPCat2021; CPID [modified 2021]), and safety data sheets, consumer uses of manganese and manufactured articles available to consumers include adhesives and sealants; non-pesticidal agricultural products; automotive, aircraft and transportation uses (for example, fuel additives); batteries; building and construction materials; cleaning and furnishing care (for example, cleaning products and odour control products); electronics; lubricants and greases; metal materials; paints and coatings; self-care products (that is, cosmetics, natural health products and non-prescription drugs); textiles; children's toys; playground and sporting equipment; and water treatment. Additional consumer uses of manganese in Canada are presented in Table 4-4.

Table 4-4. Additional uses in Canada for manganese and its compounds

Use	Manganese
Food additive[a]	Y
Food packaging materials[b]	Y
Mineral nutrient added to foods[c]	Y
Ingredient in registered plant fertilizer or supplement[d]	Y
Medicinal or non-medicinal ingredients in disinfectant, human, or veterinary drug products[e]	Y
Medicinal or non-medicinal ingredients in natural health products[f]	Y
Notified to be present in cosmetics under the *Cosmetic Regulations*[g]	Y
Active ingredient and formulant in registered pest control products[h]	Y

Abbreviations: Y, use was reported for these substances.
[a] Manganese sulfate is permitted as a pH adjusting agent in bacterial cultures and as a yeast food in ale, beer, light beer, malt liquor, porter, and stout according to good manufacturing practice. Potassium permanganate is permitted to be used to modify starch, as long as the resulting modified starches contain no more than 50 ppm manganese (Health Canada [modified 2013], [modified 2016b], [modified 2022b]).
[b] Personal communication, email from the Food and Nutrition Directorate (FND), Health Canada, to the Existing Substances Risk Assessment Bureau (ESRAB), Health Canada, dated August 9, 2021; unreferenced.
[c] Manganese is permitted as a mineral nutrient added to foods for special dietary use (for example, meal replacements and in formulated liquid diets) and as an ingredient in infant formulas and human milk fortifiers (Canada 1978).
[d] Canadian Food Inspection Agency (CFIA) [modified 2023].
[e] DPD [modified 2022]; personal communication, email from the Pharmaceutical Drugs Directorate (PDD), Health Canada, to the ESRAB, Health Canada, dated August 3, 2021; unreferenced.
[f] NHPID [modified 2021]; LNHPD [modified 2021]; personal communication, email from the Natural and Non-prescription Health Products Directorate (NNHPD), Health Canada, to the ESRAB, Health Canada, dated July 5, 2021; unreferenced.
[g] Personal communication, email from the Consumer and Hazardous Products Safety Directorate (CHPSD), Health Canada, to the ESRAB, Health Canada, dated March 12, 2021; unreferenced.
[h] Personal communication, email from the Pest Management Regulatory Agency (PMRA), Health Canada, to the ESRAB, Health Canada, dated July 5, 2016; unreferenced; Health Canada 2010a, [modified 2016b], 2020c.

5. Releases to the environment

Reporting to the National Pollutant Release Inventory (NPRI) is mandatory for manganese and its compounds (ECCC 2022). From 2015 to 2019, the average annual total quantity of manganese released to the environment from all industrial sectors was 1,306 tonnes (ranging from 1,203 to 1,451 tonnes per year) (Table 5-1; NPRI 2022). Manganese is released primarily to water, representing 82% of total manganese released to the environment. Releases of manganese to land, air, and unspecified media (where releases are less than 1 tonne per facility) represent 10.4%, 6.7%, and 0.9% of total quantities, respectively.

Table 5-1. Annual quantities (in tonnes) of manganese and its compounds released to air, land, and water from 2015 to 2019

Year[a]	Air	Land	Water	Unspecified media[b]	Annual total
2015	85	200	1,156	10	1,451
2016	82	112	994	14	1,203
2017	89	114	1,054	14	1,271
2018	83	114	1,065	12	1,274
2019	98	137	1,082	12	1,330
Mean ± standard deviation	87 ± 6	135 ± 34	1,070 ± 52	12 ± 1	1,306 ± 83

[a] Data used for this table are current as of March 30, 2022 (NPRI 2022). Facilities may periodically update their information reported to the NPRI. As such, repeated analysis with data extracted at different times may produce different results. There is a degree of complexity surrounding NPRI data reporting, such as meeting reporting thresholds and the use of various acceptable methods and data sources. Therefore, uncertainties exist in the reported quantities (see ECCC 2022 for further information).
[b] Releases can be reported as a total release to all media for Part 1A substances where releases (by the reporting facility) are less than 1 tonne (ECCC 2022).

A variety of industrial sectors reported releases of manganese to the NPRI.

The sectors with the highest average annual releases of manganese to all media (mean ± standard deviation from 2015 to 2019) were 1) pulp, paper, and paperboard mills (932 ± 44 tonnes); 2) metal ore mining (210 ± 56 tonnes); 3) water, sewage, and other systems (64 ± 3 tonnes); and 4) iron and steel mills and ferroalloy manufacturing (39 ± 5 tonnes). The first 3 sectors also represent the sectors with the highest average annual releases of manganese to water: 1) pulp, paper, and paperboard mills (895 ± 42 tonnes); 2) metal ore mining (91 ± 30 tonnes); and 3) water, sewage, and other systems (64 ± 3 tonnes). The iron and steel mills and ferroalloy manufacturing sector reported an average of 3 ± 0.6 tonnes annual releases of manganese to water. Average annual releases of manganese to water greater than 1 tonne were also reported to the NPRI by the following sectors: basic chemical manufacturing (10 ± 4 tonnes), foundries (3 ± 2 tonnes), non-ferrous metal (except aluminum) production and processing (2 ± 2 tonnes), and oil and gas extraction (2 ± 0.6 tonnes) (Table B-1, Appendix B) (NPRI 2022).

Sectors reporting the highest average annual releases of manganese to air were: 1) iron and steel mills and ferroalloy manufacturing (35 ± 6 tonnes); 2) metal ore mining (22 ± 6 tonnes); 3) pulp, paper, and paperboard mills (10 ± 0.7 tonnes); 4) coating, engraving, cold and heat treating and allied activities (1 single reported quantity of 10 tonnes in 2019); 5) electric power generation, transmission, and distribution (6 ± 0.2 tonnes); and 6) motor vehicle parts manufacturing (3 ± 0.5 tonnes). Other industrial sectors that reported greater than 1 tonne of manganese releases to air per year were foundries (2 ± 2 tonnes); agricultural, construction and mining machinery manufacturing (0.8 ± 2 tonnes); and steel product manufacturing from purchased steel (1 ± 0.7 tonnes) (NPRI 2022).

Sectors reporting the highest average annual releases of manganese to land were metal ore mining (95 ± 29 tonnes) and pulp, paper, and paperboard mills (26 ± 4 tonnes). Other industrial sectors that reported greater than 1 tonne of manganese releases to land per year were 1) electric power generation, transmission, and distribution (9 ± 3 tonnes); 2) cement and concrete product manufacturing (5 ± 0.4 tonnes); and 3) architectural and structural metals manufacturing (1 single reported quantity of 8 tonnes in 2015).

In addition to releases to air, land, and water, significant quantities of manganese are disposed both on site and off site at various facilities (Table B-2, Appendix B). From 2015 to 2019, the average annual disposal of manganese (mean ± standard deviation) was 342,705 ± 85,444 tonnes. Disposal of manganese was primarily to tailings management, which represented 88% of total manganese disposed (Table B-2, Appendix B). The sectors with the highest average annual disposal quantities for manganese were 1) metal ore mining (348,210 ± 23,453 tonnes); 2) oil and gas extraction (21,323 ± 3,950 tonnes); 3) non-metallic mineral mining and quarrying (5,244 ± 1,259 tonnes); and 4) iron and steel mills and ferroalloy manufacturing (4,986 ± 1,241 tonnes). In addition to these sectors, a number of other sectors dispose more than 100 tonnes of manganese per year, including 1) pulp, paper, and paperboard mills; 2)

electric power generation, transmission, and distribution; 3) coal mining; 4) waste treatment and disposal; 5) basic chemical manufacturing; 6) other non-metallic mineral product manufacturing; 7) other miscellaneous manufacturing; 8) water, sewage, and other systems; 9) remediation and other waste management services; and 10) veneer, plywood, and engineered wood product manufacturing.

6. Environmental fate and behaviour

6.1 Environmental distribution

Manganese and its compounds are found in air, rock, soil, water, sediments, and biota. Manganese occurs naturally in the environment and in a variety of concentrations depending on the location and underlying geology. Both natural and anthropogenic sources of manganese can be released from a given environmental compartment and transported to other environmental media.

6.1.1 Air

In general, manganese substances have negligible vapour pressure (Appendix A). Manganese is present in air as suspended particulate matter (PM) (US EPA 1984) and can be distributed over considerable distances in the atmosphere (IPCS 1981). Manganese emitted to the atmosphere via both natural and anthropogenic sources is associated with particles of various sizes, with the median fine fraction (concentration ratio of $PM_{2.5}/PM_{10}$) ranging from approximately 0.25 to 0.61 (Al Mamun et al. 2020). The fate and transport of manganese-containing PM is determined by particle size and density, as well as by wind speed and direction (IPCS 2004). Suspended PM containing manganese is removed from the atmosphere by gravitation settling or rainfall (US EPA 1984).

6.1.2 Soil

Manganese partitions between the solid and solution phase in soil, with the fraction in the solution phase being more bioavailable. The solubility of manganese and its compounds in soil is inversely proportional to both pH and redox potential (IPCS 2004). The bioavailability of manganese tends to be higher in flooded soils and other acidic and reducing environments (Stokes et al. 1988). Manganese ions tend to adsorb to organic matter in soil, rendering them less bioavailable (Stokes et al. 1988). In addition to the influence of pH, redox potential, and organic matter on the bioavailability of manganese, the chemistry and biochemistry of manganese in soils are complex due to factors such as multiple/mixed oxidation states and chemical and microbial mediated oxidation and reduction processes (Ståhlberg and Sombatpanit 1974). Manganese in soil can migrate to air and water as PM and can leach from soil in soluble forms (IPCS 2004).

6.1.3 Fresh water and sediments

Manganese decomposes to form MnO and H_2 gas in water (Zhou et al. 2001; ICSC 2003). In the aquatic environment, manganese primarily exists in manganous Mn(II) and manganic Mn(IV) forms, but it can also exist as complex ions and insoluble salts. The thermodynamically stable form of manganese is Mn(IV), which exists as insoluble manganese oxide, while the most ecotoxicologically relevant form is Mn(II) because of its bioavailability (IMnI 2012). The transition between Mn(II) and Mn(IV) occurs through abiotic and biotic oxidation and reduction reactions (Stokes et al. 1988; Heal 2001). The environmental chemistry of manganese is determined primarily by pH and redox conditions, with Mn(II) dominating at low pH and redox potential and Mn(IV) dominating at high pH and redox potential in the form of manganese oxides (Freitas et al. 2013). Mn(II) is stable in anoxic waters, whereas Mn(IV) is thermodynamically stable in well-oxygenated waters where manganese is precipitated out of solution as insoluble oxides or carbonates (Davison 1993). In acidic (pH 4 to 6) and neutral waters (pH 6 to 8), Mn(II) oxidizes slowly, especially in anoxic conditions, whereas oxidation occurs more readily in alkaline conditions (pH >8) (Davison 1993; ATSDR 2012).

In rivers, adsorbed manganese is often transported as suspended sediments (IPCS 2004) originating from weathering processes (Davison 1993). In other freshwater systems, the transport of particulate manganese can be both a source of and a sink for manganese as suspended sediments enter and exit a system. Soluble forms of manganese can also enter freshwater systems from oxygen-deficient (anoxic) soils and groundwater (Davison 1993).

In oxygen-rich (oxic or aerobic) aquatic environments, manganic forms are thermodynamically stable, whereas soluble Mn(II) may exist as soluble inorganic complexes or as insoluble carbonates and oxides (Hedgecott et al. 1998; IPCS 2004; UKTAG 2012). Mn(II) may also oxidize to insoluble manganese oxides and manganese oxyhydroxides, transferring manganese from the water column to the sediment (Davison 1993; Belzile and Morris 1995; Graham et al. 2012). The precipitated manganese oxyhydroxides readily absorb or form complexes with many dissolved metal ions, scavenging those trace metals from the water column (Belzile and Morris 1995). Mn(II) occurs more readily in alkaline conditions (pH >8) and more slowly in acidic (pH 4 to 6) and neutral waters (pH 6 to 8), with a range of metastable oxidation products (Davison 1993; Zaw and Chiswell 1999; ATSDR 2012). Therefore, Mn(II) predominates in natural waters at a pH of 4 to 7 (US EPA 1984). Manganese solubility in water can be increased by the presence of chlorides, nitrates, and sulfates, thus increasing its mobility in the water column (Reimer 1999).

In oxygen-poor (anoxic or anaerobic) and stratified waters, the sediment-water interface plays a critical role in the cycling of manganese between sediment and water. Mn(II) is stable in anoxic waters, while Mn(IV) compounds such as manganese oxides are readily reduced to form Mn(II) and remobilize from the sediment to the water column (Davison 1993). Consequently, Mn(II) can accumulate in high concentrations in anoxic waters and in sediment pore-waters (mg/L range) (Davison 1993). The reduction of

Mn(IV) may occur chemically through reactions with inorganic and organic reductants or biologically through microorganisms (Davison 1993).

6.2 Environmental persistence

Manganese is considered persistent because it cannot degrade through any processes (for example, photodegradation, biodegradation), although it can transform into different chemical species and/or partition among different environmental compartments. Degradation processes may be applicable to organic metal salts and organometallics; however, the manganese moiety in these substances is considered persistent. The persistence of parent organic metal salts and organometallics and their possible organic counter-ions or organic transformation products was not evaluated individually in this draft assessment.

6.3 Potential for bioaccumulation

Manganese is a nutritionally essential element (see sections 7.1.1 and 8.1.1 of this report) that is actively assimilated and utilized by both plants and animals (IPCS 2004). The bioaccumulation potential for manganese is affected by its bioavailability, which in turn is dependent on speciation and controlled by pH and redox potential (UKTAG 2012). Mn(II) is more soluble and therefore more bioavailable than Mn(IV) (IPCS 2004). Manganese solubility in water can be increased by the presence of chlorides, nitrates, and sulfates (Heal 2001; IPCS 2004). Manganese oxides and carbonates are generally insoluble and therefore less bioavailable (IPCS 2004). Furthermore, manganese may reversibly bind to inorganic anions or organic compounds. The overall bioavailability and toxicity of manganese in the environment is dependent largely on environmental characteristics, such as pH and water hardness. Toxicity modifying factors (TMFs) for manganese are discussed briefly in section 7.1.3 and in detail by the Canadian Council of Ministers of the Environment (CCME 2019).

Although manganese is homeostatically regulated, it can be significantly bioconcentrated by aquatic biota at lower trophic levels (IPCS 2004). Bioconcentration factors (BCFs) range from 2,000 to 20,000 for marine and freshwater plants, from 2,500 to 6,300 for phytoplankton, from 300 to 5,500 for marine macroalgae, from 800 to 830 for intertidal mussels, and from 35 to 930 for fish (reviewed in IPCS 2004). However, the BCF approach is of limited usefulness in predicting metal bioaccumulation, especially for essential elements because of its inability to distinguish between nutritional accumulation, accumulation from background levels, homeostatic control of concentrations, and internal sequestering, detoxification, and storage (McGeer et al. 2003). For metals, BCFs tend to be inversely related to exposure concentration: the uptake by aquatic organisms tends to be greater when the concentration in the surrounding water is low (and vice versa) (McGeer et al. 2003).

There is little evidence to suggest that manganese biomagnifies in food chains. Weak biomagnification was observed after the freshwater fish *Hyphessobrycon serpae* was fed tubificid worms with elevated manganese body burdens (Patrick and Loutit 1978).

However, biodilution, a decrease in concentration with increasing trophic level, appears to be more common. For example, manganese body burdens were found to be lower in higher food chain predatory fish such as pickerel compared to lower food chain opportunistic fish such as bluegill (Wiener and Giesy 1979). Manganese accumulation also decreased along a theoretical, simplified food chain consisting of the green alga *Protococcoidal chlorella*, the invertebrate *Daphnia magna*, and the freshwater fish *Pimephales promelas* (Kwasnik et al. 1978). A more recent study modelling a simplified freshwater food chain under laboratory conditions found that, while manganese accumulated significantly in zooplankton (*Daphnia pulex*) and was effectively retained in the digestive tract of zebrafish (*Danio rerio*), no biomagnification was observed (Herman et al. 2021). Overall, current evidence (for example, reviewed in IPCS 2004) suggests that, while lower trophic level species may significantly bioconcentrate manganese, higher trophic level species are able to at least partially maintain homeostasis; therefore, manganese is not expected to biomagnify along food chains.

7. Potential to cause ecological harm

7.1 Ecological effects assessment

7.1.1 Essentiality and deficiency

Manganese is an essential element for biological functioning in all organisms. It is a constituent of various enzymes and functions as an activator of enzyme systems in animals (Martin 1974 as cited in Steenkamp et al. 1994). Nutritional manganese requirements vary among species, and adverse effects may be observed at concentrations higher than those requirements (IPCS 2004). The essentiality of manganese and its toxic mode of action have been discussed by the CCME (2019) and are summarized here and in sections 7.1.2 and 8.1.1.

Manganese deficiency has been characterized in plants and fish. For example, the aquatic plant *Lemna major* developed chlorosis and produced smaller fronds when grown in a manganese-deficient environment, which eventually led to a failure to reproduce, necrosis, and mortality (McHargue and Calfee 1932). Conversely, chlorotic plants grown in a manganese-deficient solution were successfully restored to a healthy, dark green state when traces of manganese sulfate were added, providing evidence for the essentiality of manganese (McHargue and Calfee 1932). Manganese deficiency in animals can also cause reduced or deformed growth, skeletal deformities, defective eggshell formation, low manganese-superoxide dismutase (Mn-SOD), impaired glucose tolerance, or increased mortality (Leach 1974 as cited in Knox et al. 1981). Depressed growth, attributed to manganese deficiency, has been observed in a variety of fish species including rainbow trout, yellow catfish, common carp, grass carp, and gibel carp (Tan et al. 2012).

Although manganese is an essential nutrient for organism health, this ecological assessment focuses on the adverse effects associated with excess manganese concentrations in the environment.

7.1.2 Mode/mechanism of action

Manganese can be detrimental to organisms when present at concentrations in excess of an optimal range defined by its essentiality. In fish, the manganous free ion (Mn^{2+}) is mainly taken up via the gills; however, the olfactory nerve cells may be another route of uptake for manganese (Rouleau et al. 1995). Manganese is transported via fish blood and can cross biological membranes/tissue barriers into the kidney, brain, and liver (Rouleau et al. 1995). A potential mechanism of manganese toxicity in fish is the formation of reactive oxygen species (ROS), which induces oxidative stress, damage to tissues, inflammation, and neurodegeneration (Valavanidis et al. 2006; Vieira et al. 2012). The increase in ROS also disrupts the enzymatic and non-enzymatic antioxidant defence system. For example, decreased activities of the antioxidant enzyme catalase were observed in the brains of the freshwater fishes *Colossoma macropomum* (Gabriel et al. 2013) and *Rhamdia quelen* (Dolci et al. 2013); the same was observed for brain superoxide dismutase (SOD) in *Colossoma macropomum* (Gabriel et al. 2013) and *Carassius auratus* (Vieira et al. 2012). In addition, lipid peroxidation, a biomarker for oxidative cell damage, was increased in these fish species. Antioxidant activity and lipid peroxidation vary throughout the body of fish, suggesting that manganese-induced oxidative effects may be organ- and tissue-specific (Vieira et al. 2012). In some algal species, excess manganese may induce iron deficiency, which can lead to the inhibition of chlorophyll synthesis. Conversely, manganese may also mitigate the toxicity of other metals to algae (IPCS 2004).

It has been demonstrated that excess manganese may cause a Ca^{2+} pump dysfunction, thereby affecting neuro-muscular transmission in benthic marine invertebrates (Hagiwara and Takahashi 1967; Baden and Neil 1998; Holmes et al. 1999).

7.1.3 Toxicity modifying factors

The toxicity of many metals can be modified by various environmental characteristics, such as pH and water hardness (CCME 2007). Where sufficient data were available, the relationships between manganese toxicity and freshwater chemistry variables were examined in the development of the Canadian Water Quality Guidelines (CWQGs; CCME 2019) and incorporated into estimates of predicted no-effect concentrations (PNECs) in this draft assessment. A positive relationship was observed between pH and long-term manganese toxicity for algae (CCME 2019). At low pH, H^+ ions compete with free manganese ions, thus reducing manganese toxicity to algae (Peters et al. 2011). However, no effects of pH on manganese toxicity were observed in studies with fish or invertebrates (Peters et al. 2011; CCME 2019).

An inverse relationship was observed between long-term manganese toxicity and water hardness for invertebrates and fish but not for aquatic plants and algae (CCME 2019). Several other studies have also shown that hardness is an important TMF for invertebrates and fish (Stubblefield et al. 1997; Reimer 1999; Peters et al. 2011; Parametrix 2010b, 2010d as cited in CCME 2019; Davies et al. 1998 as cited in CCME 2019), likely as a result of Ca^{2+} and Mg^{2+} cations competing with free manganese ions

for binding sites on the biotic ligand (Lasier et al. 2000). Unlike some metals, there was no significant relationship between dissolved organic carbon concentrations and manganese toxicity.

In the development of CWQGs, empirical relationships were derived to normalize long-term toxicity data to water hardness (for fish and invertebrates) and pH (for aquatic plants and algae) (CCME 2019). The resulting equations were used to normalize effect concentrations for the long-term species sensitivity distribution (SSD) data set to multiple (n=132) combinations of pH and water hardness ranging from 5.8 to 8.4 pH and from 25 to 670 mg/L as $CaCO_3$, respectively (CCME 2019). As a result, long-term site-specific CWQGs can be derived on the basis of site-specific pH and water hardness levels (CCME 2019).

In this ecological effects assessment, the TMFs (that is, pH and water hardness) were used to calculate site-specific PNECs for manganese. Where measured values of pH and water hardness were unavailable, representative data were derived for Canadian ecozones and Great Lakes (Table C-1, Appendix C). Central tendencies of the TMFs were based on data identified as being in reference condition, as defined by the approach given in Kilgour & Associates Ltd. (2018) and Proulx et al. (2018). The data sets were obtained from a variety of federal and provincial surface water quality monitoring programs and data repositories covering the period of 2005 to 2015.[7] The use of geometric means for total hardness was preferred, since this parameter typically follows a log-normal distribution in the environment, whereas averages were used for pH. Central tendencies of the TMFs were also developed for the Great Lakes using data collected between 2005 and 2015.[8] Geometric means for water hardness were calculated using dissolved measurements of calcium and magnesium (US EPA 2015) as direct measurements were unavailable.[9] Where measured TMF data were unavailable for the effluent receiving environment, the central tendencies for the TMFs were used as a substitute.

7.1.4 Effects on freshwater aquatic organisms

Several empirical studies have assessed the chronic toxicity of manganese and its compounds to aquatic organisms such as algae, aquatic plants, invertebrates, and fish.

[7] BQMA 2015; FQMS 2016; NLTWQM 2016; PWQMN [modified 2018]; RAMP 2016; personal communication, data prepared by the Water Stewardship Division, Province of Manitoba, for the Ecological Assessment Division, Environment and Climate Change Canada (ECCC), dated February 24, 2016; unreferenced; personal communication, data prepared by the Environmental and Municipal Management Services, Saskatchewan Water Security Agency, for the Ecological Assessment Division, ECCC, dated February 25, 2016; unreferenced.

[8] Personal communication, data provided by the Water Quality Monitoring and Surveillance Division, ECCC for the Ecological Assessment Division, ECCC, dated June 20, 2017; unreferenced.

[9] Personal communication, data provided by the Water Quality Monitoring and Surveillance Division, ECCC for the Ecological Assessment Division, ECCC, dated July 27, 2017; unreferenced.

CWQGs for the protection of aquatic life for manganese (CCME 2019) were derived following the CCME protocol and using a statistical approach (CCME 2007). In this ecological effects assessment, long-term CWQGs were selected as freshwater PNECs for manganese and its compounds because they are based on recent scientific studies, they integrate TMFs, and they use chronic toxicity data that are an indicator of the potential for harm from long-term exposure to manganese.

The long-term CWQGs are based on chronic toxicity data for 14 species, including 2 algae (*Raphidocelis subcapitata* and *Scenedesmus quadricauda*), 1 aquatic plant (*Lemna minor*), 6 invertebrates (*Aeolosoma* sp., *Ceriodaphnia dubia*, *Chironomus tentans*, *Daphnia magna*, *Hyalella azteca*, and *Lymnaea stagnalis*) and 5 fish (*Danio rerio*, *Pimephales promelas*, *Oncorhynchus mykiss*, *Salmo trutta*, and *Salvelinus fontinalis*).

In total, 1,160 long-term freshwater toxicity data points from 13 different studies were deemed acceptable for use in the derivation of guidelines (CCME 2019). Where multiple comparable endpoints were available for the same species, effect, life stage, and exposure duration, a geometric mean was calculated. Where there was more than one long-term endpoint type for a given species and effect, the preferred endpoint was selected, as outlined in CCME (2007). The most sensitive endpoint (or geometric mean) was selected if more than one measurement was available for a given species where effect, test duration, and/or species life stage differed (CCME 2019).

Endpoints for the 14 species were used to create long-term SSDs (CCME 2019). Multiple individual SSDs (n=132) were created to incorporate the relative sensitivities of species to different combinations of pH and water hardness values (pH ranging from 5.8 to 8.4, and water hardness ranging from 25 to 670 mg/L as $CaCO_3$). For each SSD, maximum likelihood estimation was used to fit several cumulative distribution functions to the toxicity data, and model averaging was used to calculate 5% hazard concentrations (HC5) for dissolved manganese. Long-term CWQGs, and the PNECs used in this ecological effects assessment, are represented by HC5 values calculated for a given combination of pH and water hardness. For example, the HC5 is 430 µg/L dissolved manganese in fresh water normalized to a water hardness of 50 mg/L as $CaCO_3$ (for invertebrates and fish) and to pH 7.5 (for plants and algae) (CCME 2019) (Figure 7-1).

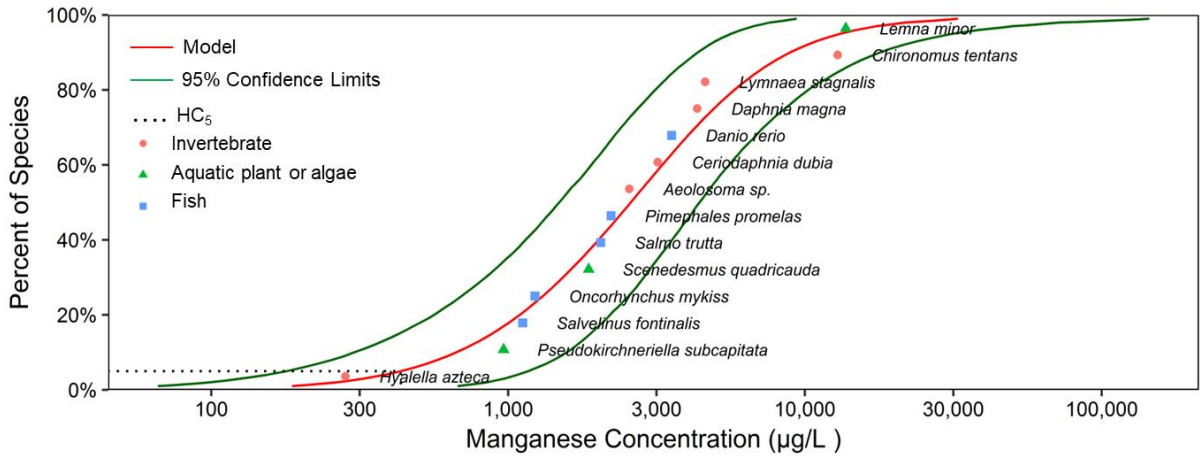

Figure 7-1. Long-term model averaged species sensitivity distribution (SSD) for dissolved manganese in fresh water, normalized to a water hardness of 50 mg/L as $CaCO_3$ (for invertebrates and fish) and to pH 7.5 (for plants and algae).

[Figure 7-1 illustrates the species sensitivity distribution (SSD) of chronic toxicity data for dissolved manganese concentrations in fresh water normalized to a water hardness of 50 mg/L as $CaCO_3$ for fish and aquatic invertebrates and to pH 7.5 for aquatic plants and algae. A model averaged distribution is shown on the graph and fit to 14 chronic datapoints for aquatic organisms. The 5th percentile of the distribution (HC5) was calculated at 430 µg/L dissolved manganese.]

Long-term CWQGs for dissolved manganese can be found manually by using a look-up table or an Excel-based calculator (CCME 2019). The CWQG table or calculator is valid between a hardness of 25 and 670 mg/L as $CaCO_3$ and a pH of 5.8 to 8.4, which are the ranges of data used to derive the water hardness and pH slopes. While extrapolation should be used with caution, the calculator can extrapolate CWQGs down to hardness concentrations of 10 mg/L as $CaCO_3$, as well as to pH values of down to 5.5 and up to 9 (CCME 2019).

Species sensitivity varies considerably across the range of water chemistry conditions. The long-term CWQG ranges from 200 to 1,500 µg/L dissolved manganese across the range of water hardness (25 to 670 mg/L as $CaCO_3$) and pH (5.8 to 8.4). For example, at a water hardness of 50 mg/L as $CaCO_3$ and a pH of 7.5, the long-term CWQG is 430 µg/L dissolved manganese. At a water hardness of 50 mg/L as $CaCO_3$ and a pH of 7.5, the most sensitive species is the invertebrate *Hyalella azteca* and the least sensitive species is the floating aquatic plant *Lemna minor*, with pH and hardness-normalized low effect concentrations of 283 µg/L and 13,725 µg/L dissolved manganese, respectively.

7.1.5 Effects on marine organisms

There is limited information regarding the ecotoxicological effects of manganese on marine organisms; in particular, effects on marine fish species are lacking (Table 7-1). The acute toxicities of manganese to marine invertebrates and a marine diatom were within the same range. Lethal or effect concentrations for 50% of test individuals ranged from 16,000 to 70,000 µg Mn/L for marine invertebrates and a marine diatom (Table 7-1). Yellow rock crab (*Cancer anthonyi*) at the embryo/larval life stage was the marine species that was most sensitive to manganese exposure; embryo hatching and mortality to hatched embryos were 38.3% and 26.9%, respectively, at the lowest test concentration of 10 µg Mn/L after a 7-day exposure (MacDonald et al. 1988).

Table 7-1. Key marine water toxicity values for manganese

Species group	Test organism	Endpoint	Value (µg Mn/L)	Reference
Invertebrates	Brine shrimp (*Artemia* sp.)	2-day LC_{50}	51,800	Gajbhiye and Hirota 1990
Invertebrates	Starfish (*Asterias rubens*)	7-day NOEC/LOEC	25,000 /50,000	Hansen and Bjerregaard 1995
Invertebrates	American or Virginia oyster (*Crassostrea virginica*)	2-day LC_{50}	16,000	Calabrese et al. 1973
Invertebrates	Blue mussel (*Mytilus edulis*)	2-day EC_{50} development	30,000	Morgan et al. 1986
Invertebrates	Harpacticoid copepod (*Nitocra spinipes*)	4-day LC_{50}	70,000	Bengtsson 1978
Invertebrates	Sea urchin (*Paracentrotus lividus*)	2-day EC_{50} development	8,850	Pinsino et al. 2010
Invertebrates	Yellow rock crab (*Cancer anthonyi*)	7-day LOEC (hatching/mortality to hatched embryos)	10	MacDonald et al. 1988
Algae	Diatom (*Phaeodactylum tricornutum*)	4-day EC_{50} growth	25,700	Rosko and Rachlin 1975

Abbreviations: EC_{50}, effect concentration affecting 50% of the test organisms; LC_{50}, lethal concentration for 50% of the test organisms; LOEC, lowest observed effect concentration; NOEC, no-observed-effect concentration.

Hook and Fisher (2002) conducted a manganese sublethal toxicity study on marine copepods (*Acartia tonsa* and *Acartia hudsonica*) following 4-hour feedings of manganese-contaminated phytoplankton food. It was found that a manganese concentration of 13,440 nmol/g (dry weight [dw]) in copepods tissue led to a 50%

depression in egg production. This value was considered to be the threshold effective body concentration for marine copepods (Hook and Fisher 2002). The remarkably lower effect concentration observed for yellow rock crab compared to other marine species suggests the need for a deeper understanding of manganese toxicity to marine environments; therefore, a marine PNEC for manganese was not derived in this draft assessment.

7.1.6 Effects on soil-dwelling organisms

Data on the chronic toxicity of manganese to soil organisms were compiled and evaluated. The data set is adequate for a long-term SSD approach, as specified in the CCME protocol on deriving a soil quality guideline for soil contact (that is, for the protection of terrestrial plants and invertebrates) (CCME 2006). Toxicity endpoints that are considered reliable are summarized in Table 7-2. Manganese increases crop yield or growth at low concentrations (Fageria 2001). At higher concentrations of manganese, decreases in grain yield and growth were observed for 7 species of plants (Table 7-2) at concentrations ranging from 44 to 971 mg Mn/kg (Fageria 2001). Soil invertebrates were more tolerant of long-term exposure to manganese than plants with reported effects on survival at 332 to 2,444 mg Mn/kg (Kuperman et al. 2002, 2004; Phillips et al. 2002; Simini et al. 2002). The reproduction of soil invertebrates was more sensitive to manganese compared to survival, with effects observed at concentrations ranging from 116 to 1,209 mg Mn/kg (Kuperman et al. 2002, 2004; Phillips et al. 2002; Simini et al. 2002; Son et al. 2017).

Table 7-2. Key soil toxicity values for manganese

Species group	Test organism	Endpoint	Value (mg Mn/kg dw)	Reference
Invertebrates	Redworm (*Eisenia fetida*)	14-day EC_{20} survival	1,718	Simini et al. 2002; Kuperman et al. 2004
Invertebrates	Redworm (*Eisenia fetida*)	28-day EC_{20} reproduction	629[a]	Simini et al. 2002; Kuperman et al. 2004
Invertebrates	Potworm (*Enchytraeus crypticus*)	42-day EC_{20} survival	332	Kuperman et al. 2002, 2004
Invertebrates	Potworm (*Enchytraeus crypticus*)	28-day EC_{20} reproduction	116[a]	Kuperman et al. 2002, 2004
Invertebrates	Compost springtail (*Folsomia candida*)	28-day NOEC/LOEC survival	1,667 /2,444	Phillips et al. 2002; Kuperman et al. 2004
Invertebrates	Compost springtail (*Folsomia candida*)	28-day EC_{20} reproduction	1,209[a]	Phillips et al. 2002; Kuperman et al. 2004

Species group	Test organism	Endpoint	Value (mg Mn/kg dw)	Reference
Invertebrates	Springtail (*Paronychiurus kimi*)	28-day EC_{50} reproduction	326[a]	Son et al. 2017
Plants	Corn (*Zea mays* L.)	28-day EC_{10} dry weight	400[a]	Fageria 2001
Plants	Rice (*Oryza sativa* L.)	28-day EC_{10} grain yield (mature)	560[a]	Fageria 2001
Plants	Soybean (*Glycine max* L. Merr.)	28-day EC_{10} dry weight	92[a]	Fageria 2001
Plants	Wheat (*Triticum aestivum* L.)	28-day EC_{10} grain yield (mature)	44[a]	Fageria 2001
Plants	Common bean (*Phaseolus vulgaris* L.)	28-day EC_{10} dry weight	128[a]	Fageria 2001
Plants	Barley (*Hordeum vulgare*)	5-day EC_{10} root length	820	ECHA 2022
Plants	Barley (*Hordeum vulgare*)	23-day EC_{10} dry weight	971[a]	ECHA 2022
Plants	Lettuce (*Lactuca sativa*)	23-day EC_{10} dry weight	494[a]	ECHA 2022

Abbreviations: $EC_{10/20/50}$, effect concentration affecting 10%, 20%, or 50% of the test organisms; NOEC, no-observed-effect concentration; LOEC, lowest-observed-effect concentration.
[a] Values selected in the SSD.

The data set (11 soil-dwelling species, including 4 invertebrates and 7 plants) was used for a long-term SSD using the ssdtools package (Dalgarno 2018; Thorley and Schwarz 2018) (Figure 7-2). When more than one endpoint was available for an individual species, the most sensitive data point was selected (Table 7-2). The model averaged (using the Akaike information criterion correction [AICc]) estimate of the fit to data) was applied, and the HC5 (5^{th} percentile, representing the concentration that is hazardous to 5% of soil-dwelling organisms) of the distribution was 49 mg Mn/kg dw (Figure 7-2; Table 7-3); this value was selected as the PNEC for long-term manganese soil toxicity.

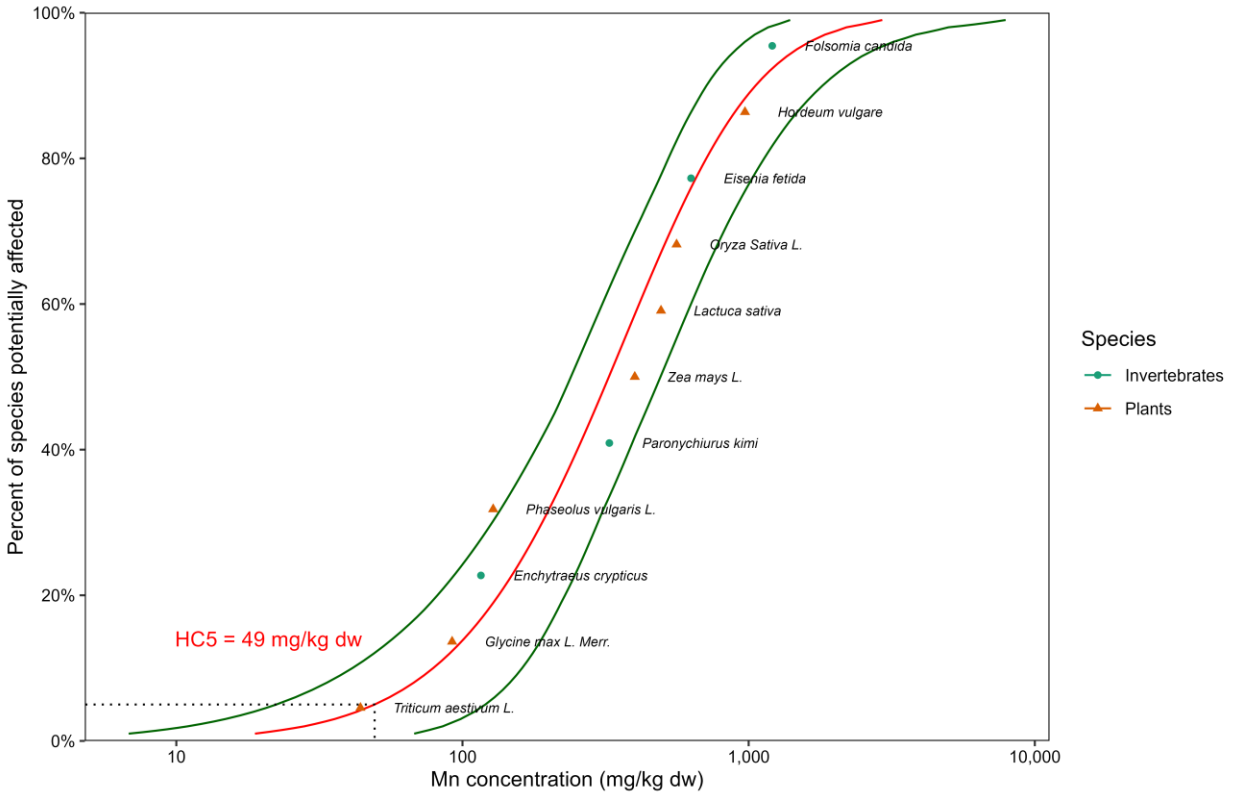

Figure 7-2. Long-term model averaged species sensitivity distribution (SSD) for manganese in soil. The 5th percentile (HC5) is 49 mg/kg dw for manganese

[Figure 7-2 illustrates the species sensitivity distribution (SSD), which is based on chronic toxicity data causing sublethal effects to 10% of the soil-dwelling organisms tested (data presented in Table 7-2). The chronic SSD is used to derive the manganese PNEC for soil-dwelling organisms. The averaged model fit (that is, normal, logistic, gamma) SSD is shown on the graph, along with the 95% confidence intervals. The 5th percentile of the average distribution (HC5) was calculated to be 49 mg/kg dw for manganese.]

Table 7-3. Long-term SSD statistics applying ssdtools

Distribution	AICc (unitless)	Predicted HC5 (95% LCL and UCL) (mg Mn/kg dw)	Weight (unitless)
Log-Normal	6.15	56 (26 to 155)	0.315
Log-Logistic	7.02	53 (19 to 160)	0.205
Gamma	5.32	43 (9.1 to 170)	0.480
Model average	N/A	49 (17 to 165)	N/A

Abbreviations: AICc, Akaike information criterion correction; dw, dry weight; LCL, lower confidence limit; N/A, not applicable; UCL, upper confidence limit.

7.2 Ecological exposure assessment

7.2.1 Approach for aquatic exposure characterization

According to data reported to the NPRI (section 5), manganese is released primarily to water, accounting for 82% of total manganese released to the environment. Detailed exposure scenarios were developed for the industrial sectors with the largest releases of manganese to water in Canada: 1) pulp, paper, and paperboard mills; 2) metal ore mining; and 3) wastewater systems (WWS).[10] In addition, since 90% of all manganese consumed is used for steel production globally, exposure scenarios for steel-related sectors were developed to the extent possible, using the information available (IMnI 2022). For this draft assessment, steel-related sectors include iron and steel mills and ferroalloy manufacturing; motor vehicle parts manufacturing; agricultural, construction and mining machinery manufacturing; and steel product manufacturing from purchased steel. Surface water quality data from multiple monitoring programs across Canada were also summarized.

Although not described in this draft assessment, preliminary aquatic exposure scenarios for manganese releases from other sectors (for example, electric power generation, transmission and distribution, basic chemical manufacturing, non-ferrous metal [except aluminum] production and processing, oil and gas extraction, and coal mining) indicated that these sectors were of lower concern, at current levels of exposure.

For each detailed exposure scenario, predicted environmental concentrations (PECs) were calculated for the aquatic environment using concentrations of manganese measured in surface waters. Both dissolved and total manganese concentrations were considered where available, with preference given to dissolved manganese. Although they are based on measured concentrations, these PECs are considered predictive owing to the extent of their spatial and temporal variation.

When measured concentrations of manganese in surface waters were unavailable, PECs were calculated using manganese effluent concentrations (C_{eff}) according to the equation below:

$$PEC\ (\mu g/L) = C_b\ (\mu g/L) + \left(\frac{C_{eff}\ (\mu g/L) - C_b\ (\mu g/L)}{DF}\right)$$

[10] In this draft assessment, the term “wastewater system” refers to a system that collects domestic, commercial, and/or institutional household sewage and possibly industrial wastewater (following discharge to the sewer), typically for treatment and eventual discharge to the environment. Unless otherwise stated, the term wastewater system makes no distinction of ownership or operator type (municipal, provincial, federal, Indigenous, private, partnerships). Systems located at industrial operations and specifically designed to treat industrial effluents will be identified by the terms “on-site wastewater systems” and/or “industrial wastewater systems”.

[Alt-text for equation: PEC (µg/L) = C_b (µg/L) + ((C_{eff} (µg/L) – C_b (µg/L)) / DF (maximum of 10, unitless)]

where C_b is the median background concentration of Mn, and C_{eff} is the concentration of Mn in effluent. For defining background concentrations, concentrations of manganese in the receiving water (upstream of the final discharge point) were preferred, followed by concentrations in the intake water, and then the median ecozone background concentration. Median ecozone (and Lake Erie, Lake Ontario, and Lake Superior) background concentrations of total manganese in surface waters were estimated by Kilgour & Associates Ltd. (2018; Proulx et al. 2018) (Table C-2, Appendix C).

Background concentrations were removed from effluent concentrations, since it was assumed that intake waters were not treated prior to use in industrial processes. A dilution factor (DF) appropriate for the given waterbody was applied to reflect conditions near the discharge point. Data collected for other recent assessments indicate that the standard maximum effective DF of 10 is applied to the majority of facilities in the 3 sectors addressed in this report.

7.2.2 Canadian surface water quality monitoring data

Monitoring data for manganese concentrations in Canadian surface waters were available from various federal, provincial, and municipal monitoring programs (Table 7-4). In total, 82,915 data points were available for the years 2011 to 2022. These data included measurements of extractable (Mn_E), dissolved (Mn_D), and total manganese (Mn_T) fractions, representing 3%, 36%, and 61% of the data points, respectively. For some samples, measurements for multiple fractions were available, while for other samples, only a single fraction was measured. Statistical summaries of the data were generated by Canadian ecozone, including the total number of measurements, the percentage of detection of manganese, and other descriptive statistics (Table 7-5). Detection of manganese was high across all data sets, ranging from 80.6% to 100% detection, with a median of 99.8% detection. For samples with non-detected measurements, a concentration of half the detection limit was assumed and used for the statistical analyses.

Manganese concentrations in surface water vary across Canada, because manganese is both naturally occurring and released through anthropogenic activities. Across all ecozones, Mn_T ranged from 0.003 to 20,900 µg/L (range of 0.09 to 810 µg/L for Mn_E and 0.025 to 20,700 µg/L for Mn_D). Median concentrations of manganese across ecozones ranged from 20 to 22 µg/L for Mn_E, 0.335 to 20 µg/L for Mn_D, and 4.2 to 137 µg/L for Mn_T.

Table 7-4. Surface water quality monitoring data sets for manganese

Data sets (organization)	Reference
National long-term water quality monitoring data sets (Environment and Climate Change Canada)	NLTWQM 2023

Data sets (organization)	Reference
Multiple programs and data sets from the Environmental Monitoring System (British Columbia Ministry of the Environment and Climate Change Strategy)	BC EMS 2023
Canada-Alberta Joint Oil Sands Environmental Monitoring Program data sets (Alberta Environment and Protected Areas, Environment and Climate Change Canada, and other partners[a])	JOSM 2023
Regional Aquatics Monitoring Program data sets (RAMP Steering Committee)	RAMP 2023
Provincial (Stream) Water Quality Monitoring Network data sets (Ontario Ministry of the Environment, Conservation and Parks)	PWQMN 2023
Regional Watershed Monitoring Program data sets (Toronto and Region Conservation Authority)	RWMP 2022
Banque de données sur la qualité du milieu aquatique data sets (Government of Québec)	BQMA 2023
New Brunswick Surface Water Monitoring Network data set (New Brunswick Department of Environment and Local Government)	NB SWMN 2023
Province of Prince Edward Island Surface Water Quality Monitoring data set (Prince Edward Island Department of Environment, Water and Climate Change)	PEI SWQM 2023
Surface Water Quality Monitoring Network Grab Sample Water Quality Data data set (Nova Scotia Environment)	NSE SWQMN 2023

[a] Regional First Nations and Métis organizations, environmental agencies, and industry stakeholders.

Table 7-5. Manganese concentrations in Canadian surface waters from 2011 to 2022 by ecozone

Ecozone	Fraction	Sample size	Median (µg/L)	P95 (µg/L)	Max (µg/L)
Arctic Cordillera	D	17	8.6	9.9	18
Arctic Cordillera	T	18	40	58	117
Atlantic Maritime	D	48	20	30	147
Atlantic Maritime	E	1,484	22	36	270
Atlantic Maritime	T	3,416	29	59	10,847
Boreal Cordillera	D	2,178	4.6	20	1,090
Boreal Cordillera	T	3,166	12	39	11,000
Boreal Plains	D	935	11	56	2,400
Boreal Plains	T	1,239	43	128	2,840
Boreal Shield	D	252	2.0	5.3	33
Boreal Shield	T	3,565	16	48	4,320
Mixedwood Plains	D	656	3.9	7	38
Mixedwood Plains	T	3,129	37	72	1,970

Ecozone	Fraction	Sample size	Median (µg/L)	P95 (µg/L)	Max (µg/L)
Montane Cordillera	D	13,268	1.9	9.6	20,700
Montane Cordillera	T	19,015	8.2	28	20,900
Northern Arctic	D	57	4.9	9.6	18
Northern Arctic	T	57	37	146	3,840
Pacific Maritime	D	6,560	3.3	14	2,505
Pacific Maritime	T	9,388	7.7	26	4,930
Prairies	D	1,265	5.0	36	3,870
Prairies	T	1,289	137	326	3,860
Southern Arctic	D	81	1.3	2.4	9.2
Southern Arctic	T	81	4.2	7.6	90
Taiga Cordillera	T	99	37	74	1,570
Taiga Plains	D	708	4.1	11	544
Taiga Plains	T	747	18	51	1,040
Taiga Shield	D	30	0.34	0.5	0.76
Taiga Shield	T	543	7.8	11	439
N/A	D	3,599	9.3	24	5,510
N/A	E	1,312	20	40	810
N/A	T	4,713	45	97	5,590

Abbreviations: D, dissolved; E, extractable; T, total; P95, 95th percentile concentration; N/A, not assignable.

7.2.3 Pulp and paper sector

According to the NPRI, the pulp and paper sector reported average annual releases of 895 ± 42 tonnes of manganese to water from 2015 to 2019 (Table B-1, Appendix B). A total of 27 facilities measured effluent manganese concentrations from 2016 to 2019 (NPRI 2021). The PECs for the receiving waters were calculated from effluent concentrations, as previously stated. The calculated PECs ranged from 18.5 to 384 µg Mn/L.

The Canadian pulp and paper sector includes facilities (mills) that produce a range of products including paper, cardboard, newsprint, and pulp. Sources of manganese vary by mill and can include furnish, intake water, processing additives, and raw materials (NCASI 2018). Furnish, consisting of materials such as virgin fibre (for example, wood chips and sawdust), old corrugated containers, and recycled paper (for example, newsprint, magazines, and copy paper), is the primary source of manganese from the pulp and paper sector (NCASI 2018). For example, D'Souza et al. (1998) reported that 78% of manganese originated from furnish. Other studies have found that ≥ 85% of manganese inputs to mills come from wood chips (Mannisto et al. 1999; Frederick et al. 2000; Backman et al. 2004). Manganese content in fibre sources from 2 data sets is

summarized by the National Council for Air and Stream Improvement (NCASI) (NCASI 2009; US EPA 2011a).

Manganese concentrations in softwood or hardwood chips and sawdust range from 13 to 265 mg/kg (median 81 mg/kg, n=24 mill averages), in old corrugated containers from 8.8 to 55 mg/kg (median 33 mg/kg, n=16 mill averages), and in secondary fibres (for example, newsprint, copier paper, magazines) from 5.6 to 76 mg/kg (median 34 mg/kg, n=9 mill averages) (NCASI 2018).

Fuels used for energy generation within the industry also contain manganese. For example, in the United States, manganese in bark fuel ranges from 20.8 to 457 mg/kg (median 144 mg/kg, n=41 mill averages), in bituminous coal from 2.67 to 322 mg/kg (median 18.5 mg/kg, n=104 mill averages), and in fuel oil No. 6 from 0.001 to 33.4 mg/kg (median 0.38 mg/kg, n=15 mill averages) (US EPA 2011a).

Other sources of manganese include manganese as an impurity in chemicals and materials used in paper manufacturing, such as in phosphoric acid at 1.48 to 113 mg/kg (median 11.4 mg/kg, n=4 samples), in sulfuric acid at 0.055 to 5.81 mg/kg (median 0.268 mg/kg, n=7 samples), and in aluminium alloys at 0.604 to 2.62 mg/kg (n=3 samples) (NCASI 2018).

Canadian pulp and paper mills are subject to the *Pulp and Paper Effluent Regulations* (PPER) under the *Fisheries Act* (Canada 2018a). Under Schedules II and IV.1 of the PPER, effluent monitoring and Environmental Effects Monitoring (EEM) are required. While there is no requirement for mills to report manganese concentrations in effluent or receiving areas, manganese and other metals are often measured as part of the "Investigation of Cause" phase after adverse biological effects of effluents have been observed (Environment Canada 2010). A total of 11 active facilities reported 176 measurements of Mn_T and 128 measurements of Mn_D surface water concentrations in exposure and reference areas from 2006 to 2019 in various EEM reports (EEM 2021). The values for Mn_T were in the range of 3.5 to 120 µg/L (Mn_D: 0.39 to 110 µg/L), with median Mn_T ranging from 14 to 78 µg/L (median Mn_D: 0.7 to 21 µg/L) for exposure areas and from 11 to 68 µg/L (median Mn_D: 1 to 20 µg/L) for reference areas, respectively. Only 3 of the 11 facilities showed elevated median Mn_T or Mn_D in the exposure areas compared to the respective reference areas. Three additional facilities reported manganese effluent concentrations in EEM reports (EEM 2021). The PECs for these 3facilities in receiving waters were calculated, as previously stated, from effluent concentrations and ranged from 3.4 to 2,700 µg Mn/L.

Data (from late August 2018 to late January 2019) for metal concentrations in final effluent for Canadian pulp and paper mills, as well as background concentrations in corresponding ambient waters (primarily raw intake water), were collected in a study sponsored by Canadian pulp and paper facilities and managed by the NCASI (2019). Samples were collected from 30 mills representing 2 mill process categories (16 chemical mills and 14 mechanical mills) and different wood fibre sources in 4Canadian provinces (British Columbia, Alberta, Ontario, and Québec). At each facility, samples

were collected over 3 consecutive days during normal process conditions (that is, stable, typical mill operating conditions associated with average production rates and excluding start-up and shutdown conditions). Total and dissolved manganese concentrations, as well as pH and total water hardness, were measured in both effluent and intake waters. Manganese concentrations in raw intake water were assumed to be representative of background concentrations in the associated final effluent-receiving waters. In cases where raw intake water and receiving waters were located on different waterbodies, receiving waters were sampled upstream of the discharge point. Facility-level data, including minimum, maximum, and mean concentrations, were provided to Environment and Climate Change Canada (NCASI 2019). Concentrations below the method detection limits (MDLs) were replaced with values equal to half of the corresponding MDL.

Manganese was detected in all samples from the 30 mills, except for Facilities C-3 and C-16, in which manganese was below the detection limit of 0.5 µg/L. The median of the mean Mn_D effluent concentrations was 522 µg/L, with concentrations ranging from below detection to 3,090 µg/L. The calculated PECs are presented in Table 7-6. For each mill, PECs were calculated by subtracting the ambient manganese concentration (that is, intake water or upstream) from the minimum, maximum, and mean effluent Mn_D, applying a DF of 10, and then adding mean manganese concentrations in the corresponding background or intake water to account for the background concentrations. Across the 30 mills, PECs ranged from 1.2 to 311 µg/L Mn_D (Table 7-6).

Table 7-6. Dissolved effluent manganese concentration (Mn_D) and predicted environmental concentrations (PECs) for the pulp and paper sector based on effluent concentrations from 16 chemical (C) (kraft) and 14 mechanical (M) mills across Canada from 2018 to 2019

Mill	Mean Mn_D effluent concentration (µg Mn/L)[a]	Effluent Mn_D range (µg Mn/L)[a]	Mean back-ground conc. (µg Mn/L)	Mean PEC (range) (µg Mn/L)
C-1	456	437 to 483	4.5	50 (48 to 52)
C-2	60.1	43.8 to 91.9	3.7	9.3 (7.7 to 13)
C-3	2.5 [b]	2.5[b]	1.2	1.3 (NA)[b]
C-4	235	229 to 242	0.8	24 (24 to 25)
C-5	590	517 to 657	9.7	68 (60 to 74)
C-6	66.8	59.4 to 72.4	7.2	13 (12 to 14)
C-7	183	158 to 197	1.5	20 (17 to 21)
C-8	541	512 to 560	49	98 (95 to 100)
C-9	644	521 to 734	1.9	66 (54 to 75)
C-10	503	423 to 579	0.8	51 (43 to 59)
C-11	909	809 to 1,020	10	100 (90 to 111)
C-12	406	355 to 450	5.2	45 (40 to 50)
C-13	561	482 to 664[c]	7.2	63 (55 to 73)[c]
C-14	587	579 to 600	7.5	65 (65 to 67)
C-15	1,267	1,210 to 1,370	9.9	136 (130 to 146)

Mill	Mean Mn_D effluent concentration (µg Mn/L)[a]	Effluent Mn_D range (µg Mn/L)[a]	Mean back-ground conc. (µg Mn/L)	Mean PEC (range) (µg Mn/L)
C-16	2.5 [b]	2.5[b]	1.1	1.2 (NA)[b]
M-1	3,010	2,920 to 3,090	2.0	303 (294 to 311)
M-2	1,827	1,550 to 2,010	20	201 (173 to 219)
M-3	243	240 to 246	6.2	29.9 (29.6 to 30.2)
M-4	655	476 to 834	13	77 (60 to 95)
M-5	590	487 to 703	14	72 (62 to 83)
M-6	44.9	38.1 to 50.1	2.0	6.3 (5.6 to 6.8)
M-7	14.4	9.2 to 18.2	3.5	4.6 (4.1 to 5.0)
M-8	1,610	1,540 to 1,690	41	198 (191 to 206)
M-9	2.5 [b]	2.5[b]	7.7	7.2 (NA)[b]
M-10	15.3	8.6 to 28.7	1.0	2.4 (1.8 to 3.8)
M-11	1,383	1,320 to 1,440	1.6	140 (133 to 145)
M-12	626	619 to 636	2.0	64 (64 to 65)
M-13	138	121 to 155	13	25 (24 to 27)
M-14	609	597 to 616	4.2	65 (63 to 65)

Abbreviations: conc., concentration; NA, not applicable; PEC, predicted environmental concentration.
[a] n=3 measurements.
[b] No range since all 3 samples were below the detection limit.
[c] Calculated from total manganese concentrations.

7.2.4 Metal ore mining sector

The Canadian metal ore mining sector includes both ore extraction and processing. The term “mining” is used in a broad sense to include ore extraction, quarrying, and beneficiating (for example, crushing, screening, washing, sizing, concentrating, and flotation), which are customarily done at the mine site (Statistics Canada [modified 2021]). Thus, mining activities can include both ore extraction via open-pit or underground mining, and ore processing at a milling facility (commonly referred to as a mill). Small quantities of valuable minerals are separated from larger quantities of waste minerals at milling facilities through grinding and crushing, chemical and physical separation, and dewatering processes (Environment Canada 2009). Manganese is not currently extracted and processed in Canada but is released as a by-product of metal ore mining activities. From 2015 to 2019, a yearly average of 91 ± 30 (48 to 136) tonnes of manganese was released to water (Table B-1, Appendix B). Of potential concern is the exposure of freshwater biota to bioavailable forms of manganese in surface waters receiving mining effluents.

Canadian metal mines that discharge effluent at any time into any water at a flow rate exceeding 50 m^3/day are subject to the *Metal and Diamond Mining Effluent Regulations* (MDMER) under the *Fisheries Act* (Canada 2018b). The EEM provisions under Schedule 5 of the MDMER include measurements of total manganese as part of both effluent characterization and water quality monitoring in reference and exposure areas. Some facilities also report dissolved concentrations of manganese, but these data are

limited. Exposure areas refer to surface waters frequented by fish that are exposed to metal ore mining effluent, whereas reference areas refer to surface water frequented by fish that are not exposed to metal ore mining effluent but which have fish habitat similar to that of a corresponding exposure area (Canada 2018b). Under the MDMER, measurements of pH and water hardness are also required for water quality monitoring.

From 2013 to 2020, 120 metal ore mining facilities submitted total manganese data at least once for a freshwater exposure area (EEM 2021). In total, there were 4,568 data points representing 2,528 samples in the exposure areas and 2,040 samples in the reference areas. Manganese concentrations below the MDLs (0.01 to 1,000 µg/L, approximately 1.1% of all samples) were replaced with values equal to half of the corresponding MDLs. In 6 non-detect cases where reported MDLs exceeded the MDMER analytical requirement (MDLs were ≤5 µg/L total manganese), the reported MDL of 500 µg/L was used.

Across the full data set, Mn_T concentrations ranged from below detection to 53,000 µg/L, excluding 1 measurement of 162,000 µg/L, which was 3 orders of magnitude higher than any other value at the same site and may indicate an error in units. The median Mn_T was 24 µg/L (average 203 ± 1,689 µg/L, ranging from below detection to 53,000 µg/L) for exposure samples compared to a median Mn_T of 16 µg/L (average 51 ± 211 µg/L, ranging from below detection to 7,650 µg/L) for reference samples. Data indicate that exposure areas receiving mining effluents were enriched in total manganese compared to reference areas with no mining effluents. In a national assessment of EEM information from metal mines, manganese was one of the metals observed to be present at elevated concentrations in the receiving environment (ECCC 2015).

The influence of the metal ore mining sector on Mn_T in the aquatic environment was examined in detail at 12 facilities. These 12 facilities were selected on the basis of high Mn_T concentrations (for example, concentrations up to mg/L), the number of samples (at least 10 samples representing at least 2 years during the 8-year period for both reference and exposure areas), and/or manganese enrichment in exposure area(s). A summary of the Mn_T values for the reference and exposure areas for these 12 facilities is presented in Figure 7-3. Manganese was detected in all samples collected from the exposure areas of 10 facilities, except for Facility 2 (98%) and Facility 8 (92%); manganese was also detected in all samples collected from the reference areas of 10 facilities, except for Facility 5 (88%) and Facility 9 (96%). Consistent with the trend observed across all the exposure area samples, exposure areas for the 12 facilities were enriched in total manganese compared to paired samples from their respective reference areas (Figure 7-3). Median enrichment factors ranged from 1.2 for Facility 3 to 72 for Facility 12.

Limited measurements of Mn_D were available for the metal ore mining sector. In total, 5 pairs each of Mn_T and Mn_D were available for the exposure and reference areas of Facility 9. The Mn_T and Mn_D are comparable for the exposure area of the facility (for example, dissolved to total ratios are 97% to 100% for 4 paired samples and 72% for 1

paired sample), while dissolved to total ratios are less consistent at the reference area, ranging between 38% and 92%.

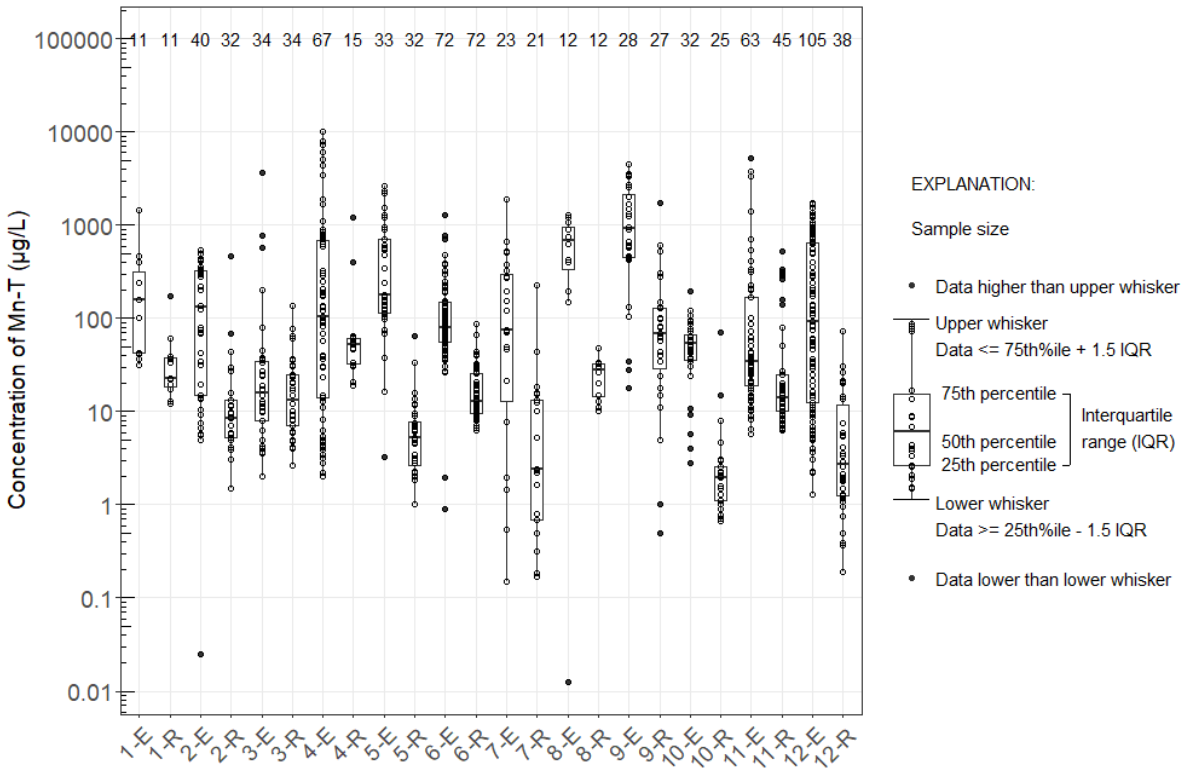

Figure 7-3. Total manganese surface water concentrations (Mn_T) in reference (R) and exposure (E) areas reported by 12 selected metal ore mining facilities subject to the MDMER from 2013 to 2020 (EEM 2021)

[Figure 7-3 presents box plots of measured Mn_T for the exposure and reference areas of 12 selected facilities subject to the *Metal and Diamond Mining Effluent Regulations* (MDMER) from 2013 to 2020 (EEM 2021). Mn_T data were combined when multiple exposure and reference areas were available. The sample sizes, detection frequency, minimum, first quartile (Q1) Mn_T, median Mn_T, third quartile (Q3) Mn_T, 95th percentile Mn_T, and maximum Mn_T are shown in the following table:

Facility	Sample size	Detection frequency (%)	Min (µg Mn_T/L)	Q1 (µg Mn_T/L)	Median (µg Mn_T /L)	Q3 (µg Mn_T/L)	95th percentile (µg Mn_T/L)	Max (µg Mn_T/L)
1-R	11	100	12	19	22	38	120	180
1-E	11	100	31	42	160	320	950	1,400
2-R	32	100	1.5	5.3	8.6	13	55	470
2-E[a,b]	40	98	0.025	15	130	330	440	540
3-R[a,b]	34	100	2.6	7.0	13	25	69	140
3-E[a,b]	34	100	2.0	8	16	35	640	3,700
4-R	15	100	19	33	53	62	650	1,200

4-E[a,b]	67	100	2	14	100	690	5,800	10,000
5-R	32	88	1	2.7	5.2	7.9	24	65
5-E	33	100	3.3	120	120	700	2,200	2,700
6-R	72	100	6.3	9.5	13	26	42	88
6-E	72	100	0.9	55	79	150	430	1,300
7-R	21	100	0.17	0.45	0.74	2.2	9.5	18
7-E[a,b]	23	100	0.15	15	74	300	640	1,900
8-R	12	100	10	14	28	33	40	48
8-E	12	92	0.012	350	700	950	1,200	1,300
9-R	27	96	0.5	30	69	130	580	1,700
9-E	28	100	18	450	910	2,200	3,500	4,500
10-R	25	100	0.67	1.1	2.0	2.6	14	71
10-E	32	100	2.8	36	54	67	110	200
11-R[a,b]	45	100	6.2	10	14	25	320	530
11-E[a,b]	63	100	5.8	19	35	170	1,300	5,200
12-R[a,b]	38	100	0.19	1.2	2.7	12	27	72
12-E[a,b]	105	100	1.3	12	94	650	1,500	1,800

Abbreviations: E, exposure area; max, maximum; min, minimum; Mn_T, total manganese concentration; Q1, first quartile; Q3, third quartile; R, reference area.
[a] Data pooled from more than 1 reference (R) and exposure (E) area.
[b] Facilities have multiple final discharging points (FDPs) for effluent.

]

7.2.5 Wastewater systems sector

Wastewater systems (WWS) may discharge effluent containing manganese from consumer, commercial, and industrial uses to surface waters. From 2015 to 2019, the NPRI reported average annual releases of manganese to water of 64 ± 3 tonnes from WWS (Table B-1, Appendix B).

Under the CMP Environmental Monitoring and Surveillance Program, empirical monitoring data were collected from February 2009 to October 2019 for 37 municipal WWS located across Canada (ECCC 2020). At each WWS, influent and final effluent were sampled as 24-hour composite samples for 3 consecutive days during summer and/or winter. A total of 224 raw influent and final effluent samples, respectively, were analyzed for total manganese. Manganese concentrations were above MDLs in all samples. Mn_T concentrations ranged from 13 to 868 µg/L for influents and from 0.7 to 985 µg/L for final effluents, respectively.

PECs for facilities in the WWS sector were derived for the 30 WWS that discharge effluent to fresh water (Table 7-7). For these 30 WWS, the median manganese concentrations for final effluents were in the range of 5.6 to 510 µg/L (Table 7-7). PECs were calculated by applying a DF of 10 to the final “total” effluent concentrations and adding the appropriate ecozone median background concentration for total manganese (that is, corresponding to a given facility’s location) (Table C-2, Appendix C). Across the

30 WWS, manganese was detected in all samples, with PECs ranging from 1.2 to 107 µg/L total manganese (Table 7-7).

Table 7-7. Total manganese (Mn_T) predicted environmental concentrations (PECs) for the wastewater sector based on effluent concentrations from 30 WWS across Canada from 2009 to 2019 (ECCC 2020)

Facility (type)	No. of samples	Median effluent conc. (µg Mn_T/L)	Median EAC[b] (µg Mn_T/L)	Median background conc. (µg Mn_T/L)	Median PEC (µg Mn_T/L)
1 (secondary)	9	63	6.3	7.1	13
2 (advanced)	12	29	2.9	52	55
3 (lagoon)	5	350	35	25	59
4 (advanced)	9	40	4.0	7.2	11
5 (secondary)	6	340	34	8.2[a]	43
6 (lagoon)	18	120	12	21	33
7 (secondary)	12	110	11	0.51	12
8 (lagoon)	6	510	51	8.2[a]	60
9 (primary)	9	49	4.9	21	26
10 (secondary)	6	14	1.4	0.80	2.2
11 (lagoon)	6	160	16	21	36
12 (secondary)	6	49	4.9	21	26
13 (secondary)	6	89	8.9	0.80	9.7
14 (secondary)	12	68	6.8	0.80	7.6
15 (lagoon)	12	200	20	52	72
16 (lagoon)	6	89	8.9	21	30
17 (secondary)	6	5.6	0.56	0.80	1.4
18 (lagoon)	9	62	6.2	25	31
19 (primary)	15	81	8.1	21	29
20 (secondary)	6	50	5.0	52	57
21 (lagoon)	6	260	26	12	38
22 (secondary)	6	15	1.5	21	22
23 (secondary)	6	16	1.6	21	22
24 (secondary)	6	7.1	0.71	21	21
25 (lagoon)	3	50	5.0	21	26
26 (lagoon)	6	4.3	0.43	21	21
27 (secondary)	6	2.7	0.27	21	21
28 (secondary)	3	62	6.2	21	27
29 (advanced)	3	60	6.0	7.2	13
30 (secondary)	3	57	5.7	7.2	13

Abbreviations: Conc., concentration; EAC, estimated aquatic concentration; No., number; Mn_T, total manganese concentration; PEC, predicted environmental concentration.

[a] Calculated from total concentrations of manganese.

[b] EAC = estimated aquatic concentration, determined by applying a DF of 10 to measured median effluent concentrations of manganese for each WWS.

Total manganese was detected in all sludge/biosolids samples (a total of 198) collected from 27 WWS from 2009 to 2019 (ECCC 2020). Concentrations of manganese ranged from 6.47 to 4,240 mg/kg in treated biosolids. Biosolids from WWS are sent to landfills, incinerated, or applied to land. The equation below was used to estimate the input of manganese to soils through biosolids land application.

$$PEC = \frac{Total\ Mn\ concentration\ in\ biosolids \times application\ rate \times number\ of\ years}{mixing\ depth \times soil\ density}$$

To simulate a worst-case exposure scenario for soil-dwelling organisms, a maximum application rate of 0.83 kg/m^2 dw per year (based on the highest existing provincial regulatory limit; Environment Canada 2006), a mixing depth of 0.2 m (plough depth; ECHA 2016), and a soil density of 1,200 kg/m^3 (Williams 1991) were used, along with the highest concentrations of manganese measured in biosolids, not destined for incineration, from each of the 23 WWS in Canada. A period of 10 consecutive years was chosen as the length of accumulation (ECHA 2016). The cumulative manganese concentrations in soil at the end of this period were in the range of 4 to 29 mg/kg for the 23 WWS. Two of the WWS facilities showed high estimated manganese PECs of 125 mg/kg and 147 mg/kg, respectively. However, there were uncertainties in calculating the estimated PECs for these 2 facilities. One facility used potassium permanganate for solids treatment, which may have contributed to the high concentrations of manganese in biosolids. The high estimated PECs for the other facility were caused by a significant increase (2 to 3 times) of manganese concentrations in biosolids in 2010 and 2011 (possibly due to the treatment processes used in those years); however, they were below 47 mg/kg in other sampling years. The PECs are based on the assumption that manganese will neither leach or run off nor be taken up by plants and removed through harvest; they are therefore conservative, considering that manganese is an essential element that will be taken up by plants and crops. In addition, the maximum provincial limits on land application rates for the 2 WWS facilities were not available for the provinces in which they are located. Therefore, the estimated manganese PECs for the 2 facilities were calculated as 24 mg/kg and 28 mg/kg, respectively, on the basis of the Ontario regulatory limit of 0.16 kg/m^2 dw per year (Environment Canada 2006).

7.2.6 Steel-related sectors

For this draft assessment, steel-related sectors include: 1) iron and steel mills and ferroalloy manufacturing; 2) motor vehicle parts manufacturing; 3) agricultural, construction and mining machinery manufacturing; and 4) steel product manufacturing from purchased steel. Globally, 90% of all manganese consumed is used for steel production (IMnI 2022). The iron and steel mills and ferroalloy manufacturing sector reported annual average releases of manganese of 39 ± 5 tonnes from 2015 to 2019 (Table B-1, Appendix B) (NPRI 2022). On average, 89% of annual releases from this sector are to air (35 ± 6 tonnes) and 7.5% are to water (3 ± 3 tonnes). Other steel-related sectors reported annual releases of manganese greater than 1 tonne to air but well below 1 tonne to water, including motor vehicle parts manufacturing (3 ± 0.5 tonnes

to air; 0.0003 ± 0.00004 tonnes to water); agricultural, construction and mining machinery manufacturing (0.8 ± 2 tonnes to air; no reported releases to water); and steel product manufacturing from purchased steel (1 ± 0.7 tonnes to air, less than 0.04 tonnes to water) (NPRI 2022).

A total of 5 facilities in the iron and steel mills and ferroalloy manufacturing sector reported measured effluent manganese concentrations from 2016 to 2019 (NPRI 2021). The PECs for the receiving waters were calculated from effluent concentrations and ranged from 0.1 to 260 µg Mn/L.

One facility each in the steel product manufacturing from purchased steel sector and motor vehicle parts manufacturing sector reported measured effluent manganese concentrations from 2016 to 2019 (NPRI 2021). The calculated PECs ranged from 18.6 to 27.7 µg Mn/L.

Measured manganese concentrations in surface waters for steel-related sectors are limited. One iron ore pelleting facility with combined effluents from a mining operation is subject to the MDMER (EEM 2021). Measured manganese concentrations in the exposure areas of this facility ranged from 0.9 to 250 µg Mn/L.

Air emission is the dominant release pathway for steel-related sectors (NPRI 2020). Manganese is present in air as suspended PM (US EPA 1984) and is removed from the atmosphere by dry or wet depositions. Surface water and soils in the vicinity of steel facilities are likely to be enriched by manganese from atmospheric depositions. A decrease of almost 50% in atmospheric manganese concentrations in Montreal in the early 1990s was attributed to the closing of a large manganese alloy production plant located about 25 km southwest of Montreal (Boudissa et al. 2006). In 2003, more than 10 years after the plant had closed, manganese concentrations in soils remained extremely high in both surface (0 to 10 cm) and subsurface (10 to 25 cm) soils. The mean manganese concentrations in surface soils were 226,277, 6,232, and 3,079 mg/kg for sampling sites located 10 m, 50 m, and 800 m from the closed facility, respectively. The mean manganese concentrations in subsurface soils were 283,001, 3,409, and 2,986 mg/kg for the 3 sampling locations, respectively (Boudissa et al. 2006). Both surface and subsurface soils within 10 m of the closed facility had significantly higher manganese concentrations (for example, 36 to 95 times higher) relative to sites farther away.

7.3 Characterization of ecological risk

The approach taken in this ecological assessment was to examine assessment information and develop proposed conclusions using a weight-of-evidence approach and precaution. Evidence was gathered to determine the potential for manganese and its compounds to cause harm in the Canadian environment. Lines of evidence considered include those evaluated in this draft assessment that support the characterization of ecological risk in the Canadian environment. Reliable secondary or indirect lines of evidence are considered when available, including regulatory decisions

and classification of hazard or fate characteristics made by other regulatory agencies. The potential for cumulative effects was considered in this assessment by examining cumulative exposures to the manganese moiety.

7.3.1 Risk quotient analysis

Risk quotient (RQ) analyses were performed by comparing the various estimates of exposure (PECs; see the Ecological Exposure Assessment section) with ecotoxicity information (PNECs; see the Ecological Effects Assessment section) to determine whether there is potential for ecological harm in Canada. Site-specific aquatic PNECs were derived by considering the TMFs (that is, pH and water hardness) using site-specific measurements where these data were available, and using the ecozone level medians reported in Table C-1, Appendix C (see also Kilgour & Associates Ltd. 2016) when site-specific measurements were not available. Central tendencies (medians) were chosen as realistic estimates, which are neither overly conservative nor under conservative. RQs were calculated by dividing the PEC by the PNEC for relevant environmental compartments and associated exposure scenarios. RQs greater than 1 are indicative of a potential for ecological risk. RQs were calculated for the aquatic compartment (surface fresh waters) for the: 1) pulp and paper, 2) metal ore mining, 3) wastewater treatment systems, and 4) steel-related sectors. RQs were also calculated for Canadian surface water monitoring data. In addition, RQs were calculated for the soil compartment for WWS where biosolids are applied to agricultural lands.

RQs were summarized using box plots to illustrate their distribution at a given facility. The lower and upper edges of each box represent the 25th and 75th percentiles, which are the first and third quartiles (Q1 and Q3), respectively, whereas the horizontal line within each box represents the 50th percentile (median). The average is represented by an “x”. The distance between the 25th and 75th percentile is called the interquartile range (IQR) and represents the difference between the first and third quartiles (that is, IQR = Q3−Q1). The lower and upper whiskers represent the lowest or highest data that are within Q1 − 1.5 × IQR or the Q3 + 1.5 × IQR, respectively. Data exceeding these thresholds appear as circles or as their values in cases where the RQs exceed the y-axis scale.

Canadian surface water quality monitoring data*:* RQs for Canadian surface water quality monitoring data were calculated using PECs estimated from measured dissolved, extractable, or total manganese concentrations (listed in order of preference) and PNECs derived using site-specific (when available) or ecozone pH and water hardness. Median PNECs ranged from 6.2×10^{-5} to 21.9 µg Mn/L. The distribution to RQs by ecozone is presented in Table 7-8. Across ecozones, RQs ranged from 0.00001 to 42. Median RQs were all well below 1 and ranged from 0.005 to 0.11. Although the RQs were generally well below 1, elevated RQs may occur across ecozones.

Table 7-8. Canadian surface water quality monitoring risk quotients (RQs) across ecozones from 2011 to 2022

Ecozone	Sample size	RQ min	RQ 25th	RQ median	RQ 75th	RQ 95th	RQ max
Arctic Cordillera	18	0.01800	0.027	0.043	0.063	0.099	0.13
Atlantic Maritime	4,939	0.00001	0.052	0.089	0.163	0.481	32.87
Boreal Cordillera	3,167	0.00007	0.006	0.020	0.080	0.922	27.46
Boreal Plains	1,240	0.00031	0.010	0.043	0.177	0.907	5.70
Boreal Shield	3,565	0.00012	0.024	0.056	0.162	0.606	12.34
Mixedwood Plains	3,130	0.00012	0.040	0.114	0.224	0.553	5.84
Montane Cordillera	20,177	0.00003	0.003	0.012	0.050	0.348	42.18
Northern Arctic	57	0.00008	0.004	0.019	0.039	0.071	0.10
Pacific Maritime	9,454	0.00005	0.004	0.016	0.053	0.400	10.41
Prairies	1,290	0.00086	0.007	0.020	0.099	0.718	5.06
Southern Arctic	81	0.00040	0.003	0.005	0.011	0.022	0.03
Taiga Cordillera	99	0.01223	0.061	0.113	0.234	1.621	4.24
Taiga Plains	748	0.00003	0.003	0.015	0.038	0.136	1.90
Taiga Shield	543	0.00011	0.024	0.036	0.051	0.112	1.69
N/A	6,124	0.00005	0.017	0.061	0.203	0.968	14.84

Pulp and paper sector: For this sector, the site-specific Mn_T and/or Mn_D in surface fresh waters were available for 11 facilities from EEM (2021); these values were compared with PNECs that incorporated the TMFs (pH and water hardness). Median PNECs derived using site-specific (when available) or ecozone pH and water hardness ranged from 270 to 1,200 µg Mn/L. No sampling sites had PECs exceeding the PNECs (that is, RQs at 0.002 to 0.4). Manganese concentrations in effluent were available for 3 additional facilities (EEM 2021). For 2 of the 3 facilities, the RQs were below 0.1. One facility had only 2 effluent concentrations available: a RQ of 9.9 in 2006, which was reduced to 0.08 in 2015.

A total of 27 facilities reported effluent manganese concentrations to the NPRI from 2016 to 2019 (NPRI 2021). PNECs were calculated using the ecozone pH and water hardness at the location of the mills. Across the 27 facilities, PNECs ranged from 260 to 390 µg Mn/L. One facility exhibited PNEC exceedances (RQs from 1.07 to 1.20). This same facility also collected Mn_D data from the receiving water (EEM 2021), with the resulting RQs for this facility ranging from 0.01 to 0.02 based on the Mn_D measured in the exposure area.

RQs calculated from effluent concentration data collected by NCASI (2019) for 30 mills across Canada were summarized in a bar graph, using average Mn_D in effluents (Figure 7-4). PNECs ranging from 200 to 1,400 µg Mn_D/L were calculated using mill-specific mean pH and total mean water hardness values (Table C-3, Appendix C). RQs

calculated using minimum and maximum concentrations are shown as lower and upper error bars, respectively. Across the 30 mills, each mill had 3 measurements of 100% manganese detection, with the exception of mills C-3 and C-16, in which manganese was below the MDL. Average RQs were typically well below 1 (average 0.16 ± 0.13) and ranged from 0.003 to 0.56.

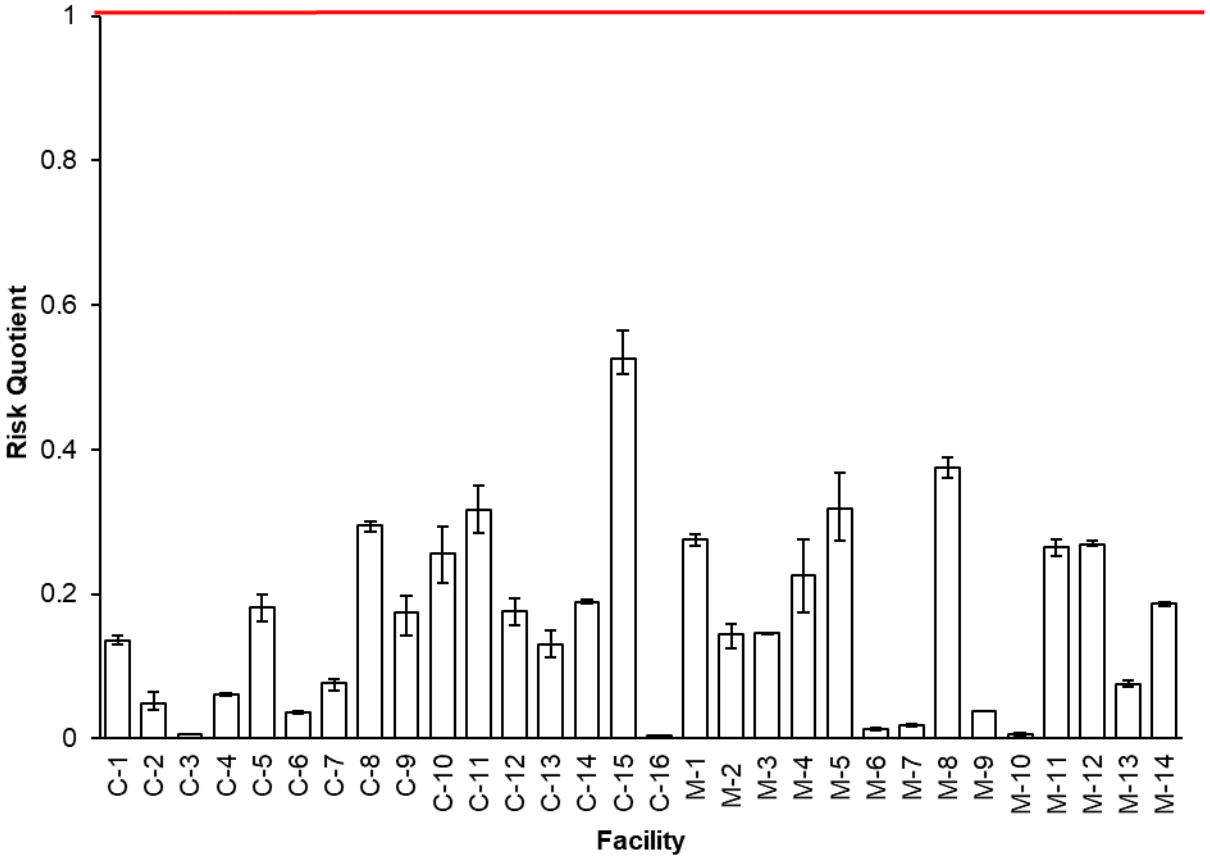

Figure 7-4. Pulp and paper sector risk quotients for 30 facilities releasing manganese to surface fresh waters from 2018 to 2019 (NCASI 2019)

[Figure 7-4 presents a bar graph of risk quotients (RQs) for 30 pulp and paper mills (16 chemical and 14 mechanical mills) releasing manganese to surface fresh waters. RQs were calculated from average Mn_D in effluent concentrations from 2018 to 2019 (NCASI 2019). Minimum and maximum RQs are represented by error bars. The horizontal red line represents a RQ = 1. The sample sizes, detection frequencies, minimum RQ, mean RQ, and maximum RQ are shown in the following table:

Mill	Sample size	Detection frequency (%)	Minimum RQ	Mean RQ	Maximum RQ
C-1	3	100	0.1	0.1	0.1
C-2	3	100	0.04	0.05	0.06

Mill	Sample size	Detection frequency (%)	Minimum RQ	Mean RQ	Maximum RQ
C-3	3	0	0.005	0.005	0.005
C-4	3	100	0.06	0.06	0.06
C-5	3	100	0.2	0.2	0.2
C-6	3	100	0.03	0.04	0.04
C-7	3	100	0.07	0.08	0.08
C-8	3	100	0.3	0.3	0.3
C-9	3	100	0.1	0.2	0.2
C-10	3	100	0.2	0.3	0.3
C-11	3	100	0.3	0.3	0.3
C-12	3	100	0.2	0.2	0.2
C-13	3	100	0.1	0.1	0.1
C-14	3	100	0.2	0.2	0.2
C-15	3	100	0.5	0.5	0.6
C-16	3	0	0.003	0.003	0.003
M-1	3	100	0.3	0.3	0.3
M-2	3	100	0.1	0.1	0.2
M-3	3	100	0.1	0.1	0.1
M-4	2	100	0.2	0.2	0.3
M-5	3	100	0.3	0.3	0.4
M-6	3	100	0.01	0.01	0.01
M-7	3	100	0.02	0.02	0.02
M-8	3	100	0.4	0.4	0.4
M-9	3	100	0.03	0.03	0.03
M-10	3	100	0.004	0.005	0.008
M-11	3	100	0.3	0.3	0.3
M-12	3	100	0.3	0.3	0.3
M-13	3	100	0.07	0.07	0.08
M-14	3	100	0.2	0.2	0.2

Abbreviations: C, chemical mill; M, mechanical mill; RQ, risk quotient.

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Metal ore mining sector: The ecological risk characterization for the metal ore mining sector was conducted using water quality monitoring data for samples collected from 2013 to 2020 under the EEM provisions of the MDMER (EEM 2021). PECs were estimated using measured concentrations of total manganese from exposure areas receiving mining effluent and their corresponding reference areas. In total, 160 samples (3.5%) had RQs of greater than 1 (126 exposure area and 34 reference area samples). Of the 120 facilities with available manganese concentrations in receiving waters, average and Q3 (75th percentile) RQs for exposure areas were below 1 for 111 facilities and 110 facilities, respectively.

Of the 12 metal ore mining facilities examined in detail in this ecological assessment, manganese was detected in all samples from the exposure and reference areas of 10 facilities. Detection frequencies ranged from 92% to 98% in the other 2 exposure areas and from 88% to 96% in the other 2 reference areas (see section 7.2.4). For each sample, site-specific PNECs were calculated using measured values of pH and total water hardness as TMFs (Table C-4, Appendix C). Where pH or water hardness data were missing, values were substituted with the average pH and median water hardness for the same sampling sites on other sampling dates, when available, or values were substituted with the ecozone average pH or median water hardness. Where pH or water hardness values were outside the valid ranges of the CWQGs, values were substituted with a pH of 5.5 (that is, a pH lower than 5.5) or 9.0 (that is, a pH higher than 9.0) and a water hardness of 10 mg/L as $CaCO_3$ (that is, a water hardness lower than 10 mg/L as $CaCO_3$) or 670 mg/L as $CaCO_3$ (that is, a water hardness higher than 670 mg/L as $CaCO_3$), respectively, as recommended by the CCME (2019). For some facilities, the TMF values differed between reference and exposure areas, most notably for water hardness. Water hardness may be higher in exposure areas compared to reference areas owing to the addition of lime during effluent treatment in order to precipitate dissolved metals and control pH levels (Lane and Associates Limited 1990). The site-specific median PNECs in exposure areas, which range from 240 to 1,400 µg/L across facilities, are generally higher than site-specific median PNECs in reference areas, which range from 210 to 350 µg/L (Table C-4, Appendix C).

The distribution of RQs for 12 selected facilities are presented in Figure 7-4. Across all of the individual RQs calculated for the 12 facilities, RQs ranged from 0.0005 to 2.4 for reference areas and from 0.00002 to 15 for exposure areas. The median RQs for reference areas ranged from 0.003 to 0.27 and from 0.07 to 2.7 for exposure areas (Figures 7-5 and 7-6). In several cases, averages that were higher than the medians were driven by very high manganese concentrations (that is, tens of mg/L) in some samples (Figures 7-5 and 7-6).

Four facilities with the highest median RQs (Facilities 5, 9, and 1 of the multiple final discharging points [FDPs] at each of Facilities 11 and 12) had median RQs of 0.7, 1.3, 0.8, and 2.7 in their exposure areas, respectively (Figures 7-5 and 7-6). For Facility 5, 27% of samples (9 out of 33, Figure 7-4) exceeded site-specific PNECs, with RQs ranging from 1.0 to 3.4. The water chemistry, especially pH values, in the exposure area may have contributed partially to the PNEC exceedance, where 7 of the 9 exceedances in the exposure area had pH values of below 6. For Facility 9, 61% of samples (17 out of 28, Figures 7-5 and 7-6) exceeded site-specific PNECs, with RQs ranging from 1.2 to 5.9, and water hardness varied significantly (from 17 to 721 mg/L as $CaCO_3$) at the exposure area of the facility. All PNEC exceedances in the exposure area have elevated manganese concentrations that ranged from 886 to 4500 µg/L. Five samples (18%) collected from the reference area also exceeded PNECs, with RQs from 1.1 to 2.4 (a sixth sample that was 3 orders of magnitude higher compared to other values, likely due to an error in the units, was excluded). However, when measurements taken on the same sampling dates in the exposure and reference areas of Facility 9 were compared, the median manganese concentration was 10-fold higher in the exposure

areas, and RQs were 3.8 times higher compared to reference areas. Five reference and exposure areas were defined for both Facility 11 and Facility 12. Manganese concentrations were only available for Facility 11 from 2013 to 2014 (before its temporary cessation of operations) and from 2018 to 2020 (reopening) and for Facility 12 from 2019 to 2020 (after reopening). The median RQ for 1 of the exposure areas of Facility 11 was 0.82, and 40% of measured concentrations (8 out of 20) exceeded the corresponding PNEC, with RQs ranging from 1.1 to15 (11-E FDP-B in Figure 7-5). All 24 manganese measurements sampled in 1 of the exposure areas of Facility 12 (12-E FDP-C in Figure 7-5) exceeded the PNEC, with RQs ranging from 1.1 to 5.5 (median 2.7). High values for water hardness were present in this exposure area, ranging from 765 to 1,400 mg/L as $CaCO_3$.

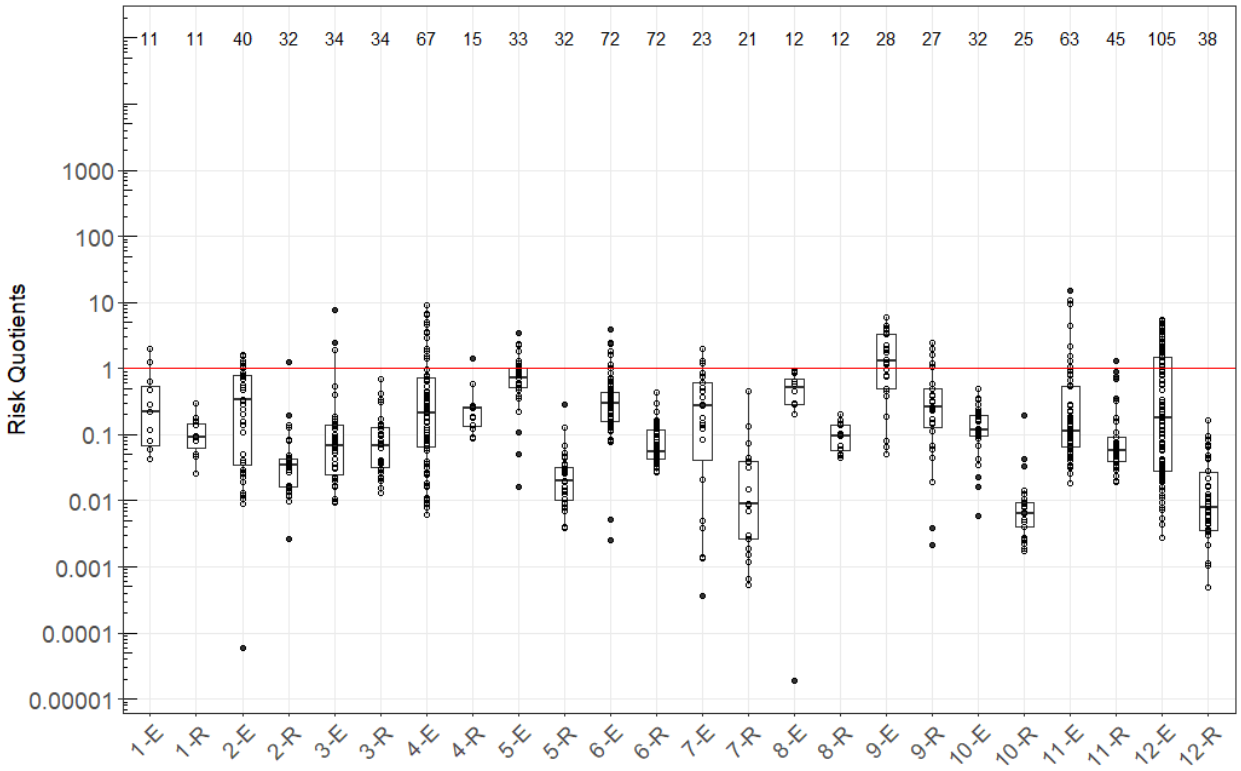

Figure 7-5. Metal ore mining sector risk quotients for reference (R) and exposure (E) areas for 12 facilities releasing total manganese to surface fresh waters from 2013 to 2020.

[Figure 7-5 presents box plots of risk quotients (RQs) based on measured Mn_T calculated for the exposure and reference areas of 12 selected metal ore mining facilities subject to the MDMER from 2013 to 2020 (EEM 2021). Mn_T data were combined when multiple exposure and reference areas were available. The horizontal red line represents a RQ = 1. The sample sizes, detection frequencies, minimum RQ, first quartile (Q1) RQ, median RQ, third quartile (Q3) RQ, 95th percentile RQ, and maximum RQ are shown in the following table:

Facility	Sample size	Detection frequency (%)	Min RQ	Q1 RQ	Median RQ	Q3 RQ	95th RQ	Max RQ
1-R	11	100	0.03	0.07	0.09	0.15	0.24	0.30
1-E	11	100	0.04	0.07	0.22	0.56	1.6	2.0
2-R	32	100	0.003	0.02	0.03	0.04	0.16	1.2
2-E[a,b]	40	98	0.0001	0.04	0.33	0.79	1.3	1.6
3-R[a,b]	34	100	0.01	0.03	0.07	0.13	0.36	0.68
3-E[a,b]	34	100	0.01	0.02	0.07	0.14	2.1	7.6
4-R	15	100	0.09	0.13	0.25	0.27	0.83	1.4
4-E[a,b]	67	100	0.006	0.06	0.22	0.73	5.0	9.2
5-R	32	88	0.004	0.01	0.02	0.03	0.10	0.28
5-E	33	100	0.017	0.51	0.73	1.0	2.4	3.4
6-R	72	100	0.027	0.04	0.06	0.12	0.17	0.44
6-E	72	100	0.003	0.16	0.29	0.44	1.7	3.9
7-R	21	100	0.001	0.001	0.003	0.009	0.04	0.07
7-E[a,b]	23	100	0.0004	0.05	0.27	0.62	1.3	2.0
8-R	12	100	0.04	0.06	0.10	0.14	0.18	0.20
8-E	12	92	0.00002	0.29	0.52	0.70	0.91	0.91
9-R	27	96	0.002	0.13	0.27	0.50	1.9	2.4
9-E	28	100	0.051	0.50	1.3	3.3	4.4	5.9
10-R	25	100	0.002	0.004	0.01	0.01	0.04	0.19
10-E	32	100	0.006	0.10	0.12	0.20	0.34	0.50
11-R[a,b,c]	45	100	0.019	0.04	0.06	0.09	0.74	1.3
11-E[a,b,c]	63	100	0.018	0.07	0.11	0.53	4.2	15
12-R[a,b,c]	38	100	0.0005	0.004	0.01	0.03	0.08	0.16
12-E[a,b,c]	105	100	0.003	0.03	0.16	1.3	4.2	5.5

Abbreviations: E, exposure area; max, maximum; min, minimum; Q1, first quartile; Q3, third quartile; R, reference area; RQ, risk quotient.

[a] Data pooled from more than 1 reference (R) and exposure (E) area.

[b] Facilities have multiple FDPs. One or more exposure FDPs were considerably enriched in manganese compared to the reference FDP(s); additional details have therefore been provided to characterize the FDP.

[c] The water hardness value exceeded the valid range for calculating the manganese PNEC; the estimated PNEC and derived RQ should therefore be used with caution.

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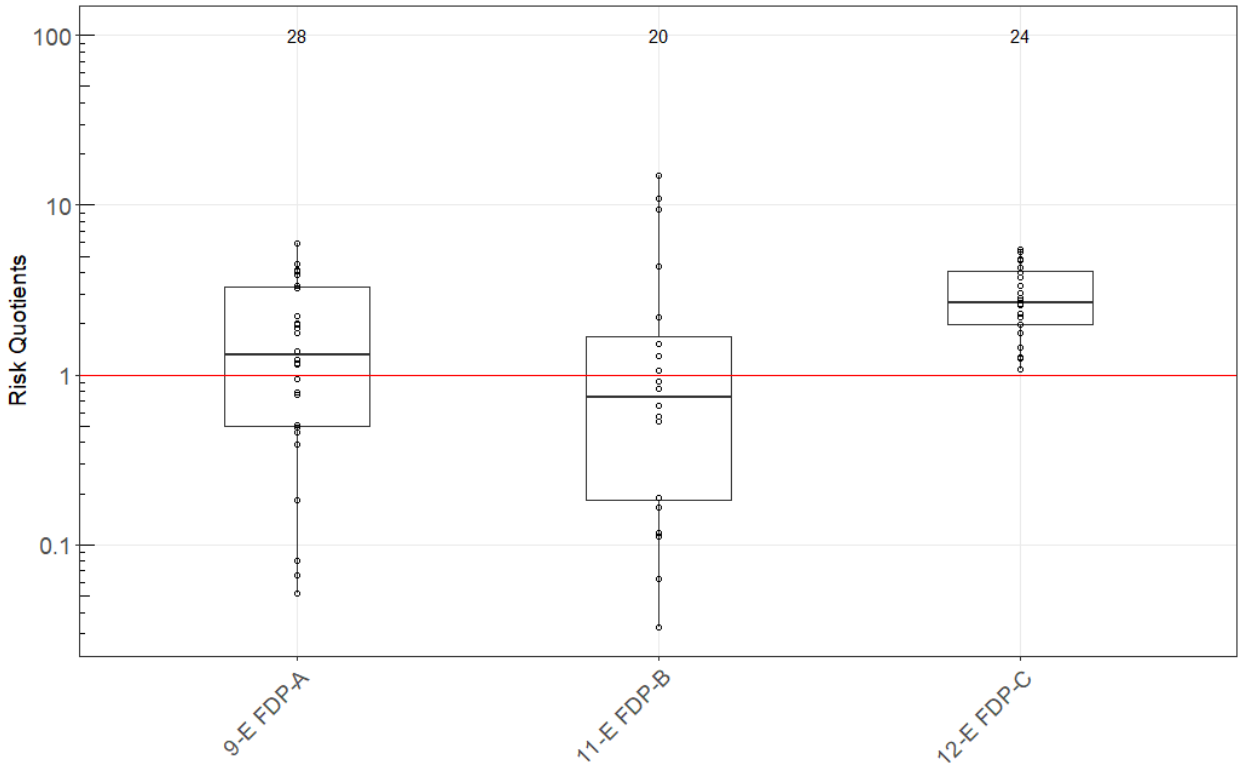

Figure 7-6. Metal ore mining sector risk quotients for 3 final discharging points (FDPs) from 3 facilities releasing total manganese to surface fresh waters from 2013 to 2020.

[Figure 7-6 presents box plots of risk quotients (RQs) that are based on measured Mn_T calculated for the exposure areas for 3 FDPs from Facilities 9, 11, and 12. The horizontal red line represents a RQ = 1. The sample sizes, detection frequencies, minimum RQ, first quartile (Q1) RQ, median RQ, third quartile (Q3) RQ, 95th percentile RQ, and maximum RQ are shown in the following table:

FDP	Sample size	Detection frequency (%)	Min RQ	Q1 RQ	Median RQ	Q3 RQ	95th RQ	Max RQ
9-E FDP-A	28	100	0.05	0.5	1.3	3.3	4.4	5.9
11-E FDP-B	20	100	0.03	0.2	0.8	1.7	11	15
12-E FDP-C	24	100	1.1	2.0	2.7	4.1	5.4	5.5

Abbreviations: E, exposure area; FDP, final discharging point; max, maximum; min, minimum; Q1, first quartile; Q3, third quartile; RQ, risk quotient.

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Wastewater systems sector: RQs for WWS releasing manganese to water were calculated using PECs modelled from total manganese concentrations in effluent from 30 WWSs, and PNECs for each facility were generated from the ecozone or Great Lakes central tendencies of TMFs (Table C-1, Appendix C). Across the 30 WWS, PNECs ranged from 260 to 390 µg/L total manganese (Table C-5, Appendix C). The RQs were well below 1 (range of 0.003 to 0.266) for all 30 WWS (Figure 7-7).

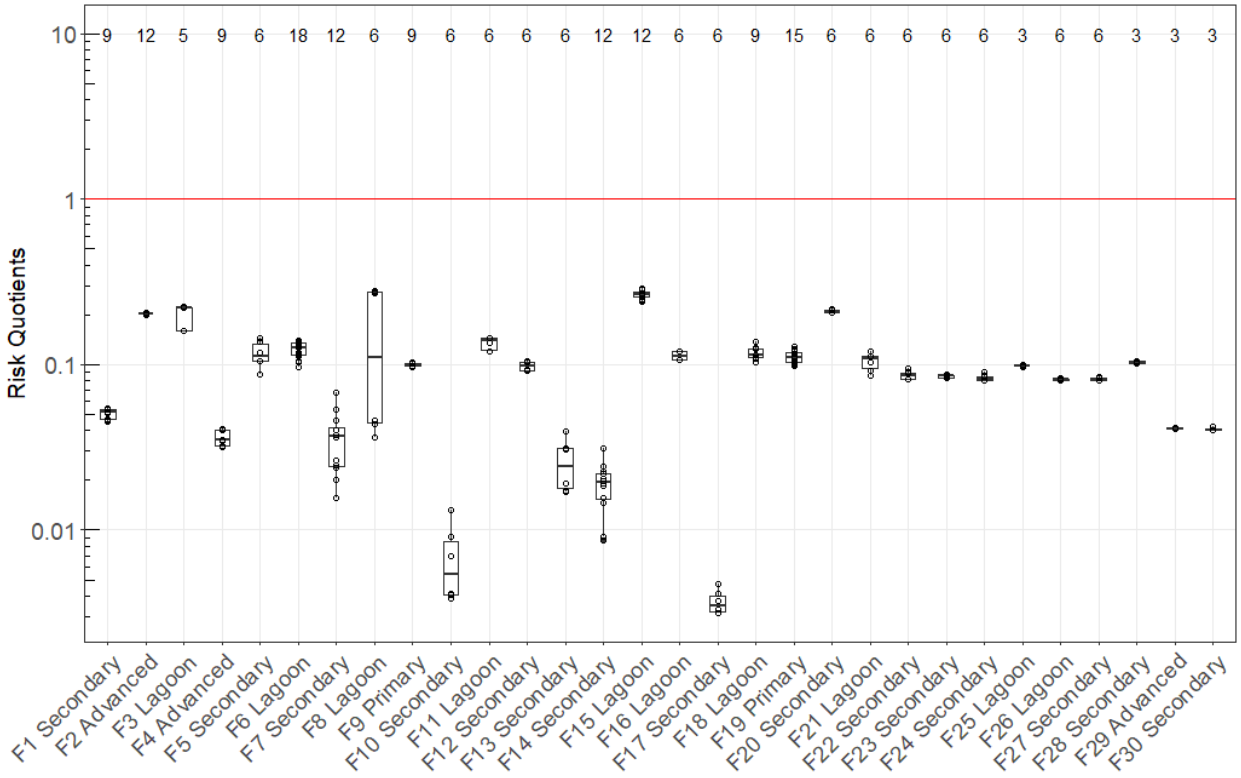

Figure 7-7. Wastewater system risk quotients for 30 facilities releasing manganese to surface fresh waters from 2009 to 2019 (ECCC 2020).

[Figure 7-7 presents box plots of risk quotients (RQs) based on measured manganese concentrations in effluents for the receiving waters of 30 selected WWS facilities. The horizontal red line represents a RQ = 1. Manganese was detected in all samples and all are below a RQ of 1. The sample sizes, minimum RQ, median RQ, 95th percentile RQ, and maximum RQ are shown in the following table:

Facility (type)	Sample size	Minimum RQ	Median RQ	95th RQ	Maximum RQ
1 (secondary)	9	0.04	0.05	0.05	0.05
2 (advanced)	12	0.2	0.2	0.2	0.2
3 (lagoon)	5	0.2	0.2	0.2	0.2
4 (advanced)	9	0.03	0.04	0.04	0.04

Facility (type)	Sample size	Minimum RQ	Median RQ	95th RQ	Maximum RQ
5 (secondary)	6	0.09	0.1	0.1	0.1
6 (lagoon)	18	0.1	0.1	0.1	0.1
7 (secondary)	12	0.02	0.04	0.06	0.07
8 (lagoon)	6	0.04	0.2	0.3	0.3
9 (primary)	9	0.1	0.1	0.1	0.1
10 (secondary)	6	0.004	0.006	0.01	0.01
11 (lagoon)	6	0.1	0.1	0.1	0.1
12 (secondary)	6	0.09	0.1	0.1	0.1
13 (secondary)	6	0.02	0.02	0.04	0.04
14 (secondary)	12	0.009	0.02	0.03	0.03
15 (lagoon)	12	0.2	0.3	0.3	0.3
16 (lagoon)	6	0.1	0.1	0.1	0.1
17 (secondary)	6	0.003	0.003	0.005	0.005
18 (lagoon)	9	0.1	0.1	0.1	0.1
19 (primary)	15	0.1	0.1	0.1	0.1
20 (secondary)	6	0.2	0.2	0.2	0.2
21 (lagoon)	6	0.08	0.1	0.1	0.1
22 (secondary)	6	0.08	0.08	0.09	0.1
23 (secondary)	6	0.08	0.08	0.09	0.09
24 (secondary)	6	0.08	0.08	0.09	0.09
25 (lagoon)	3	0.1	0.1	0.1	0.1
26 (lagoon)	6	0.08	0.08	0.08	0.08
27 (secondary)	6	0.08	0.08	0.08	0.08
28 (secondary)	3	0.1	0.1	0.1	0.1
29 (advanced)	3	0.04	0.04	0.04	0.04
30 (secondary)	3	0.04	0.04	0.04	0.04

Abbreviation: RQ, risk quotient.

]

RQs for releases of manganese to soils via biosolids land application were derived by comparing PECs calculated from the highest total manganese concentration in the treated biosolids of 23 WWS in Canada with PNECs generated for soil-dwelling organisms (section 7.1.6). RQs were in the range of 0.1 to 0.6 for 21 WWS. The PECs were estimated conservatively using the highest manganese land application rate available in Canada (section 7.2.5). However, when the lowest Ontario land application rate standard was applied, the RQs of 2.6 and 3.1 for the remaining 2 WWS facilities decreased to 0.51 and 0.59, respectively.

Steel-related sectors: Multiple sectors were considered for environmental releases of manganese from steel-related industries. RQs of 0.0002 to 0.96 were calculated from the effluent concentration data for 7 facilities with PNECs generated from ecozone TMFs. Although soil concentrations were above the PNEC, soil RQs resulting from

atmospheric deposition were not calculated due to the uncertainty associated with the limited information available for this compartment.

7.3.2 Consideration of the lines of evidence

To characterize the ecological risk of manganese and its compounds, technical information for various lines of evidence was considered (as discussed in the relevant sections of this report) and qualitatively weighted. The key lines of evidence supporting the assessment conclusion are presented in Table 7-9, with an overall discussion of the weight of evidence provided in section 7.3.3. The level of confidence refers to the combined influence of data quality and variability, data gaps, causality, plausibility, and any extrapolation required within the line of evidence. The relevance refers to the impact the line of evidence has when determining the potential to cause harm in the Canadian environment. Qualifiers used in the analysis ranged from low to high, with the assigned weight having 5 possible outcomes.

Table 7-9. Weighted lines of key evidence considered in order to determine the potential for manganese and its compounds to cause harm in the Canadian environment

Line of evidence	Level of confidence[a]	Relevance in ecological assessment[b]	Weight assigned[c]
Environmental fate and behaviour	Moderate	Moderate	Moderate
Persistence in the environment	High	Moderate	Moderate to high
Bioaccumulation in aquatic organisms	High	Moderate	Moderate to high
PNEC for aquatic organisms based on sample-specific TMFs data	High	High	High
PNEC for aquatic organisms based on central tendencies of ecozone and Great Lakes TMFs data	Moderate	High	Moderate to high
PNEC for soil-dwelling organisms	Moderate	High	Moderate to high
PECs for surface waters based on measured data (metal ore mining, and pulp and paper)	High	High	High
PECs for surface waters based on modelled data (pulp and paper, wastewater, and steel-related sectors)	Moderate	High	Moderate to high
PECs in land application-wastewater treatment	Low	High	Moderate

Line of evidence	Level of confidence[a]	Relevance in ecological assessment[b]	Weight assigned[c]
RQ(s) for surface fresh water based on measured PECs and PNECs derived with sample-specific TMF data (metal ore mining and pulp and paper)	High	High	High
RQ(s) for surface fresh water based on modelled PECs and PNECs derived with ecozone/Great Lakes TMF data (WWS)	Moderate	High	Moderate to high
RQ(s) for land application-wastewater treatment	Low	Moderate	Low to moderate

Abbreviations: PEC, predicted environmental concentration; PNEC, predicted no-effect concentration; RQ, risk quotient; TMF, toxicity modifying factor; WWS, wastewater systems.
[a] Level of confidence is determined according to data quality, data variability, and data gaps (that is, are the data fit for purpose?).
[b] Relevance refers to the impact of the evidence in the ecological assessment.
[c] Weight is assigned to each line of evidence according to the overall combined weights for level of confidence and relevance in the ecological assessment.

7.3.3 Weight of evidence for determining potential to cause harm to the Canadian environment

Once released into the environment, manganese-containing substances may dissolve, dissociate, or degrade to release manganese ions into the environment. The fate and behaviour of manganese is governed by both physical and chemical properties in the receiving environment (for example, pH and redox conditions). Changes in environmental conditions (for example, from oxic to anoxic conditions) also have the potential to transform manganese from biologically unavailable to bioavailable forms, and vice versa.

Manganese is persistent and can therefore accumulate in the environment over time, resulting in long-term exposure in environmental media. Manganese is an essential element that can accumulate in certain organisms. However, there is little evidence that manganese biomagnifies in ecosystems.

In the aquatic environment, the bioavailability, and thus toxicity, of manganese is modified by pH and water hardness. Long-term CWQGs were used to incorporate these parameters into the calculation of freshwater PNECs for manganese. Long-term CWQGs are expressed as concentrations of Mn_D. Therefore, Mn_D concentrations were preferred for the ecological risk characterization. However, Mn_D concentrations were seldom available for sector-specific data, and Mn_T concentrations were generally used to calculate PECs. There is greater uncertainty associated with PECs derived from Mn_T, since less soluble forms of manganese may be present in the Mn_T measurements and these PECs are considered to be conservative. PNECs were primarily calculated using

available site-specific TMF data (for example, pulp and paper and metal ore mining sectors). Where such TMF data were unavailable, ecozone and Great Lakes central tendencies were used (for example, WWS and steel-related sectors). The chronic toxicity data were sufficient to use an SSD approach to derive a PNEC for soil-dwelling organisms, but there were insufficient data to incorporate potential TMFs affecting manganese bioavailability, such as pH and redox potential.

Exposure scenarios were developed for the pulp and paper, metal ore mining, WWS, and steel-related sectors. Surface water PECs and RQs were calculated from measured manganese concentrations in the receiving environments (metal ore mining, and pulp and paper) or by deriving surface water PECs from effluent concentrations, assuming that the effluent would be diluted by a maximum factor of 10x in the receiving environment (pulp and paper, steel-related sectors, and WWS). The PECs and RQs for a land application wastewater treatment for the WWS sector is estimated by simulating a worst-case exposure scenario for soil-dwelling organisms, using the highest concentrations of manganese measured in biosolids not destined for incineration from each of the 23 WWS in Canada.

There was limited evidence to indicate that manganese releases from the pulp and paper sector are potentially contributing to ecological harm in the Canadian aquatic environment at current levels. For the pulp and paper sector, the exposure scenarios considered 3 sources of exposure data, including from a study sponsored by a stakeholder (NCASI 2019), and surface water and effluent concentrations reported to the PPER and NPRI. The data sets collected from mills were representative of different mill process categories, wood fibre sources, and multiple regions across Canada. The data sets also included both total and dissolved manganese concentrations, increasing confidence in the PECs and RQs calculated for this sector. One facility in the pulp and paper sector had a high RQ of 9.9, which was calculated from a single effluent concentration in 2006. This RQ decreased to 0.08 in 2015, which may indicate that the manganese discharge from this facility has been reduced in recent years.

Information on manganese concentrations in receiving surface waters or in effluents is available for 120 metal ore mining facilities that were in operation from 2013 to 2020 (EEM 2021). Manganese releases for most metal ore mining facilities are limited and suggest a low potential for ecological harm on the basis of a conservative approach using Mn_T concentrations (RQs reported in section 7.3.1). However, 3 facilities or sites (that is, Facility 9, and 1 of the multiple discharging points at each of Facilities 11 and 12) had occurrences of samples with highly elevated total manganese concentrations (Figures 7-5 and 7-6). Median and Q3 RQs in the exposure areas at these facilities or sites ranged from 0.7 to 2.7 and 1.7 to 4.1, respectively, suggesting that there is potential for a small number of facilities in the metal ore mining sector to be of ecological concern. Some manganese concentrations are elevated in both the reference and exposure areas of Facility 9, which may imply that background manganese concentrations also contributed, if only partially, to the manganese concentration measured in the exposure area. Median and Q3 RQs for Facility 5 were 0.7 and 1.0 in the exposure areas, respectively, suggesting that there may be some potential for

ecological concern. Most of the PNEC exceedances were associated with low pH (that is, below 6) in the exposure area at Facility 5.

Confidence in the aquatic PECs and RQs estimated for facilities in the WWS sector was lower than for the pulp and paper and metal ore mining sectors, because the TMF values were based on ecozone and Great Lakes central tendencies rather than measured values. However, the risk characterization scenario using Mn_T effluent concentrations suggests a low potential for ecological harm from the WWS sector. A conservative approach to estimating manganese concentration in biosolids land use was used (for example, PECs were calculated using the highest application rate in Canada and the highest concentration measured for each WWS, and facilities using $KMnO_4$ in wastewater treatment were included). The existing provincial regulatory limits for biosolids land application rates vary between provinces (that is, by up to 5 times); therefore, estimating PECs and RQs on the basis of the highest regulatory limit could result in overestimation.

Aquatic RQs derived for steel-related sectors, including primarily the iron and steel mills and ferroalloy manufacturing sectors, were below 1. Aquatic RQs for other steel-related sectors considered in this report, including the motor vehicle parts manufacturing sector; the agricultural, construction, and mining machinery manufacturing sector; and the steel product manufacturing from purchased steel sector, are anticipated to be lower, considering that releases to water reported to the NPRI are lower for these sectors.

Overall, exposure of the environment to manganese and its compounds is not of concern at current levels for the pulp and paper sector, the WWS sector, and steel-related sectors; however, manganese concentrations in effluents discharged from a small number of facilities in the metal ore mining sector are considered to be of potential environmental concern.

7.3.4 Sensitivity of conclusion to key uncertainties

This draft assessment focuses on the manganese moiety and includes all substances that have the potential to dissolve, dissociate, or degrade to release manganese through various transformation pathways and that can potentially contribute to the combined exposure of living organisms to manganese. This approach is precautionary and reduces uncertainty regarding the environmental fate and behaviour of the release of manganese-containing substances under dynamic environmental conditions. Additional information on the environmental fate and behaviour, as well as the persistence and bioaccumulation potential, of manganese would have a low impact on the proposed conclusion.

In this draft assessment, chronic PNECs for manganese were only derived for the freshwater and soil compartments. Long-term CWQGs were selected as freshwater chronic PNECs; this approach is considered to be robust, because it is based on recent chronic toxicity data and incorporates TMFs. Although long-term CWQGs are primarily based on laboratory toxicity studies conducted with highly soluble manganese salts that

readily dissociate and release the free Mn^{2+} ion, the most bioavailable and toxic form of manganese, TMFs (that is, water hardness and pH) were incorporated into the calculation of the site-specific freshwater PNECs to reflect realistic environmental conditions. Additional toxicity data would have a low impact on the proposed conclusion. Measured TMF data were not always available and needed to be estimated. There is little uncertainty when PNECs are calculated using site-specific TMFs but some uncertainty when PNECs are calculated using ecozone values as it is unknown how well these estimates represent site-specific conditions. Geometric means and medians or averages were chosen, since these statistics do not represent extreme values and therefore provide realistic values for the TMFs that are unlikely to systematically under- or overestimate the potential for ecological harm. Where ecozone values were used, the low potential for ecological concern was supported by additional data sets that used site-specific PNECs for the pulp and paper sector and by generally low RQs for the WWS sector. For the metal ore mining sector, site-specific TMF data were available, reducing uncertainty in the PNECs.

There is some uncertainty regarding the long-term PNEC of manganese in soil under varying environmental conditions (for example, low pH), but this uncertainty could be reduced if sufficient data were available to incorporate TMFs into the calculation of soil PNECs. However, this uncertainty has a low impact on the proposed conclusion. The effects of manganese on the aquatic stages of some sediment-dwelling organisms are incorporated into the freshwater PNECs, but there were insufficient data to derive a separate sediment PNEC. Effects of manganese on marine organisms are not well characterized. Additional refinement of data on ecotoxicity in marine organisms is needed to assess the potential risk to the marine environment. While additional information on the ecological effects of manganese in the soil, sediment, and marine compartments would be valuable, it would have a limited impact on the estimates of risk for the exposure scenarios presented in this draft assessment.

There are some uncertainties related to the exposure scenarios for the pulp and paper, metal ore mining, and WWS sectors. Some data sets of measured environmental concentrations contained non-detects, and these were replaced with half of the reported MDL. However, when detection frequencies are high (>85%), as is the case for the majority of measurements presented, the choice of substitution method (for example, zero, one-half MDL) typically becomes irrelevant (US EPA 2006). Therefore, the presence of non-detects here is unlikely to affect the conclusion of the ecological assessment. Exposure and reference areas may be located downstream and upstream of the same waterbody or located on different waterbodies (that is, not necessarily upstream and downstream paired). In some cases, the manganese concentration in the reference area may be influenced by natural or anthropogenic factors that lead to higher values compared to the designated exposure area. While potentially observed for some facilities, this confounding factor does not influence the proposed conclusion, because EEM provisions are based on no effect observed at the reference sites.

For the pulp and paper sector, there were several RQs greater than 1. In each case, additional refinement of the exposure scenario resulted in a RQ of less than 1. For

example, RQs of less than 1 were observed when additional years of data were considered (NPRI data set) or when measured PECs were considered in addition to effluent data (EEM data set). There is some uncertainty regarding potential releases of manganese during atypical mill operations, as well as uncertainty where site-specific TMF data are unavailable. However, the general consensus between the 3 data sets and their representation of a diversity of mills across Canada reduced the uncertainties in any individual data set.

The exposure analysis for the metal ore mining sector considered measurements of Mn_T in surface waters receiving effluents from metal mines. Although PECs (and PNECs) based on Mn_T may be conservative, the limited data available for paired Mn_T and Mn_D in the exposure area of 1 facility (Facility 9) were comparable, suggesting that Mn_T may provide reasonable worst-case estimates of exposure for the metal ore mining sector. For 4 facilities or FDPs, approximately 25% or more of the measurements taken at the exposure areas exceeded site-specific PNECs. The variations in pH and water hardness values, particularly the former, in effluent-receiving waters could influence the site-specific PNECs calculated. These PNEC exceedances were obtained at irregular occasions (for example, 0 to 2 in quarterly samples) and may be caused primarily by variation in TMFs in measurements (for example, Facility 2 and, to a lesser degree, Facility 5). High manganese concentrations were observed in more than 50% of samples measured over a 2- to 3-year duration for Facility 9, and in 1 from each of the exposure areas of Facilities 11 and 12, indicating potential concern for manganese in exposure areas. High levels of water hardness beyond the valid ranges of the CWQGs in the exposure areas of Facilities 11 and 12 may be conservative with respect to fish and invertebrates; however, the protective effects of water hardness for algae and aquatic plants may be less certain. Collection of additional data on dissolved manganese concentrations at these facilities would be valuable, since it could provide further lines of evidence to refine the exposure scenarios for the sector.

The exposure analysis for the WWS sector was based on relatively small subsets of Canada's many WWS facilities. However, these subsets are considered representative, because a variety of treatment types in municipalities of various sizes across Canada were included. A relatively high uncertainty is associated with the worst-case exposure scenario and risk characterization for releases of manganese to soils via biosolids land application. The approach is precautionary and has a low impact on the proposed conclusion.

The exposure analysis for the steel-related sectors considered manganese PECs derived from effluent concentrations. The potential contribution of air releases to aquatic manganese concentrations could not be addressed quantitatively due to the lack of measured concentrations in surface waters, which may lead to an underestimation of the potential risks for these sectors. High manganese soil concentrations measured near a closed manganese alloy facility in Montreal (Boudissa et al. 2006) suggested a potential contribution from PM deposition in the vicinity of such facilities. Data for the soil compartment are generally limited, representing a key uncertainty for steel-related sectors.

8. Potential to cause harm to human health

8.1 Health effects assessment

Several national and international organizations have reviewed the health effects of exposure to manganese (IOM 2001; US EPA 2002, 2004; NHMRC 2011; WHO 2011, 2021; ATSDR 2012). Manganese was reviewed by Health Canada's Water and Air Quality Bureau (WAQB; Health Canada 2010a, 2019a), Natural and Non-prescription Health Products Directorate (NNHPD) (Health Canada 2018a), Food and Nutrition Directorate (FND, Health Canada [modified 2006], 2016), and the Federal Contaminated Sites Risk Assessment in Canada program (Health Canada 2010b). These existing assessments were used to inform the health effects assessment of manganese and its compounds.

To more easily compare the different sources of manganese, all concentrations and doses described in this health effects assessment have been adjusted to give amounts of manganese in its elemental form.

8.1.1 Essentiality

Manganese is an essential element that is required for normal amino acid, lipid, protein, and carbohydrate metabolism. It also serves as an essential enzyme cofactor for a variety of enzymes, including arginase, glutamine synthetase, phosphoenolpyruvate decarboxylase, and manganese superoxide dismutase (IOM 2001; Health Canada 2010a, 2019a). Manganese-containing enzymes serve multiple functions in development, digestion, reproduction, antioxidant defense, energy production, immune response, and the regulation of neuronal activities (Chen et al. 2018).

Manganese requirements are usually met adequately via food. Manganese deficiency is rare, and symptoms are not well-defined (Dupont and Tanaka 1985 as cited in Health Canada 2019a; IOM 2001). Skin anomalies, slow growth of nails, reduced bone density, hair depigmentation, and hypocholesterolemia (abnormally low cholesterol) have been observed in individuals with low levels of manganese in their diet (Health Canada 2019a). Estimated average requirements (EAR) have not been established due to a lack of sufficient data. However, adequate intake (AI) levels, which are average daily nutrient intake levels recommended to ensure nutritional adequacy when evidence is insufficient to develop an EAR, have been derived for people aged 1 year and older on the basis of median manganese intake data from the United States Food and Drug Administration Total Diet Study (IOM 2001). For infants, the AI values were based on literature data on average consumption through human milk (0- to 6-months old) and foods (7 to 12 months old; Gibson and De Wolfe 1980). AI values range from 0.003 mg/day for infants 0 to 6 months of age to 2.6 mg/day for lactating adult females (IOM 2001; Health Canada [modified 2006]). In Canada, the mean manganese intake for all age groups meets or exceeds the AI, indicating a low prevalence of inadequate intake among people in Canada.

Although manganese is an essential nutrient for human health, this health effects assessment focuses on the adverse health effects associated with excess manganese exposure in the general population.

8.1.2 Toxicokinetics

Manganese absorption via the oral route is influenced by its bioavailability in the gastrointestinal (GI) tract, its chemical form, the amount ingested, iron status, sex, and age (Health Canada 2019a). In adults, 3% to 5% of ingested manganese is generally absorbed through the GI tract, with females tending to have a higher absorption rate than males (Finley et al. 1994); however, a high degree of inter- and intra-individual variability has been observed. Increased absorption (up to 40% of ingested manganese) has been reported in neonates (Neal and Guilarte 2013). With respect to GI bioavailability from food, manganese absorption has been shown to be influenced by the presence of other trace minerals (for example, iron, calcium, zinc) and dietary constituents (for example, cellulose, pectin, phytate, ascorbic acid) (Aschner et al. 2005). Total diet, rather than the actual medium of exposure, appears to be more of a determining factor for the uptake of manganese from the GI tract (US EPA 2002). Under most conditions, the bioavailability of manganese ingested through food or drinking water is similar; however, in fasted individuals, relative bioavailability through water may increase to approximately 2 times that of food (Ruoff 1995 as cited in US EPA 2002). From the GI tract, manganese enters portal circulation through passive diffusion or active transport via divalent metal transporter 1 (Harischandra et al. 2019).

Absorption within the respiratory tract is not likely to be under homeostatic regulation, but is rather dependent on particle size, deposition, and chemical solubility (ATSDR 2012). In addition, exposure via the inhalation route bypasses hepatobiliary excretion, such that manganese can be transported to the brain directly through the olfactory or circulatory systems (Aschner et al. 2005; Crossgrove and Yokel 2005; Bock et al. 2008 as cited in Health Canada 2019a).

Limited dermal absorption data are available for manganese. One *in vitro* dermal absorption study, which was Good Laboratory Practice certified and conducted according to the Organisation for Economic Co-operation and Development (OECD) test guidelines, was available for review (IMnI 2010; REACH dossier [modified 2020]). The study was conducted for 24 hours with flow-through diffusion chambers, using previously frozen human skin samples from 4 donors. Two experiments with 6 replicates each were conducted, for a total of 12 replicates. Manganese dichloride ($MnCl_2$) was applied at 5 mg/cm^2 and left on the skin for 24 hours, followed by a wash with a phosphate-buffered saline. The study authors excluded 4 out of the 12replicates as they showed low recovery (less than 85%) or were considered to be outliers. The study authors reported an average dermal absorption value of 1.82% from 8 replicates based on the manganese recovered in the bioavailable portion (receptor fluid + epidermis + dermis) over 24 hours (IMnI 2010). Health Canada did not consider any replicates to be outliers; the average recovery based on all 12 replicates was 80.7%.

Using all 12 replicates, Health Canada calculated an average dermal absorption value of 8.3% over 24 hours.

Once absorbed, manganese is distributed throughout the body via systemic circulation. The plasma elimination half-life was reported as 4.56 hours in male rats administered manganese chloride via oral gavage (Zheng et al. 2000). The highest concentrations of manganese have been reported in the liver, kidneys, and some regions of the brain including the olfactory bulb, with the lowest concentrations found in bone, muscles, and fat (Aschner et al. 2005; Merian et al. 2004 as cited in Health Canada 2019a). Tissues rich in mitochondria and pigments, such as retina, dark skin, and hair, also tend to have high concentrations (Dorman et al. 2006a). Despite its low concentration, bone acts as the largest tissue store of manganese (accounting for 25% to 40% total body burden) because of its mass (Aschner et al. 2005; Roth 2006 as cited in Health Canada 2019a). In rodents, approximately 8% of ingested manganese is transferred to the developing brain in the early neonatal period (Aschner and Aschner 2005). In the human brain, manganese primarily accumulates within the basal ganglia region (Health Canada 2010a). Manganese can also readily cross the placental barrier during pregnancy (Kostial et al. 2005), and maternal manganese levels increase during pregnancy to meet the fetal demand for manganese (Arbuckle et al. 2016).

Elemental manganese does not undergo metabolism; therefore, it is absorbed and excreted unchanged (Health Canada 2019a). Manganese is primarily removed from the blood by the liver via biliary excretion into the intestine (Miller et al. 1967 as cited in Health Canada 2019a). It has been estimated that about 33% of the manganese burden in blood is removed with each pass through the liver (Thompson and Klaassen 1982). Fecal elimination is the primary route of excretion for both unabsorbed and biliary excreted (that is, absorbed) manganese (Dorman et al. 2006a). Urinary excretion of manganese is generally low. Estimated whole-body retention half-times are between 13 and 37 days in humans who have ingested trace levels of radioactive manganese as manganese chloride (Mena et al. 1969; Sandstrom et al. 1986; Davidsson et al. 1989a as cited in Health Canada 2019a). The half-life of manganese in the brain was estimated to be from 51 to 74 days in rats and 53 days in humans and the macaque monkey (Cotzias et al. 1968; Newland et al. 1987; Takeda et al. 1995 as cited in Health Canada 2019a). In macaque monkeys, the half-life in the brain was significantly longer (223 to 267 days) after a single intratracheal exposure of manganese chloride compared to exposure by subcutaneous administration (54 days) (Newland et al. 1987).

Clearance of PM from the respiratory tract includes both absorptive (dissolution) and non-absorptive (transport of intact particles) processes and generally depends on the deposition site and the size, solubility, and possibly the mass of the particles (US EPA 2004 as cited in Health Canada 2019a). The main mechanisms of homeostatic control of blood manganese are the regulation of manganese absorption from the GI tract and the hepatobiliary excretion following ingestion (Health Canada 2010a, 2019a; ATSDR 2012). Maternal manganese is also excreted into human milk, with manganese concentrations generally being highest in colostrum; these levels then decline over the first few days or weeks, after which they remain relatively stable (Mitchell et al. 2020).

Infants have a reduced capacity for biliary excretion compared to adults; as such, exposure during this developmental stage may result in the increased delivery of manganese to the brain and other tissues (Dorman et al. 2006a; Health Canada 2010a). Animal studies have shown that although absorption and retention of manganese is higher in neonates, they return to the levels of older animals at approximately postnatal day (PND) 17 to 18 (Miller et al. 1975; Kostial et al. 1978; Lonnerdal et al. 1987;Rehnberg et al. 1981 as cited in ATSDR 2012). Similarly, people with liver dysfunction are likely to accumulate manganese to an elevated level in the body despite low daily exposure (Taylor et al. 2020).

Blood (whole blood, plasma, and serum) manganese and urinary manganese have been commonly investigated as possible biomarkers to quantify external manganese exposure (Dorman et al. 2006a; Health Canada 2010a, 2019a; ATSDR 2012). Due to the homeostatic regulation of manganese, blood manganese is not considered a sensitive biomarker of exposure in the interpretation of population-level biomonitoring data (Ge et al. 2018). Urinary excretion of manganese is generally not responsive to external manganese exposure (Davis and Greger 1992; Andersen 1999; Vitarella et al. 2000; as discussed in Health Canada 2010a), likely because the fraction of manganese excreted is so low.

Several physiologically based pharmacokinetic (PBPK) models for manganese have been developed for rats (Teeguarden et al. 2007a; 2007b; 2007c; Na et al. 2008; Nong et al. 2008, 2009; Yoon et al. 2009a, 2009b; Song et al. 2018), monkeys (Nong et al. 2009; Schroeter et al. 2011, 2012), and humans (Schroeter et al. 2011; Yoon et al. 2011, 2019; Gentry et al. 2017; Ramoju et al. 2017; Song et al. 2018). A summary of the models published between 2007 and 2012 can be found in Health Canada (2019a), and an overview can be found in Taylor et al. (2012). Recently published models were developed for humans and are based on specific population data, such as for workers, infants, and adults (Gentry et al. 2017; Ramoju et al. 2017; Song et al. 2018; Yoon et al. 2019). However, owing to limitations, the models had limited applicability in this draft assessment.

8.1.3 Health effects via the oral route of exposure

Existing assessments by Health Canada and other international organizations were used to inform the section on health effects associated with oral exposure. In addition, a literature search was conducted from May 2018 to January 2022 to identify additional studies of adequate quality and relevance for inclusion in the assessment of oral toxicity.

For this health effects assessment, in line with Health Canada (2019a), the critical endpoint identified for the risk characterization of oral manganese exposures is the lowest-observed-adverse-effect level (LOAEL) of 25 mg Mn/kg bw/day for neurotoxic effects in the young, as described in the Kern et al. (2010), Kern and Smith (2011), and Beaudin et al. (2013) studies. A subsequent study by Conley et al. (2020) was also considered, as heightened behavioural reactivity was noted in animals with the same

dosing regimen. This endpoint is from neonatal rodent neurodevelopmental studies with exposures from PND 1 to 21, which coincides with brain development during the third trimester (*in utero*) up to approximately 2 to 3 years of age, in humans (Semple et al. 2013).

Health Canada used this endpoint to set a maximum acceptable concentration (MAC) in drinking water designed to be protective of neurotoxic effects in formula-fed infants (Health Canada 2019a). The MAC is calculated by considering the LOAEL of 25 mg/kg bw/day with a total uncertainty factor (UF) of 1,000; the calculation also takes into account a 7 kg infant consuming 0.75 L/day, along with a source allocation factor of 0.5 to allow for some manganese content in the formula itself.

Neonatal rodent development during the early postnatal period coincides with *in utero* brain development beginning in the third trimester in humans (Semple et al. 2013). Studies also suggest that children exposed to elevated levels of manganese in drinking water during infancy may be at an increased risk for neurodevelopmental deficits that may persist into adulthood (Kern and Smith 2011; Beaudin et al. 2013). The selection of the developing fetus, infants, and children (based on studies in neonate rats) as susceptible subpopulations for manganese oral exposure, together with the selection of neurodevelopmental effects as the critical health effects, are considered protective against other adverse effects of oral exposure to manganese across the entire population.

The studies summarized here are limited to key studies that are relevant for characterizing risk, in addition to those published after the most recently published assessment on manganese (Health Canada 2019a). Results from newer studies are consistent with the health effects noted in earlier studies, providing support for the choice of a developmental neurotoxic point of departure (POD). Although effects were noted at doses lower than the LOAEL of 25 mg/kg bw/day, the studies in which these effects were noted had limitations in their study design and reporting and/or were not considered strong enough to be used as a POD for risk assessment due to these study limitations.

Human studies

Drinking water

Several human epidemiological studies have evaluated the association between manganese exposure via drinking water and neurological effects in children (Wasserman et al. 2006, 2011; Bouchard et al. 2011, 2018; Khan et al. 2011, 2012; Oulhote et al. 2014; Kullar et al. 2019).

A cross-sectional study conducted in southern Quebec analyzed the relationship between manganese exposure from residential tap water (range of 1 µg Mn/L to 2,700 µg Mn/L, median of 34 µg Mn/L, geometric mean of 20 µg Mn/L, and an arithmetic mean of 98 µg Mn/L) and intelligence quotient (IQ) scores in children aged 6

to 13 years (n=362) (Bouchard et al. 2011). Children were specifically recruited from communities supplied by groundwater. Higher concentrations of manganese in drinking water were associated with lower IQ scores. The authors also measured the concentration of manganese in children's hair and reported that the concentration of manganese in hair increased with higher manganese concentrations in drinking water, but not with increased manganese intake from food. It was suggested that this result is consistent with a difference in the bioavailability of manganese from water compared to in food. A study conducted within the same population of children aged 6 to 13 from southern Quebec (n=375) assessed the relationship between concentrations of manganese in drinking water and neurobehavioural functions (memory, attention, motor function, and hyperactivity) (Oulhote et al. 2014). The authors reported significant inverse associations between standardized levels of manganese (log_{10} transformed) in water and memory. In addition, there was a significant association between motor function and estimated intake of manganese from water consumption. The associations between hyperactivity or attention and manganese concentrations in drinking water or estimated intake of manganese from water consumption were not statistically significant (Oulhote et al. 2014).

To examine whether the results from Bouchard et al. (2011) could be replicated in another population, Bouchard et al. (2018) performed a second cross-sectional study in southeastern New Brunswick. Children aged 5.9 to 13.7 years (n=259) from rural households using groundwater wells were recruited. Manganese concentrations in well water spanned a range of <0.03 µg/L to 1,046 µg/L, with a median value of 5 µg/L, a geometric mean of 6.3 µg/L, and an arithmetic mean of 62.1 µg/L. The relationship between manganese concentrations in drinking water and IQ scores was insignificant. The authors attributed this lack of significant association to the lower levels of manganese measured in this region.

These studies considered several covariates that may confound the association between manganese exposure and cognitive abilities, such as the presence of lead and arsenic in drinking water, socioeconomic status, and maternal factors (Bouchard et al. 2011, 2018).

Kullar et al. (2019) conducted a pooled analysis combining the data from Bouchard et al. (2011) and Bouchard et al. (2018) (n=630). The objective was to estimate the concentration of manganese in drinking water associated with pre-defined levels of cognitive impairment in children (that is, a 1%, 2%, and 5% decrease in Performance IQ scores) using the Bayesian Benchmark Dose Analysis System. The authors derived weight-averaged median estimates for the benchmark concentration (BMC) of manganese in water and the lower bound of the credible interval (BMCL). The BMCs (BMCL) for manganese in drinking water associated with a 1%, 2%, and 5% decrease in Performance IQ scores were 133 µg/L (78 µg/L), 266 µg/L (156 µg/L), and 676 µg/L (406 µg/L), respectively.

Several cross-sectional studies from Bangladesh have examined the associations between cognitive performance in children and manganese concentrations in drinking

water obtained from household wells (Wasserman et al. 2006, 2011; Khan et al. 2011, 2012).

Wasserman et al. (2006) observed a significant negative association between manganese concentrations in drinking water (average: 793 µg/L, range: 4 µg/L to 3,908 µg/L) and full-scale performance and verbal raw scores in children aged 10 (n=142). In comparison, Wasserman et al. (2011) did not observe an association between manganese concentrations in drinking water (median: 527.25 µg/L, average: 725.54 µg/L, range: 40 µg/L to 3,442.45 µg/L) and IQ scores in children aged 8 to 11 (n=299); however, the authors noted a significant relationship between blood manganese concentration and decreases in working memory and perpetual reasoning scores. Both studies adjusted for maternal education and intelligence, house type, family ownership of a television, child height, and head circumference.

The association between manganese exposure from drinking water and academic achievement was assessed in children aged 8 to 11 years (n=840) (Khan et al. 2012). A significant relationship was observed between manganese drinking water concentrations >400 µg/L and decreased mathematics test scores. In a previous study by the same authors, which used a similar protocol, increasing manganese concentrations in drinking water (mean: 889.2 µg/L, median: 649.5 µg/L, range: 40 µg/L to 3,442.5 µg/L) were associated with negative classroom behaviours in children aged 8 to 11 years (n=201) (Khan et al. 2011).

A prospective study assessed the behaviour and cognitive abilities of children from rural Bangladesh (n=1,265) exposed to manganese via drinking water (Rahman et al. 2017). The study involved a mother-child cohort that covered early pregnancy up to children 10 years of age. Manganese concentrations were measured in drinking water during pregnancy (median: 204 µg/L, range: 1.3 µg/L to 6,550 µg/L), and at 5 years of age (median: 228 µg/L, range: 0.1 µg/L to 6,550 µg/L) and 10 years of age (median: 339 µg/L, range: 0.1 µg/L to 8,680 µg/L). The authors reported that early-life exposure to manganese increased the risk of conduct problems, particularly in boys. However, prenatal manganese concentrations were positively associated with cognitive abilities in girls but not in boys (Rahman et al. 2017).

Overall, the above studies support an association between exposure to elevated levels of manganese in drinking water and neuropsychological issues in children (Health Canada 2019a). However, these studies do not allow the temporality of the association to be determined. Additionally, the risk of spurious associations was estimated to be high, and exposure measurements were generally poor, since they relied on a single measurement of a single sample (Health Canada 2019a).

Although there is a large database that examines manganese-induced neurotoxicity in humans exposed via drinking water, the effects of manganese exposure through diet have been sparsely studied. At present, no studies have been identified that examine the potential neurological effects in children exposed to excess levels of manganese via the diet or supplements.

Diet

In a review by Greger (1999), people eating Western-type and vegetarian diets were estimated to have manganese intakes in the range of 0.7 mg/day to 10.9 mg/day, as measured by food consumption recall surveys, total diet study analyses, or duplicate diet composite analyses conducted in various countries, including Canada. An earlier study by Davis and Greger (1992) identified a LOAEL of 15 mg/day, where significant increases in serum manganese concentration after 25 days of supplementation and increases in lymphocyte Mn-SOD activity after 90 days of supplementation were observed (as reported in IOM 2001). It should be noted that neither of these studies were designed to assess toxicity, including neurotoxicity. Instead, they were used to estimate average intakes for generally healthy-appearing individuals and to demonstrate that increased Mn-SOD activity is associated with increased manganese intake through supplementation. Neurotoxicity was not assessed in either of these studies.

In a study by Finley et al. (2003), 17 healthy young women were exposed to diets containing radiolabelled manganese (^{54}Mn) at either 0.8 or 20 mg Mn/day for 8 weeks in a metabolic unit. During the dietary period, blood analysis and neuropsychological tests were administered at regular intervals. Manganese intake up to 20 mg/day did not show any effect on neurological measures or hand steadiness; however, this dose level was associated with decreased self-confidence, which is a measure of assertiveness. Manganese absorption, as percent of administered dose, was almost 40% lower in the high manganese diet group compared to the low diet group. Consequently, a 25-fold increase in manganese intake resulted in only a 3- to 4-fold increase in retention of whole-body manganese after 60 days. The biological half-life was twice as long in the low diet group compared to the high diet group. On the basis of the study results, the authors concluded that a dietary intake of 0.8 mg/day to 20 mg/day for 8 weeks likely does not result in manganese deficiency or toxicity symptoms in healthy adults. However, it was acknowledged that continued intake at 20 mg/day may have resulted in the accumulation of manganese over time.

Kresovich et al. (2018) examined circulating inflammatory markers relative to dietary manganese intake in 633 healthy elderly male veterans (average age of 73 years). Total estimated dietary intakes of manganese and other macro- and micronutrients were calculated using self-administered, semi-quantitative food frequency questionnaires. Participants were divided into quartiles based on estimated manganese intakes (≤2.68, 2.69 to 3.86, 3.87 to 5.47, and ≥5.48 mg/day, respectively). After adjustment for multiple comparisons, estimated dietary manganese intake was positively associated with 1) circulating concentrations of interleukin 8, which has been increasingly recognized as a risk factor for a multitude of chronic diseases and 2) methylation of 2 gene bodies (NKAP and NKAPP1) that regulate the NF-κβ pathway, a major contributor to interleukin production.

The Institute of Medicine (IOM; 2001) set a Tolerable Upper Intake Level (UL) for manganese (11 mg/day for adults), identifying neurotoxicity and elevated blood

manganese as the critical adverse effects on which to base this value. Following their review of the data, they preferred to use human data rather than animal data to support this endpoint. The upper value for the average intakes cited by Greger (1999; 11 mg/day Mn in food) and the LOAEL of 15 mg/day from Davis and Greger (1992), as discussed above, were designated as the no-observed-adverse-effect level (NOAEL) and LOAEL for this value, respectively. The IOM applied a UF of 1, citing a lack of evidence of human toxicity from doses less than 11 mg/day of manganese from food; however, none of the studies in their review assessed neurotoxicity associated with dietary intakes in a healthy population. The UL values for children and adolescents were extrapolated from those established for adults. For infants, the UL was deemed "not determinable" by the IOM due to a lack of data on adverse effects in this age group and concerns about an infant's ability to handle excess amounts. To prevent high levels of manganese intake, the only source of intake for infants should be from food or formula (IOM 2001).

In utero exposure

Associations between *in utero* manganese exposure and outcomes in children at birth (Zota et al. 2009; Chen et al. 2014; Ashley-Martin et al. 2018) have been investigated in studies with mother-child pairs. Throughout pregnancy, maternal blood manganese concentrations rise to meet the nutritional requirements of the fetus during the prenatal growth period, with even higher levels measured in umbilical cord blood at birth (Arbuckle et al. 2016). However, the threshold at which manganese shifts from being beneficial to toxic is unclear (Anglen Bauer et al. 2021). Mothers with low and high manganese concentrations have been observed to have smaller infants, which suggests an inverted U-shaped association (Zota et al. 2009; Chen et al. 2014; Ashley-Martin et al. 2018). There was no association between birth weight and manganese concentrations in cord blood. In a prospective study with 1,179 mother-child pairs, Dai et al. (2021) observed that prenatal manganese exposure (as measured by concentration in cord blood) was positively related to ponderal index (relationship between body weight and height) at birth and negatively related to physical growth in childhood (up to and including age 3). Possible biological mechanisms underlying the associations between maternal blood manganese levels and birth outcomes may include effects on key pregnancy-related enzymes and pathways, such as matrix metalloproteinases (Au et al. 2016).

Associations between manganese levels *in utero* (as measured by maternal and/or umbilical cord blood) and lasting effects on neurodevelopment have also been reported in infants and children aged 6 months to 6 years old (Takser et al. 2003; Lin et al. 2013; Chung et al. 2015; Claus Henn et al. 2017). Manganese concentrations increase in maternal blood during gestation and accumulate in cord blood, which is associated with greater transfer to the fetus. After adjusting for potential confounders, Takser et al. (2003) noted negative relationships between manganese levels in cord blood and several psychomotor sub-scales (attention, non-verbal memory, and hand skills) at 3 years. In a study by Chung et al. (2015), associations between maternal blood

manganese and mental and psychomotor developmental index scores in 6-month-old infants followed an inverted U-shaped dose-response curve, after adjustment for potential confounders. A shift from positive to negative outcomes was noted at blood manganese concentrations of 24 µg/L to 28 µg/L. In a similar study by Claus Henn et al. (2017), cord manganese concentrations were not associated with neurodevelopment scores at 2 years of age; however, cord/maternal and cord/total manganese ratios were associated with mental and psychomotor developmental indexes. Associations with neurodevelopment scores were negative for pairs with high maternal, high cord, or high maternal and cord manganese. In addition, a series of recent studies (Oppenheimer et al. 2021a, 2021b, 2022) have found negative associations between prenatal manganese exposure and concentration/attention, cognitive flexibility, and working memory in adolescents. Effects were observed in the presence of a 2-fold increase in manganese concentrations in umbilical cord blood at birth.

Leonhard et al. (2019) reported results from a systematic review, examining studies with manganese biomarkers that assessed neurodevelopmental outcomes from birth to 15 years old. However, the study results were of questionable quality due to study limitations.

Animal studies

The acute oral toxicity of manganese varies depending on the chemical species, solubility, and route of exposure (dietary versus gavage) but is generally considered low. In several gavage studies conducted on adult rats, the median oral lethal doses (LD_{50} values) ranged from 250 mg Mn/kg bw (as manganese chloride) to 1,082 mg Mn/kg bw (as manganese acetate) (Hazaradze 1961; Smyth et al. 1969; Kostial et al. 1989, all cited in Health Canada 2019a; WHO 2011). Manganese sulfate has an LD_{50} of 782 mg/kg bw when administered in water via gavage; however, survival was not affected when manganese sulfate was administered via the diet up to 1,300 mg/kg bw/day over 14 days (NTP 1993). This demonstrates the relevance of route and vehicle.

Neurological effects (decrease in total activity, delayed acquisition of an avoidance reaction, increased latency of conditioned reflex activity, and delayed learning) were noted in rats following a single exposure of 50 mg/kg bw aqueous manganese chloride by gavage. However, these effects were reversible.

Kern et al. (2010) provided a detailed investigation of the neurodevelopmental effects of manganese exposure in rats. In this study, neonate rats were gavage-dosed daily, via micropipette, with 0, 25, or 50 mg/kg bw/day of manganese as $MnCl_2$ in sucrose solution from PND 1 to 21 (early life). The neonates were nursed by the dams, and after weaning, the animals were fed rodent chow. Although rat milk and rodent chow contain manganese, the test dose levels do not incorporate the contribution of manganese from these sources. The animals had access to municipal water (manganese levels were below the city's detection limit) *ad libitum*.

Behavioural performances were evaluated using open arena (PND 23), elevated plus maze (PND 23), and 8-arm radial maze (PND 33 to 46) paradigms to assess the development of attention, learning, and memory. In addition, levels of dopamine receptor and transporter proteins (that is, D1, D2, and DAT) were measured in the brain to coincide with behavioural testing on PND 24 and 36. On the basis of changes in neurobehavioural effects (impaired spatial learning and stimulus response), along with reductions in D1-like receptors in the dorsal striatum, a LOAEL of 25 mg Mn/kg bw/day was established. At 50 mg/kg bw/day, impacts on learning and memory were more pronounced. In addition, hyper-reactivity and/or disinhibition of exploratory behaviour, decreased DAT in the nucleus accumbens and dorsal striatum, and increased D2 receptors in the prefrontal cortex were noted. A NOAEL was not achieved, as adverse effects were present at the lowest dose tested. The data suggest that excess exposure to manganese during early development can cause significant alterations to dopaminergic regions that mediate control of executive function behaviours, such as impulsivity, hyper-reactivity, and cognitive flexibility.

In a follow-up study using the same dosing regimen, Kern and Smith (2011) investigated whether early exposure to manganese would cause neurobehavioural and neurochemical effects lasting into adulthood. Rats were exposed to 0, 25, or 50 mg/kg bw/day $MnCl_2$ via gavage from PND 1 to 21, without further exposure, and examined for effects that persisted later in life despite cessation of dosing. Behavioural performance in the open arena (PND 97), levels of dopamine receptor and transporter proteins in the prefrontal cortex, striatum, and nucleus accumbens (PND 107), and astrocyte marker glial fibrillary acidic protein (GFAP) levels in these same brain regions (PND 24 and 107) were assessed. Behavioural performance was also assessed on PND 98 in the presence of a d-amphetamine challenge. Although blood and brain levels of manganese had returned to background levels upon termination of the study, lasting changes in the dopaminergic system and elevations in GFAP (a marker of neuronal death) in the brain regions that mediate executive function behaviours were observed at dose levels of 25 mg/kg bw/day and above. Motor activity levels were unaffected in exposed animals on PND 97; however, an enhanced locomotor response was observed following the d-amphetamine challenge, which may be indicative of greater susceptibility to other neurotoxic agents, following manganese exposures in early life. Taken together, the results of the Kern et al. (2010) and Kern and Smith (2011) studies suggest that children exposed to elevated levels of manganese as infants could be at increased risk for neurodevelopmental deficits that may persist into adulthood.

A subsequent study by Beaudin et al. (2013) was designed to compare effects of manganese exposure on neonate rats, with one group exposed daily in early life only (0, 25, or 50 mg/kg bw/day of manganese as $MnCl_2$, via gavage from PND 1 to 21) and one group receiving lifelong exposure (0, 25, or 50 mg/kg bw/day from PND 1 to ~400). From PND 1 to 21, manganese was administered through a solution via micropipette, while exposure during post-weaning (PND 22 to end of study) occurred via the animal's drinking water (Beaudin et al. 2013). Manganese concentrations on PND 24 increased by approximately 2.7x and 3.1x, relative to controls, for 25 or 50 mg/kg bw/day, respectively. Manganese concentration in the brain was similar to controls on PND 64

for all groups, with the exception of concentration measured in the lifelong 50 mg Mn/kg bw/day dose group, which remained elevated. Both dosing regimens (early life and lifelong) resulted in significant neurological effects compared to the control animals. In animals exposed during early life only, impairments in all performance outcomes were noted at 50 mg Mn/kg bw/day but not at 25 mg Mn/kg bw/day. In animals with lifelong exposure, greater impairment in reaching and grasping/retrieval performance was noted in the 25 mg Mn/kg bw/day dose group, relative to the 50 mg Mn/kg bw/day dose group. In comparing early life to lifelong exposure, it was found that animals with lifelong exposure to 25 mg Mn/kg bw/day performed significantly worse than their counterparts exposed to manganese in early life only. However, the observed impairments were similar between the 50 mg Mn/kg bw/day lifelong and early life exposures, indicating that continuous exposure at this dose caused little additional impairment in skilled motor behaviour beyond that produced by early life exposure (Beaudin et al. 2013). These results demonstrate the ability of manganese exposure in early life to cause persistent effects into adulthood, even after levels of manganese in the brain have returned to normal, which is indicative of lasting changes.

Building on the findings from Beaudin et al. (2013), a subsequent study by Conley et al. (2020) used the same early postnatal and lifelong dosing regimens in rats described above, and reported additional effects. Heightened behavioural reactivity during the first 5- to 10-minute intervals of daily open field test sessions, suggestive of impaired arousal regulation, was noted at ≥ 25 mg/kg bw/day for both dosing regiments, although prolonged exposure did not exacerbate this effect. Manganese exposure also reduced the evoked release of norepinephrine (NE) and decreased protein levels of tyrosine hydroxylase (TH), dopamine (DA) and NE transporters, and DA D1 receptors. DA D2 receptors were increased. An increase in reactive astrocytes was indicated by increased levels of GFAP, which were predominantly of the A1 proinflammatory phenotype. The results suggest that elevated levels of manganese exposure in early life results in hypofunction of the medial prefrontal cortex catecholaminergic systems, which may be a contributor to neurological impairment reported in children exposed to manganese.

Neurodevelopmental effects have also been investigated in mice (Foster et al. 2018; Batschauer et al. 2021). Increased brain manganese concentrations, along with a negative correlation between striatal manganese concentration and motor activity were observed at doses of 11 and 25 mg/kg bw/day in a pilot study examining developmental manganese exposures; however, the study authors also noted body weight effects, which may have contributed to the findings on motor activity and cautioned against coming to a conclusion without further study (Foster et al. 2018). In a modified one-generation reproductive toxicity study (Batschauer et al. 2021), indications of anxiety-like behaviour and alterations in memory were observed for animals exposed to 1.3 mg/kg bw/day through parental animals (premating, gestation, and lactation), followed by direct dosing via gavage. Minimal changes (decreased immobility, which may be indicative of hyperactivity) were observed in animals that were administered the same dose but that were not dosed after weaning. The methods used in the Batschauer et al. (2021) study to assess learning and memory (object recognition test) were not

consistent with validated paradigms for developmental neurotoxicity testing, calling into question the validity of the test. In addition, some parameters showed high variability, with greater differences between/within duplicate control groups than those observed between treatments and controls.

Anxiety-like behaviour and learning and memory impairment have also been observed in adult Swiss albino mice (Anjum et al. 2019) exposed to 10 mg/kg bw/day manganese chloride in drinking water for 60 days. Significantly decreased levels of brain cholinesterase were noted, along with significantly increased levels of manganese in the brains of treated mice. Effects on the enteric nervous system (ENS) were also investigated in a study with adult C57BL/6 mice exposed to 15 mg/kg bw/day manganese (as $MnCl_2 \cdot 4H_2O$) via gavage (Ghaisas et al. 2021) for 30 days. Manganese exposure triggered inflammation in the gut, as well as slower peristalsis, with mitochondrial damage to enteric glial cells from exposed rats in an *in vitro* component from the same study. Considering the communication between the ENS and central nervous system (CNS) via the gut–brain axis, it was suggested that additional studies be conducted to assess whether these effects contribute to gradual impairment in CNS functioning.

Manganese has been reported to alter the development of the reproductive system (Health Canada 2019a; ATSDR 2012). Precocious pubertal development was observed in rats exposed to between 10 mg/kg bw/day and 25 mg/kg bw/day $MnCl_2$ by oral gavage in early postnatal development (Pine et al. 2005; Lee et al. 2006). Manganese exposure advanced the age of vaginal opening in female rats (Pine et al. 2005; Yang et al. 2020) and increased the rate of daily mature sperm production in male rats (Lee et al. 2006).

Results from newer studies are consistent with the health effects noted in earlier studies, providing support for the choice of a developmental neurotoxic POD. The rat is the preferred species for neurotoxicity testing in rodents (NAFTA TWG Pesticides 2016) and has been more thoroughly studied, with more robust studies being conducted for developmental neurotoxicity associated with oral manganese exposure. Mice appear to be more sensitive than rats, with effects being noted at a lower dose in mice (1.3 mg/kg bw/day); however, these effects were not observed later in life in animals for which dosing stopped on PND 21. The mouse studies also examined a limited number of animals and parameters. None of the mouse studies above were considered adequate for setting a POD for use in risk characterization.

Data on carcinogenicity, mutagenicity, and genotoxicity are inconclusive (Assem et al. 2011). The United States Environmental Protection Agency (US EPA) has classified manganese as Group D (not classifiable as a human carcinogen) due to the inadequate number of studies that exist to assess the carcinogenicity of manganese (US EPA 1996). In a carcinogenicity study by the National Toxicology Program, rats (30 mg to 331 mg of Mn/kg bw/day in males, 26 mg to 270 mg of Mn/kg bw/day in females) and mice (63 mg to 722 mg of Mn/kg bw/day in males and 77 mg to 905 mg of Mn/kg bw/day in females) were fed manganese sulfate via diet for 2 years (NTP 1993). No

treatment-related carcinogenic activity was reported in rats for both sexes. In mice, there was a significant increase in follicular cell hyperplasia of the thyroid at the highest doses tested. In addition, a marginal increase in the incidence of thyroid gland follicular cell adenoma was observed in treated mice compared to controls (US EPA 2003; WHO 2021).

The results of *in vitro* genotoxicity testing of manganese are dependent on the test system and the associated protocol used (Assem et al. 2011; Health Canada 2019a), and the results of *in vivo* testing in mammals are inconsistent (US EPA 2003; Health Canada 2019a). Overall, no conclusion can be made about the genotoxicity of manganese compounds in humans (Health Canada 2019a).

The available data examining the health effects associated with manganese exposure through diet are insufficient to derive a POD for risk assessment. The gavage-dosed drinking water studies in neonatal rats were considered to provide the best available data to characterize risk, as they were conducted on the most sensitive subpopulation and thoroughly assessed the critical effect (that is, developmental neurotoxicity). Although differences have been noted in the bioavailability of manganese in food versus in drinking water for adult individuals in a fasted state, manganese bioavailability was similar under other (non-fasted) conditions, and it is unknown whether these differences also apply to or exist in the subpopulation of interest, that is, the young.

Health Canada set the drinking water guideline for manganese (that is, MAC) at 120 µg/L (Health Canada 2019a), incorporating an uncertainty factor (UF) of 1,000, which accounts for interspecies extrapolation (x10), intraspecies variation (x10), and the use of a LOAEL rather than a NOAEL (x10). The LOAEL of 25 mg of Mn/kg bw/day is appropriate for both short- and long-term exposure, as behavioural neurological effects were noted following a short-term exposure in early life (PND 1 to 21).

It should be noted that the above critical POD was not based on the lowest neurotoxicological endpoint available in the literature for oral exposure to manganese in experimental animals. Other studies indicated neurotoxicity or reproductive toxicity for oral exposure to manganese at lower dose levels (Golub et al. 2005; Pine et al. 2005; Vezer et al. 2005, 2007 as cited in Health Canada 2019a; Anjum et al. 2019; Yang et al. 2020); however, these studies were not selected due to various study limitations, including the lack of a clear account of animal dosing, lack of information on chronic effects, and confounding factors that hindered the interpretation of dose-response data.

8.1.4 Health effects via the inhalation route of exposure

The previous assessments by Health Canada (1994, 2010a) and other international organizations (EC 2011; ATSDR 2012; MAK 2005, as discussed in Triebig et al. 2012) were used to inform the section on health effects associated with inhalation exposure. In addition, searches were conducted of published literature from between 2009 and January 2022 to identify additional studies of adequate quality and relevance for inclusion in the assessment of inhalation toxicity.

Following a review of the available information, the Health Canada (2010a) reference concentration (RfC) for inhaled manganese, set at 0.05 µg/m^3 remains the most suitable guideline for the risk characterization of manganese exposure via the inhalation route in the general population. This RfC was established using a neurofunctional endpoint, which is considered to be the most sensitive marker associated with exposure to low concentrations of manganese via inhalation. A $BMCL_{05}$ of 19.2 µg/m^3 for fine motor control (Luria Nebraska sum) was derived from the Lucchini et al. (1999) data set. This value was converted from an occupational exposure regime (8 hours/day, 5 days/week) to a continuous exposure scenario, and a UF of 100 (10x for inter-individual variation and 10x for database uncertainty) was applied. An additional database UF was applied to account for variations in the solubility of manganese compounds, a lack of information on the impact of prenatal manganese exposure on the fetus, and unknowns associated with the significance of changes in prolactin values in the general population (Health Canada 2010a). Consequently, this value is expected to be protective of developmental neurotoxic effects that may occur. It should be noted that this value is in line with the US EPA RfC of 0.05 µg/m^3, which was established in 1993 (US EPA 2002) on the basis of a study by Roels et al. (1992).

Both human and animal studies have found the CNS and the lungs to be the primary target organs for the toxicity of manganese and its inorganic compounds following inhalation exposure (Triebig et al. 2012). Inhaled manganese is not regulated by homeostasis and enters systemic circulation directly from the lungs, making manganese more readily available for distribution and accumulation in the body. Manganese can also travel directly to the brain via the olfactory and trigeminal nerves; uptake via these pathways is influenced by solubility and particle size. These direct pathways to the brain are the primary reason that the inhalation route is associated with increased susceptibility to manganese toxicity compared to the oral route (Dorman et al. 2006a; Health Canada 2010a, 2019a).

Respiratory and lung effects associated with manganese exposure do not appear to occur at levels below those at which identifiable neurological changes can be detected, indicating that neurotoxicity is the more sensitive POD for chronic exposures. As a result, it is expected that risk characterization based on a neurotoxic POD will be protective of effects (respiratory, reproductive, and developmental) that may occur with higher doses.

Health Canada (2010a) provides a more comprehensive discussion of the occupational studies and experimental animal data up until 2010. The studies referenced in this document are limited to critical studies and informative data subsequent to 2009.

Human studies

Health effects associated with inhaled manganese have been investigated in a large number of epidemiological studies. As the CNS is the most sensitive target tissue, these studies primarily assessed effects on subclinical neurofunctional outcomes such as fine motor control, tremor, memory, and aspects of cognitive ability (Health Canada 2010a),

though subtle mood changes (emotional instability, compulsive behavior) may occur earlier (Bjørklund et al. 2020).

A Canadian epidemiological study conducted in adults near the location of a former ferromanganese plant in southwestern Quebec (Mergler et al. 1999 as cited in Health Canada 2010a) was one of the first to identify adverse effects on non-occupationally exposed individuals. Elevated blood manganese was associated with poorer outcomes for hand tremor, postural sway, and Luria Nebraska sum scores, while no effects on finger tapping or motor function were discernable. Effects were more pronounced in men and individuals over 50 years old (Lucchini et al. 2015). Older adults were more sensitive in tests of coordinated upper limb movements, attention and memory (males only), and mood. However, the study did not include adequate inhalation exposure data, and, consequently, neither a dose-response nor a RfC could be derived.

The 2010 Health Canada risk assessment considered details from 17 occupational studies and 1 general population study (Mergler et al. 1999, as detailed above) that used sensitive neurofunctional tests to assess subclinical manganese toxicity. The most frequently noted effects were deficits in motor skills and reaction speed. Finger tapping, hand tremor, and hand dexterity/speed and digit symbol tests were most frequently able to detect decrements induced by manganese exposure. Negative associations were also reported for memory, attention, and concentration; however, results were not consistent.

Health Canada (2010a) identified the Lucchini et al. (1999) study as the critical study for establishing the revised Health Canada RfC for inhaled manganese. Lucchini et al. (1999) was an occupational study conducted with 61 exposed Italian silico- and ferromanganese workers (mean exposure of 15.2 years) and 87 control subjects. To investigate manganese toxicity, the study administered a battery of neuropsychological tests assessing motor function, short-term memory, cognitive function, and tremor. Serum levels of the hormone prolactin were measured to assess dopamine activity levels, as the secretion of prolactin is inhibited by dopamine activity. Prolactin levels have been investigated as a possible biomarker of manganese exposure and effect in a number of studies (Health Canada 2010a). Motor functions requiring alternating and rapid movements, short-term memory, and some tremor parameters were negatively altered in manganese-exposed workers, relative to the unexposed control group (Lucchini et al. 1999). The study also demonstrated that serum prolactin levels increased significantly as manganese exposure increased.

BMC analysis was conducted on the original data set obtained from Lucchini et al. (1999). A $BMCL_{05}$ (BMCL associated with a bench mark response of 5%) of 19.2 $\mu g/m^3$, which was based on changes in fine motor skills, was selected as the critical POD for the Health Canada guidance value for inhaled manganese. Of the endpoints assessed, this provided the lowest POD. This value was converted from an occupational exposure regime (8 hours/day, 5 days/week) to a continuous exposure scenario, and a UF of 100 (10x for inter-individual variation and 10x for database uncertainty) was applied to

derive an inhalation RfC of 0.05 µg/m^3 for the respirable fraction ($PM_{3.5}$) of manganese, applicable to continuous exposure by the general population.

Data from an occupational study of dry alkaline battery factory workers (Roels et al. 1992) were used in previous derivations of the inhalation RfC. RfCs set using this study ranged from 0.05 µg Mn/m^3 to 0.30 µg Mn/m^3 (Health Canada 1994; WHO 1999; US EPA 2002; ATSDR 2012). In 1994, Health Canada selected a NOAEL of 0.102 mg/m^3 average respirable exposure for eye-hand coordination (Health Canada 1994) and a composite assessment factor of 300 to derive the inhalation RfC of 0.11 µg/m^3 (converted to continuous exposure).

In another occupational study by Gibbs et al. (1999), a group of manganese metal (electrolytic) production workers did not report any adverse effects, relative to a matched control group with no known occupational exposure to manganese. Assessment of mood, memory, and fatigue as well as several neurobehavioral tests including hand steadiness, eye-hand coordination, and rapidity of motion were conducted. However, in 2003, Clewell et al. re-examined this data set using BMC methodology and identified $BMCL_{10}$ values ranging from 65 µg/m^3 to 360 µg/m^3 (30-day cumulative respirable manganese) for fine motor effects (eye-hand coordination, hand steadiness, tapping time, and reaction time). These endpoints were identified from data that had been previously thought to show no dose-responses and no significant effects associated with airborne manganese exposure (as detailed in Health Canada 2019a).

Recent systematic reviews of the literature have identified studies that examined airborne manganese exposure in the general population (non-occupational) and associated neurological effects, or biomarkers of exposure (Martins et al. 2020; Fernández-Olmo et al. 2021; Ruiz-Azcona et al. 2021). Studies identified in these systematic reviews were mainly carried out in areas near industrial activities or in urban areas, where methylcyclopentadienyl manganese tricarbonyl (MMT) can be used as a gasoline additive. The majority are cross-sectional studies, which prevent a temporal sequence from being established. Behavioural and cognitive effects noted in these studies were likely attributable to past exposures, rather than current or recent exposure, which is what is reported. In addition, age-related changes in vulnerability, and therefore the critical windows of exposure, remain uncertain.

Fernández-Olmo et al. (2021) concluded that, although neurological/neuropsychological impairments (mainly motor) have been associated with manganese exposure, predominantly measured by manganese concentrations in hair, this association is not always statistically significant. Moreover, it is challenging to compare studies due to their heterogeneous design (different measures of airborne manganese, different biomarkers of exposure, different tests to assess the same neurological/neuropsychological outcomes, different data analysis strategies, and the use of different potential confounders in statistical models). In a meta-analysis of 11 studies conducted on adults, Ruiz-Azcona et al. (2021) reported statistically significant negative correlations between manganese exposure and both cognitive and motor

functions (the higher the manganese levels, the poorer the scores), using a pooled correlation approach.

Although there were numerous studies (≥25) describing airborne manganese exposure in children, only 5 included both measures of air concentration and assessment of neurotoxicological effects (Riojas-Rodríguez et al. 2010; Lucchini et al. 2012; Torres-Agustín et al. 2013; Hernández-Bonilla et al. 2016; Haynes et al. 2018). Biomarkers of exposure were measured in each of the studies, although there was some variation in the biomarkers chosen. The key findings from these studies are summarized below.

A cross-sectional study reported by Lucchini et al. (2012) examined associations between manganese air concentrations and behavioural, cognitive, and motor functions in a group of Italian adolescents (n=154) living in Valcamonica, a community near a manganese alloy plant where an increased prevalence of Parkinsonism was previously observed. Average airborne (PM_{10}) and mean soil manganese concentrations were 0.0495 µg/m^3 (median: 0.0314 µg/m^3, range: 0.0012 µg/m^3 to 0.517 µg/m^3) and 958 mg/kg (median: 897 µg/m^3, range: 465 µg/m^3 to 1,729 µg/m^3) respectively, representing levels approximately 2-fold higher than those in a non-industrial reference area, with 157 adolescents included for comparison. Regression models showed significant impairment of motor coordination, hand dexterity, and odour identification associated with soil manganese concentration, which is indicative of past airborne exposures. A significant association was also observed between tremor intensity in the dominant hand and manganese concentrations in hair (mean = 0.16 mg/g) and blood (mean = 10.99 mg/L), in addition to a borderline association between tremor intensity and soil manganese concentration. A sex difference was also observed, with lower performance for odour identification and increased tremor intensity noted in boys. The authors suggested that manganese concentration in soil is more representative of historical cumulative exposure to manganese from ferroalloy emission, rather than present activity.

A study by Riojas-Rodríguez et al. (2010), part of a series of studies reviewed here, examined the effects of airborne manganese on neurofunction in a population of school children (7 to 11 years) in the Molango mining district in Mexico. Children in the exposed area (n=79) were compared with a reference group of 93 children outside the mining district. The 24-hour median air concentration of manganese (PM_{10}) in the exposed communities (0.13 µg/m^3) was higher than in the control communities (0.02 µg/m^3). Both groups had mean IQ levels (indicated by Wechsler Intelligence Scale for Children [WISC]-R scores) that were below expected levels (90 to 110 IQ) (Wechsler 1983 as cited in Riojas-Rodríguez et al. 2010); however, the prevalence was significantly higher for the exposed group (92%) than for the control group (73%). The exposed group had significantly lower total, verbal, and performance IQ scores relative to the control group, with the same trend continuing for most of the subtests. Based on manganese concentrations measured in hair, young girls were most affected in comparison to boys. The study authors commented that the cognitive effects were not likely attributable to current or recent exposure and that critical windows of manganese exposure in children remain uncertain due to a lack of longitudinal studies.

A follow-up study by Torres-Agustín et al. (2013) examined effects on verbal memory and learning in a cross-sectional study targeting the same population in Mexico's Molango mining district. The Children's Auditory Verbal Learning Test, with subscales on learning curve, immediate recall, delayed recall, recognition accuracy, immediate memory span, and level of learning, was administered to assess cognitive ability. Median outdoor (0.08 µg/m^3) and indoor area (0.07 µg/m^3) $PM_{2.5}$ manganese concentrations were higher in the exposed community compared to the reference community (0.02 µg/m^3). Long-term memory test scores, adjusted for relative covariates, were on average lower for the exposed group than for the non-exposed group of children. A negative association between manganese exposure, as measured by manganese in the hair, and long-term memory was more pronounced in girls than in boys.

Hernández-Bonilla et al. (2016) also examined the effects associated with airborne manganese exposure in 148 school-aged children (7 to 11 years) from the same mining district, compared with a group of 119 children in the same reference community. Visual perception and short-term memory were assessed using the Rey–Osterrieth Complex Figure (ROCF) test. Manganese concentrations in ambient air had previously been reported in 2006 (0.080 µg/m^3 for $PM_{2.5}$, 0.470 µg/m^3 for PM_{10}) and 2013 (0.010 µg/m^3 for $PM_{2.5}$, 0.240 µg/m^3 for PM_{10}) for the mining area. Manganese air concentrations in the reference area remained constant at 0.020 µg/m^3 for PM_{10} during this time, as reported in Fernández-Olmo et al. (2021). Manganese exposure, as estimated by manganese levels in hair, was also associated with alterations in visuoperception and short-term visual memory, with a greater impact on the accuracy of visuoperceptive function in girls.

Haynes (2018) investigated the impact of air manganese on the neurodevelopment of children 7 to 9 years of age (n=106) from East Liverpool, Ohio, and its surrounding communities. Environmental health concerns were identified in connection with a hazardous waste incinerator and a manganese processor in the community, as well as with airborne manganese concentrations exceeding the US EPA RfC (0.050 µg/m^3) for over a decade. A significant inverse association between manganese concentrations in hair and Full Scale IQ was identified, which was most apparent in working memory and processing speed subscales; however, correlations with manganese concentrations in air were not reported. No significant difference was observed between the sexes.

Associations between airborne manganese and neurological effects were examined in 288 adults (120 men and 168 women; aged 20 to 87 years) living in a mining district in Molango, Mexico (Rodríguez-Agudelo et al. 2006; Solís-Vivanco et al. 2009). Rodríguez-Agudelo et al. (2006) evaluated motor function in this population using a neuropsychological battery. Airborne manganese concentrations ranged from 0.003 µg/m^3 to 5.86 µg/m^3, with an average concentration (geometric mean) of 0.13 µg/m^3. Approximately ¾ of the study group were exposed to levels of airborne manganese greater than the US EPA-recommended guideline level for non-occupational environments (0.05 µg/m^3). Mean blood manganese concentration was 9.44 µg/L (range of between 5.0 µg/L and 31.0 µg/L). A statistically significant

association was identified between manganese in air and motor tests that assessed position changes in hand movements (OR 3.09; CI 95% 1.07, 8.92). An association was also found between verbal regulations of movements and airborne manganese (OR 2.30; CI 95% 1.00, 5.28). Solís-Vivanco et al. (2009) also examined the association between airborne manganese and cognitive functions in the same population. Airborne manganese was associated as a risk factor for attention impairment (OR 1.75, 95% CI 1.01 to 3.06). There was no association between manganese concentrations in blood and motor activity or cognitive function in these 2 studies.

Lucchini et al. (2014) examined neurobehavioural effects (motor, cognitive, and sensory functions) in the elderly associated with long-term exposure to manganese. Average airborne manganese was 0.0264 µg/m^3 in Valcamonica and 0.0210 µg/m^3 in the reference area. Differences in surface soil were more pronounced, with 1,026 mg/kg in Valcamonica and 421 mg/kg in the reference area. Lifelong exposure to manganese was significantly associated with changes in odour discrimination, motor coordination, cognitive abilities, and serum prolactin levels. A $BMDL_{01}$ of 0.0227 µg/m^3 (PM_{10}) was generated for the association between airborne manganese and motor coordination. As air manganese (air-Mn) levels were higher in the years prior to ferromanganese operations ceasing in 2001, and as subjects' age and residence histories indicate that they likely suffered greater environmental exposures over the majority of their lifespan, the confidence in the true relevance of this value is low.

A series of studies examined the association between manganese in ambient air and neurological effects in adults from Marietta, Ohio, where a large ferro- and silico-manganese smelter has been active for more than 50 years (Kim et al. 2011; Bowler et al. 2012, 2015, 2016; Kornblith et al. 2018).

Kim et al. (2011) compared results from the Unified Parkinson's Disease Rating Scale (UPDRS), a postural sway test, and a comprehensive questionnaire exploring demographics and general health in 100 exposed subjects to 90 individuals from a reference community with low levels of exposure to airborne manganese. Modelled estimates of residential airborne manganese concentrations ranged from 0.04 µg/m^3 to 0.96 µg/m^3 and averaged 0.18 µg/m^3 in the exposed group but were not reported for the comparison group. The average concentration of manganese in blood was similar for both the exposed and reference areas. After adjusting for covariates, including blood levels of lead, cadmium, and mercury, the risks of abnormal UPDRS Motor and Bradykinesia scores (odds ratios) were 2.42- and 5.18-fold higher, respectively, in the exposed group relative to the comparison group. Bowler et al. (2012) analyzed the same data set as Kim et al. (2011) and reported an association between generalized anxiety and cumulative exposure on the basis of modelled manganese air concentration and length of residence. Higher generalized anxiety scores were related to poorer performance in motor-related activities of daily living, bradykinesia, and movement.

In a follow-up study by Bowler et al. (2015), individuals from East Liverpool, Ohio, were added on the basis of the same inclusion/exclusion criteria used for the Marietta community (minimum of 10 years residency, 30 to 75 years of age, no major illness or

exposure to toxic substances requiring hospitalization, without a diagnosis of psychiatric or degenerative disorder, and no work history at a manganese-emitting facility). This study included 86 individuals from East Liverpool and 100 individuals from Marietta, with no additional low exposure group. A comprehensive screening test battery of cognitive function, including the domains of abstract thinking, attention/concentration, executive function, and memory, was administered. Modelled estimates of airborne manganese concentration for PM_{10} ranged from 0.03 μg/m^3 to 1.33 μg/m^3 in Marietta and from 0.005 μg/m^3 to 2.21 μg/m^3 in East Liverpool, with arithmetic means of 0.18 and 0.31 μg/m^3 for Marietta and East Liverpool, respectively. Significant inverse relationships occurred between modelled concentrations of manganese in air and performance on tests for cognitive measures of visuospatial memory and verbal skills. In addition, relationships approached significance between modelled manganese in air and performance on tests of cognitive flexibility, executive function, immediate and delayed visual memory, working memory, attention, and learning, indicating that higher exposures were associated with poorer performance. In a subsequent report on this data set by Bowler et al. (2016), modelled manganese exposure in air was significantly correlated with tremor, with proximity to the manganese exposure point source affecting the frequency and acceleration of the tremor oscillations.

The data collected on neurological, neuropsychological, physiological, mood, and health measures in residents from Marietta and East Liverpool were further examined by Kornblith et al. (2018) to develop symptom profiles associated with manganese exposure. These profiles were then compared with the effects identified for Parkinson's disease, as reported in the literature. While tremor and no tremor clusters were identified, similar to what has been observed with Parkinson's disease, executive dysfunction did not cluster along with other non-tremor symptoms (gait disturbance and bradykinesia/rigidity). The different symptom patterns associated with manganese exposure and Parkinson's disease point to different pathophysiology and developmental courses for these 2 conditions.

Limitations noted across population studies, both in children and adults, include the lack of a temporal relationship, as mentioned earlier, which limits the observation of progression in effects over time. Subclinical effects noted in groups exposed to manganese may reflect early subtle effects associated with chronic low-level exposure to manganese in air; however, these early subtle effects may also be partly due to chance. In addition, many studies used modelled estimates for air concentrations or provided individual manganese exposures at current concentrations only, making it difficult to calculate past and/or cumulative exposures. Particle size fractions of manganese measured and reported varied between studies, making comparison between studies difficult. Previous studies in occupational populations involved mainly male populations, with little representation of effects in females. While the studies summarized here included details on both males and females, the influence of sex on the development and progression of neurodegenerative diseases, including the potential impact of hormonal effects on pharmacokinetics, remains to be discerned. The lack of a reliable biomarker also limits the exploration of associations between exhibited health effects and internal manganese concentrations. In addition, many known co-

exposures may influence neurotoxicity, including the presence of other metals such as lead and mercury. While adjustments were made for potential confounding factors where possible, the failure to consider concomitant exposures, as well as other unknown confounders, may have contributed to the outcomes noted.

Animal studies

Acute exposure to inhaled manganese has been observed to cause respiratory effects, including pulmonary edema and inflammation in experimental animals at concentrations ≥ 2.9 mg Mn/m^3 as manganese oxide (Adkins 1980 as cited in OEHHA 2014; Bergström 1977).

Transient, site-of-contact inflammatory lesions have been noted in the respiratory tract of young adult rats and rhesus monkeys, following repeated exposures (6 hours/day, 5 days/week, ≥65 days) to manganese sulfate. Inflammation, characterized by pleocellular inflammatory infiltrates and fibrinonecrotic debris, was observed in the nasal respiratory epithelium of Sprague-Dawley rats that were administered 0.5 mg Mn/m^3 (Dorman et al. 2004b as cited in ATSDR 2012). Effects were not noted in animals exposed to a lower concentration of 0.1 mg Mn/m^3. In a separate study, lesions in the lower respiratory tract (mild subacute bronchiolitis, alveolar duct inflammation, and proliferation of bronchus-associated lymphoid tissue) were noted in rhesus monkeys exposed to 1.5 mg Mn/m^3 as manganese sulfate (Dorman et al. 2005 as cited in ATSDR 2012). Effects were not observed in monkeys exposed to ≤0.3 mg Mn/m^3. Reversibility of effects was noted for both species, following recovery periods of 45 days.

Portal-of-entry effects were also noted in studies reported in the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers for manganese and $MnCl_2$; however, original study reports or reviews from other regulatory jurisdictions were not available for these studies. Lung effects (increased lung weights, alveolar histiocytosis, and alveolitis) were noted in rats after repeated exposures (13 weeks) to manganese as a metallic powder (unknown author 2016 as cited in REACH dossier [modified 2021]). Respiratory tract effects (squamous metaplasia with submucosal inflammation, and bronchoalveolar hyperplasia, degeneration/ulceration in some animals) were also observed in studies with young adult rats exposed (nose-only) to ≥15 mg Mn/m^3 $MnCl_2$ (McGough and Jardine 2017; Dettwiler 2016 as cited in REACH dossier [modified 2020]). Clinical signs, including wheezing and crackling/gasping respiration, and dyspnea, were also noted. Phagocytic alveolar macrophage foci and granulolymphocytic alveolar inflammation were noted at necropsy, along with dose-related increases in incidence and severity.

The general inflammatory response noted in the lung (that is, pneumonitis), accompanied by increased numbers of macrophages and leukocytes, is mainly considered to be an adaptive response of the immune system to inhaled particulate manganese compounds (ATSDR 2012); however, lasting effects were noted at ≥5 mg Mn/m^3 in animals.

In non-human primates examined for behavioural effects, hyperactivity is frequently reported as an early symptom, with symptoms progressing to include abnormal movements, muscular rigidity, and limb flexion (Health Canada 2010a). Tremor is also frequently reported. Behavioural effects often correlate with the occurrence of brain lesions, particularly of the basal ganglia, involving gliosis, depigmentation, and neuronal degeneration and loss (Mella 1924; Gupta et al. 1980; Eriksson et al. 1987; as cited in Health Canada 2010a). The majority of studies available involved oral, intravenous, or subcutaneous exposure. Studies conducted via inhalation are limited. Neurological signs were not observed in female rhesus monkeys (n=4) exposed to manganese dioxide dust (<5 µm) at 30 mg Mn/m^3 for 2 years despite a 60% to 80% increase in manganese concentration in the basal ganglia and significantly decreased dopamine concentrations in the caudate and globus pallidus; however, neurobehavioural effects were not specifically assessed (Bird et al. 1984). Separate studies by Dorman et al. (2006b, 2006c) exposed rhesus monkeys to $MnSO_4$ for 90 days. Behavioural effects were not noted; however, no specific testing was performed. At exposures ≥ 0.06 mg Mn/m^3, increased concentrations of manganese in the globus pallidus, putamen, white matter, and cerebellum were noted, with increases in the caudate, pituitary, frontal cortex, and trigeminal nerve noted at higher concentrations.

In contrast, in exposed rodents, transient modifications of spontaneous motor activity appear to be the most sensitive and frequently reported effect (Health Canada 2010a). Results from these studies have not been entirely consistent, likely due to methodological differences, particularly with regards to the time at which activity was measured following the initiation of dosing (Health Canada 2010a). Alterations in locomotor activity have been noted to occur in rodents following repeat-inhalation exposures (13 weeks) to manganese sulfate (≥0.009 mg Mn/m^3), a manganese phosphate/sulfate mixture (0.01 mg Mn/m^3), and metallic manganese (3.75 mg Mn/m^3), but not with manganese phosphate (≤1.1 mg Mn/m^3) (St-Pierre et al. 2001; Normandin et al. 2002, 2004; Salehi et al. 2003, 2006; Tapin et al. 2006; as detailed in ATSDR 2012). However, results were varied, with some studies reporting increases in total activity levels, while others reported decreases; some studies also lacked dose-response data. These effects were associated with increased levels of manganese in the brain, mainly in the frontal cortex, globus pallidus, and caudate putamen; however, at higher doses, effects were more widespread, including in the olfactory bulb and cerebellum regions. Corresponding decreases in neuronal cell counts in the globus pallidus were observed following exposures to manganese sulfate or the manganese phosphate/sulfate mixture. Decreased cell counts in the caudate putamen were also associated with the mixture only (as detailed in ATSDR 2012). Increases in manganese concentration were noted in the cortex, striatum, and pallidus of rats after 13 weeks of treatment with ≥0.5 mg Mn/m^3, with slight reversal after cessation of dosing (unknown author 2016, REACH dossier [modified 2021]).

Behavioural effects have been observed in rodents following repeated inhalation exposures (90 days) to concentrations ≥ 3 mg Mn/m^3 (Salehi et al. 2003; Normandin et al. 2004; as detailed in Health Canada 2010a). Learning impairments have also been reported in rodents following manganese exposure. Inhalation exposure to manganese

sulfate concentrations ranging from about 0.1 mg Mn/m^3 to 1 mg Mn/m^3 for acute or intermediate durations were noted to differentially affect brain biochemical markers of neurotoxicity (decreased glutamine synthase protein, decreased metallothionein mRNA, decreased TH protein and glutamate transporter-1 mRNA and protein) (ATSDR 2012); however, the impact of these alterations, including the impact on functional measures, is unclear.

Neonatal rodents are more sensitive than adult animals to the accumulation of manganese in the brain after inhalation exposure, as demonstrated by elevated levels of manganese in the striatum following inhalation exposure to 0.05 mg Mn/m^3 for neonatal rats (*in utero* plus neonatal exposure), to ≥0.1 mg Mn/m^3 for young adult male rats, and to >0.5 mg Mn/m^3 for young female adult rats (Dorman et al. 2004a, 2005; as detailed in Health Canada 2010a). A linear dose-related relationship to the lactational transfer of manganese to pups was observed in maternal animals administered $MnCl_2$ dust via inhalation (REACH dossier [modified 2020]). An increase in post-implantation losses and decreased pup survivability (PND 0 to 4) were reported in a reproductive toxicity study (McGough and Jardine 2017); however, these effects occurred along with respiratory effects in paternal animals at doses ≥10 mg Mn/m^3. Developmental effects (enlarged fetal thyroid, with diffuse follicular hypertrophy and/or hyperplasia, and delayed ossification and wavy ribs) were observed in fetuses from maternal animals administered 26 mg Mn/m^3 as $MnCl_2$ in a developmental toxicity study reported in the REACH dossier [modified 2020] (Dettwiler 2016, study report not available). No treatment-related effects were reported for uterine and reproductive parameters. The developmental effects reported above, while concerning, were noted to occur at doses much higher than those associated with neurotoxicity; consequently, a neurotoxic POD provides additional margins for these effect levels.

As stated by Health Canada (2010a), the effects of manganese on systems other than the nervous, pulmonary, and reproductive systems have not been extensively studied, because they are not considered to be primary targets of this metal; however, there is no substantial evidence linking inhaled manganese to significant adverse effects on other organ systems such as the liver, kidney, or pancreas.

8.1.5 Health effects via the dermal route of exposure

The Agency for Toxic Substances and Disease Registry (ATSDR 2012) reported that there were no animal or human studies that examined systemic toxicity, including neurotoxicity, following dermal exposure to inorganic manganese. Several international assessments (WHO 1999; ATSDR 2012) report that exposure to manganese through the dermal route does not appear to be a significant health concern. As neurotoxicity has not been evaluated via the dermal route, it is considered appropriate to compare dermal exposure to the oral endpoint (systemic dose), while taking into account dermal absorption in the risk characterization.

8.1.6 Consideration of subpopulations who may have greater susceptibility

Within Canada there are groups of individuals who, due to greater susceptibility, may be more vulnerable to experiencing adverse health effects. The potential for susceptibility during different life stages or by sex are considered based on the results from the available studies. In this health effects assessment, the studies considered include experimental animal studies that examined developmental and neurodevelopmental effects in the young, including reproductive toxicity studies. In addition, studies that examined neurotoxic effects in human populations near point sources at various life stages (*in utero* and postnatal exposure with mother-infant pairs, children, adolescents, and the elderly) to assess the potential for susceptibility during these critical life stages (as discussed in section 8.1.3) were assessed. Many studies in the hazard database examined differences between the sexes. Overall, the prenatal and postnatal stages, as well as the elderly, were identified as the most susceptible developmental stages for adverse health effects. A developmental neurotoxicity endpoint was used as 1 of the critical health effects to characterize risk from exposure to manganese.

8.2 Exposure assessment

This exposure assessment considers combined exposure to the manganese moiety, from natural or anthropogenic sources. Manganese is a naturally occurring element and it is widely distributed in air, water, and soil. Numerous studies have measured manganese in various media, including whole blood, serum, urine, air, drinking water, food, soil, dust, and products available to consumers. The concentration of manganese in environmental media varies widely depending on the environmental conditions and proximity to anthropogenic sources such as ferroalloy industry facilities (US EPA 2004).

8.2.1 Biomonitoring

Total manganese concentrations have been measured in blood or urine in many national and international population-level biomonitoring surveys, including the Canadian Health Measures Survey (CHMS). Manganese concentrations in whole blood and urine were measured in CHMS participants aged 6 to 79 years in cycle 1 (2007 to 2009) and 3 to 79 years in cycle 2 (2009 to 2011). According to cycle 2 data, the median and 95th percentile whole blood concentrations in the Canadian population aged 3 to 79 years were 9.5 and 15 µg/L, respectively, with a detection rate of 100%, while manganese in urine was detected in only 29% of the samples and the 95th percentile was 0.61 µg/g creatinine (Health Canada 2023). The Maternal-Infant Research on Environmental Chemicals (MIREC) study, which is a national pregnancy cohort study, has also measured manganese in maternal blood, umbilical cord blood, and infant meconium samples (collected between 2008 and 2011). The manganese concentrations in first (8.8 µg/L) and third trimester (12.6 µg/L) maternal blood were comparable to the blood concentration reported for the general population in the CHMS study. A significantly elevated median manganese concentration (31.9 µg/L) was observed in cord blood compared to maternal blood; this was expected, given that manganese crosses the placental barrier (Arbuckle et al. 2016).

Although many authors have studied the suitability of manganese in blood, urine, and other biological matrices as biomarkers to quantify exposure, manganese in blood and urine are not sensitive enough to be considered as biomarkers of exposure for the purposes of this draft assessment. Blood manganese is not considered a sensitive biomarker of exposure for the interpretation of population-level biomonitoring data due to the tightly regulated homeostasis of manganese in blood, while urinary excretion of manganese is generally not responsive to external manganese exposure.

8.2.2 Daily exposure from environmental media, drinking water, and food

8.2.2.1 Air

Airborne manganese in particulate matter (PM) can originate from both natural and anthropogenic sources. Manganese concentrations in outdoor air in Canada can vary depending on the sampling location. Ambient air concentrations of manganese in PM have been measured across Canada as part of the National Air Pollution Surveillance (NAPS) program, by air monitoring networks in Hamilton, Sarnia, and Montreal, and in other studies conducted in Halifax, Windsor, Ottawa, Toronto, and the Ring of Fire region in northern Ontario. Overall, the median and 95th percentile concentrations of manganese in measured outdoor $PM_{2.5}$ ranged from 0.00013 µg/m^3 to 0.0047 µg/m^3 and from 0.00017 µg/m^3 to 0.013 µg/m^3, respectively (NAPS data 2015 to 2019 from NAPS [modified 2021]; Wolf and Ollson 2019; Su et al. 2021; Rasmussen et al. 2022; personal communication, email from the WAQB, Health Canada, to the ESRAB, Health Canada, dated October 26, 2018; unreferenced).

Manganese has also been measured in indoor air samples collected in Halifax, Ottawa, and Windsor. The median and 95th percentile concentrations of manganese measured in household indoor $PM_{2.5}$ ranged from 0.00006 µg/m^3 to 0.0018 µg/m^3 and from 0.0035 µg/m^3 to 0.0097 µg/m^3, respectively (Rasmussen et al. 2022; personal communication, email from the WAQB, Health Canada, to the ESRAB, Health Canada, dated October 26, 2018; unreferenced). Manganese has also been measured in personal air ($PM_{2.5}$ samplers worn on individuals through the day) collected from a study conducted in Windsor, Ontario, in 2005 and 2006 (Rasmussen et al. 2022). Median and 95th percentile concentrations of manganese measured were 0.0019 and 0.0063 µg/m^3, respectively. In this study, the highest manganese concentration in $PM_{2.5}$ was measured in outdoor samples, followed by personal and indoor air samples, (Rasmussen et al. 2022).

From 2010 to 2013, the Urban Transport Exposure Study conducted in Montreal, Ottawa, Toronto, and Vancouver sampled $PM_{2.5}$ inside and outside (monitored on rooftops) private cars, subways, and buses (Van Ryswyk et al. 2017, 2020; personal communication, email from the WAQB, Health Canada, to the ESRAB, Health Canada, dated October 26, 2018; unreferenced). The median and 95th percentile air concentrations of manganese in cars, subways, and buses ranged from 0.0032 µg/m^3 to 0.431 µg/m^3 and 0.0056 µg/m^3 to 0.513 µg/m^3, respectively. Concentrations in subways

and buses were higher than in outdoor air, suggesting that public transit may be a source of exposure to manganese. The highest average manganese concentration was measured in Toronto subways (0.431 µg/m^3). The elevated concentration of manganese was a result of "rail dust" formed from the steel wheels and steel track subway system in Toronto, coupled with predominantly below-grade stations (Van Ryswyk et al. 2017, 2024). Assuming a daily 70-minute commute, subway commuters in Toronto would be exposed to average manganese concentrations of 0.022 µg/m^3 over 24 hours in $PM_{2.5}$, and the subway commute would account for 93% of the manganese in air to which commuters are exposed (Van Ryswyk et al. 2017).

In 2017 and 2018, the Subway Air Quality Initiative and Toronto Transit Commission conducted a health impact assessment and measured manganese concentrations in different microenvironments of the subway. The manganese concentrations measured in $PM_{2.5}$ on the platform were 3 times higher than in the train. Using these concentrations, ambient air concentrations, and time spent on platforms (5 minutes) and in subway trains (1 hour), it was estimated that subway commuters were exposed to a daily time-weighted average concentration of 0.007 µg/m^3 (Wolf and Ollson 2019). These concentrations were higher than the average manganese concentration in ambient $PM_{2.5}$ of 0.0036 µg/m^3, which was measured simultaneously (Wolf and Ollson 2019).

Concentrations of manganese in outdoor air may be influenced by anthropogenic emissions in urban areas, in areas with industrial activity, and from point sources of release. Manganese concentrations have been measured in urban environments with various sources contributing to total manganese in air. Median manganese concentrations in $PM_{2.5}$ measured at NAPS sites in Toronto, Montreal, and Vancouver from 2015 to 2019 ranged from 0.0011 µg/m^3 to 0.0022 µg/m^3 (NAPS [modified 2021]). Manganese was also monitored by air quality networks in Sarnia, Ontario, and in Montreal (RSQA [modified 2021]; CASA [modified 2022]). The median concentration of manganese in total suspended particulate (TSP) in Sarnia from 2015 to 2019 was 0.006 µg/m^3, and the median manganese concentration measured in PM_{10} at 3 sites in Montreal in 2020 was 0.0054 µg/m^3.

Releases of manganese and its compounds to air in the form of particulates by industrial facilities are required to be reported to the NPRI. According to the NPRI data, 267 industrial facilities in 43 Canadian industrial sectors (based on the North American Industry Classification System [NAICS]-4) have reported releases of manganese to air between 2015 and 2019 (Table B-3, Appendix B) (NPRI 2020). Annual emissions to air by these facilities from 2015 to 2019 ranged from 0 tonnes to 17.7 tonnes of manganese (NPRI 2020).

To characterize exposure from industrial facilities and point sources of release, air concentrations in the vicinity of the facilities with the highest reported manganese emissions to air across different industrial sectors in Canada were considered on the basis of the 5-year average emissions from these facilities that were reported to the NPRI database from 2015 to 2019. Exposure was estimated for all industry sectors with

facilities that had average emissions to air of greater than 1 tonne per year from 2015 to 2019. The industry sectors with facilities reporting releases to air of over 1 tonne per year were the metal ore mining (NAICS 2122); iron and steel mills and ferroalloy manufacturing (NAICS 3311); agricultural, construction, and mining machinery manufacturing (NAICS 3331); electric power generation, transmission, and distribution (NAICS 2211); motor vehicle parts manufacturing (NAICS 3363); pulp, paper, and paperboard mills (NAICS 3221); and steel product manufacturing from purchased steel (NAICS 3312) industry groups (NPRI 2020). To characterize air concentrations, a search of the literature was conducted for measured and modelled manganese air concentration data in proximity to facilities from these industrial sectors.

The SCREEN3 dispersion model was used to estimate air concentrations of manganese in the vicinity of facilities where representative monitoring or modelled estimates for an industrial sector were not available. SCREEN3 is a screening-level Gaussian air dispersion model for assessing pollutant concentrations from various sources (SCREEN3 2011). Annual manganese concentrations in $PM_{2.5}$ at the closest residential receptor for 5 facilities from the metal ore mining sector (NAICS 2122); the agricultural, construction, and mining machinery manufacturing sector (NAICS 3331) ; the motor vehicle parts manufacturing sector (NAICS 3363); the pulp, paper, and paperboard mills sector (NAICS 3221); and the steel product manufacturing from purchased steel industry sector (NAICS 3312) were modelled. A summary of this analysis is presented below.

Forty-nine metal ore mining and refining facilities (NAICS 2122) reported releases of manganese to air between 2015 and 2019 (NPRI 2020). Five-year average releases from these facilities ranged from 0.000002 tonnes to 16.5 tonnes per year (NPRI 2020). Two mining facilities in Labrador City, Newfoundland and Labrador, reported the highest average releases to air from 2015 to 2019 (NPRI 2016, 2020). Annual ambient air quality reports that include monitoring of $PM_{2.5}$ from industrial facilities are available from the Government of Newfoundland and Labrador; however, no data are available on concentrations of metals (NL ECC 2021). Monitoring data are available near other metal ore mining and refining facilities in Canada with lower reported releases. Manganese concentrations measured at 9 ambient air particulate sampling stations, operated to measure emissions from the smelter and the copper cliff nickel refinery, in Sudbury, Ontario, are available. In 2018, manganese concentrations (PM_{10}) were measured (on a 24-hour, 6-day sampling schedule) at 5 air monitors located within or just outside the boundary of the facilities; concentrations ranged from 0.002 µg/m^3 to 0.051 µg/m^3, and the mean concentration was 0.008 µg/m^3 (VALE 2018). The median manganese concentration in $PM_{2.5}$ measured at a NAPS site in Sudbury, Ontario, from 2018 to 2019 was 0.0015 µg/m^3 (NAPS [modified 2021]). Manganese releases from metal ore mining facilities in Sudbury, Ontario, are lower than releases from Labrador City, Newfoundland; therefore, SCREEN3 estimates were used to characterize manganese air concentrations around the facilities with the highest releases.

Twelve iron and steel mills and ferroalloy manufacturing (NAICS 3311) facilities across Canada reported releases of manganese to air from 2015 to 2019 (NPRI 2020). Five-

year average releases from these facilities reported to the NPRI ranged from 0.02 tonnes to 7.1 tonnes per year (NPRI 2020). The highest manganese releases were reported from facilities in Hamilton, Ontario, and Contrecoeur, Quebec (NPRI 2016, 2020). Manganese was measured in PM_{10} at 4 air monitoring stations in proximity (1.7 km to 5 km away) to ArcelorMittal Inc. in Contrecoeur, Quebec, from April to June 2016 (Lamarche and Dao 2020). The median manganese concentrations in PM_{10} at the 4 air monitoring stations ranged from 0.011 µg/m^3 to 0.026 µg/m^3. Manganese concentrations were also measured at 6 sites in proximity to steel mills in Hamilton, Ontario, by the Hamilton Air Monitoring Network (HAMN 2022). The median manganese air concentration in TSP from 2015 to 2019 was 0.136 µg/m^3 (HAMN 2022). In compliance with Ontario provincial environmental regulations, manganese air concentrations in proximity to the steel mills are also modelled annually by ArcelorMittal Dofasco for iron and steel mill facilities in Hamilton, Ontario. According to the reports from 2017 to 2019, manganese concentrations in total PM at the maximum point of impingement, modelled using AERMOD and averaged over 24 hours, ranged from 0.944 µg/m^3 to 1.31 µg/m^3 (ArcelorMittal Dofasco 2018, 2019, 2020). Additionally, 2 studies conducted by Health Canada reported median manganese air concentrations of 0.0042 µg/m^3 and 0.014 µg/m^3 near the steel plant in Sault St. Marie, Ontario, a city containing an iron and steel manufacturer with lower reported manganese emissions than Hamilton, Ontario or Contrecoeur, Quebec (Cakmak et al. 2014; NPRI 2020; personal communication, email from the WAQB, Health Canada, to the ESRAB, Health Canada, dated October 26, 2018; unreferenced). A decrease of almost 50% in atmospheric manganese concentrations in Montreal in the early 1990s was attributed to the closing of a large manganese alloy production plant located about 25 km southwest of Montreal (Boudissa et al. 2006). However, air concentrations in the vicinity of the plant remained higher than ambient levels, even after the plant was closed. In 2003, more than 10 years after the closing of the ferroalloy plant, air concentrations beside the nearest house (800 m away from the closed plant) were 0.13 µg/m^3 (Boudissa et al. 2006). Air monitoring data from the Hamilton Air Monitoring Network were considered the best data available to characterize air concentrations in proximity to large iron and steel mills and ferroalloy manufacturing facilities.

Two agricultural, construction, and mining machinery manufacturing (NAICS 3331) facilities reported releases of manganese to air from 2015 to 2019 (NPRI 2020). Five-year average releases from these facilities reported to the NPRI ranged from 0.0001 tonnes to 3.9 tonnes per year (NPRI 2020). The facility with the highest average emissions to air from 2015 to 2019 was located in Saskatoon, Saskatchewan (NPRI 2016, 2020). No modelled or measured data from this facility were found. Monitoring data from the NAPS site in Saskatoon, located approximately 7.5 km from the facility, reported a median air concentration in $PM_{2.5}$ from 2015 to 2019 of 0.0016 µg/m^3. However, there are residential receptors located closer to the facility, within 7.5 km; therefore, SCREEN3 estimates were generated to characterize manganese air concentrations from this sector.

Twelve electric power generation, transmission, and distribution facilities (NAICS 2211) reported releases of manganese to air between 2015 and 2019 (NPRI 2020). Five-year

average releases from these facilities reported to the NPRI ranged from 0.0026 tonnes to 3.4 tonnes per year (NPRI 2020). The facility with the highest average emissions to air from 2015 to 2019 was located in Williams Lake, British Columbia (NPRI 2016, 2020). Modelled air concentrations of manganese released from this facility were generated as part of an application to amend the air permit issued by the British Columbia Ministry of the Environment (BC MOE) (Atlantic Power Corporation 2016; BC MOE 2016). Manganese air concentrations at this facility were modelled using CALPUFF, assuming the use of 100% used railway ties as fuel, which may not be representative of current practices at the facility. The BC MOE indicated that the use of railway ties was not expected to influence manganese emissions to air (BC MOE 2016). According to the report, the maximum predicted air concentration in TSP from this facility, averaged over 24 hours, in the permit amendment was 0.0017 µg/m^3 (Atlantic Power Corporation 2016). No monitoring data for air concentrations in proximity to this facility were found.

Sixteen motor vehicle parts manufacturing (NAICS 3363) facilities reported releases of manganese to air between 2015 and 2019 (NPRI 2020). Five-year average releases from these facilities reported to the NPRI ranged from 0.00017 tonnes to 3.0 tonnes per year (NPRI 2020). The facility with the highest average emissions to air from 2015 to 2019 was located in Elora, Ontario. No monitoring or modelled data from the facility with the highest reported releases were found; therefore, air concentrations were modelled using SCREEN3.

Forty-five pulp, paper, and paperboard mill (NAICS 3221) facilities reported releases of manganese to air between 2015 and 2019 (NPRI 2020). Five-year average releases from these facilities reported to the NPRI ranged from 0.0001 tonnes to 2.5 tonnes per year (NPRI 2020). The highest average releases were reported by a facility in The Pas, Manitoba. No monitoring or modelled data from the facility with the highest reported releases were found; therefore, air concentrations were modelled using SCREEN3.

Seven steel product manufacturing from purchased steel (NAICS 3312) facilities reported releases of manganese to air between 2015 and 2019 (NPRI 2020). Five-year average releases from these facilities reported to the NPRI ranged from 0.0004 tonnes to 1.2 tonnes per year (NPRI 2020). The highest average releases were reported by a facility in Calgary, Alberta. Searches that were conducted found no modelled or measured data from this facility. Monitoring data from 2 NAPS sites in Calgary, Alberta, located approximately 6.5 km to 10 km from the facility, were considered. The median air concentration measured in $PM_{2.5}$ at the monitoring stations in Calgary from 2015 to 2019 was 0.0016 µg/m^3 (NAPS [modified 2021]). However, there are residential receptors located closer to the facility, within 6.5 km; therefore, SCREEN3 estimates were generated to characterize manganese air concentrations for this sector.

In addition, manganese air concentrations in the vicinity of oil and gas extraction facilities were considered. These facilities had lower reported releases of manganese to air compared to the other industry groups above; however, they were still considered based on the availability of monitoring data. Three oil and gas extraction (NAICS 2111)

facilities reported releases of manganese to air from 2015 to 2019 (NPRI 2020). Average releases to air reported to the NPRI ranged from 0.0079 tonnes to 0.48 tonnes per year from 2015 to 2019 (NPRI 2020). Median manganese concentrations measured in $PM_{2.5}$ at sites within 30 km of the Athabasca oil sands from 2015 to 2019 ranged from 0.00067 µg/m^3 to 0.00094 µg/m^3 (WBEA 2021). Multiple oil and gas extraction facilities reporting manganese releases to air from 2015 to 2019 are located in this area (NPRI 2020). The air concentration of manganese measured in proximity to the oil and gas extraction facilities is lower than in many other industrial sectors, as well as lower than the ambient outdoor air concentration in Sarnia, Ontario.

Annual manganese concentrations in $PM_{2.5}$ at the closest residential receptor ranged from 0.051 µg/m^3 to 0.807 µg/m^3 for distances between 350 m and 2,500 m from the facility fence lines. The highest manganese concentration was estimated at the receptors of the motor vehicle parts manufacturing facility (0.807 µg/m^3), followed by the agricultural, construction, and mining machinery manufacturing facility (0.208 µg/m^3). Details of the SCREEN3 model and input parameters for each facility, including source type, distance to the receptor (residence), and modelled annual air concentration at the receptor, are presented in Table E-1, Appendix E.

Several air concentration values were selected to bring forward for the characterization of potential risk from the exposure to manganese in air via inhalation. For the general population, the highest average outdoor manganese concentration measured in TSP from Sarnia Ontario, (0.006 µg/m^3) was selected to characterize risk via inhalation exposure and to characterize exposure in the background daily intake from environmental media, drinking water, and food. This value is protective of indoor air, personal air, outdoor air in residential areas, outdoor air in urban and industrial areas with no significant point source influence, and outdoor air in the vicinity of oil and gas refining facilities. The average manganese air concentration in $PM_{2.5}$ over 24 hours, influenced by emissions from transit, was calculated as 0.022 µg/m^3 for 70 minutes per day (Van Ryswyk et al. 2017) and was selected to account for a potential increase in exposure from subways during commuting. To estimate potential inhalation exposure and risk for people living in the vicinity of industrial facilities, a manganese air concentration from each industrial sector, based on measured or modelled data, will be brought forward for risk characterization. Air concentrations to be brought forward for risk characterization are outlined below in Table 8-1.

Table 8-1. Mean daily air concentrations of manganese

Air source influence	Avg. release for highest facility[a] (tonnes)	Location	Data type/model	PM fraction	Air conc. (µg/m^3)
Outdoor air	N/A	Sarnia, Ontario	Monitoring data	TSP	0.006 (median)

Air source influence	Avg. release for highest facility[a] (tonnes)	Location	Data type/model	PM fraction	Air conc. (µg/m^3)
Transit influence	N/A	Subway in Toronto, Ontario	Monitoring data	$PM_{2.5}$	0.022 (median)
Metal ore mining	16.5	Labrador City, Newfoundland and Labrador	SCREEN3	$PM_{2.5}$	0.071
Iron and steel mills and ferroalloy manufacturing	7.1	Hamilton, Ontario	Monitoring data	TSP	0.136 (median)
Agricultural, construction, and mining machinery manufacturing	3.9	Saskatoon, Saskatchewan	SCREEN3	$PM_{2.5}$	0.208
Electric power generation, transmission, and distribution	3.4	Williams Lake, British Columbia	CALPUFF estimates, Atlantic Power Corporation	TSP	0.002 (maximum)
Motor vehicle parts manufacturing	3.0	Elora, Ontario	SCREEN3	$PM_{2.5}$	0.807
Pulp, paper, and paperboard mills	2.5	The Pas, Manitoba	SCREEN3	$PM_{2.5}$	0.051
Steel product manufacturing from purchased steel	1.2	Calgary, Alberta	SCREEN3	$PM_{2.5}$	0.180

Abbreviations: avg., average; conc., concentration; N/A, not applicable; PM, particulate matter; $PM_{2.5}$; particulate matter with a median aerodynamic diameter of less than 2.5 µm; TSP, total suspended particulate.
[a] 5-year average release to air from the facility with the highest emissions from 2015 to 2019 reported to the NPRI.

8.2.2.2 Dust

Total and bioaccessible manganese concentrations in dust in Canada are available from the Canadian House Dust Study (CHDS). Between 2007 and 2010, household dust samples were collected as part of a nationally representative random sample from 1,025 homes in 13 cities in Canada in order to provide national baseline estimates of

typical urban metal concentrations in household dust. The median and 95th percentile concentrations of total manganese in freshly vacuumed household dust were 267 and 597 mg/kg, respectively (personal communication, email from the Environmental Health Science and Research Bureau [EHSRB], Health Canada, to the ESRAB, Health Canada, dated July 20, 2016; unreferenced). In another study, house dust samples and soil samples were collected from 50 residences located in 10 neighbourhoods across Ottawa. Median manganese concentrations in indoor dust samples (267 mg/kg) were lower than in outdoor soil (532 mg/kg) (Rasmussen et al. 2001).

In a study conducted in Toronto (2015 to 2016), manganese concentrations were measured in dust from road sweepings. These samples were collected from local and arterial roads and from a municipal expressway. Median manganese concentrations in road dust were 814, 719, and 702 mg/kg for dust obtained from arterial roads, local roads, and the expressway, respectively (Wiseman et al. 2021). The inter-elemental association of manganese with crustal elements indicated that the source was lithogenic and not associated with automotive exhaust (Wiseman et al. 2021). These concentrations of manganese in road dust were higher than the concentrations reported in the CHDS.

The bioaccessibility of manganese from dust in simulated stomach fluids has been examined in several studies. Bioaccessible concentrations ranged from 54% to 68% (Turner and IP 2007; Dupuis 2013; Reis et al. 2015; l 2018). The median manganese concentration of 267 mg/kg reported in the CHDS (personal communication, email from the EHSRB, Health Canada, to the ESRAB, Health Canada, dated July 20, 2016; unreferenced) and the highest dust bioaccessibility of 68% (Reis et al. 2015) were selected to characterize general population exposure in the background estimates of daily intake from environmental media, drinking water, and food.

8.2.2.3 Soil

The major pool of manganese in soils originates from the earth’s crust. Additional sources of manganese include direct atmospheric deposition, plants, dead plant and animal material, and animal excrement (Stokes et al. 1988). Manganese-containing fertilizers may be added to soil to enhance crop growth and is an essential plant nutrient. Manganese in soil exists as dissolved Mn(II), as well as insoluble Mn(III) and Mn(IV) oxides (Brandhuber et al. 2013).

Concentrations of manganese in soil from the Appalachian, Canadian Shield, St. Lawrence Lowlands, Interior Plains, and Cordilleran regions as well as from British Columbia, Manitoba, and Ontario are available. Median concentrations range from 190 mg/kg to 621 mg/kg, and concentrations in Canada range from 2 mg/kg to 8,620 mg/kg overall (McKeague et al. 1979; McKeague and Wolynetz 1980; Haluschak et al. 1998; Reimer 1999; Rasmussen et al. 2001; SARA 2008; ON MOECC 2015). A study conducted in Toronto on soil from high traffic areas did not show elevated levels of manganese when compared to the background concentrations, indicating that

automotive exhaust did not contribute significantly to concentrations in roadside soil (Wiseman et al. 2013).

Bioaccessibility of manganese from soil in simulated stomach fluids has been investigated in a number of studies and ranged from 9% to 66% (Sialelli et al. 2010; Laird 2010; Izquierdo et al. 2015; Ngole-Jeme et al. 2018; personal communication, email from the EHSRB, Health Canada, to the ESRAB, Health Canada, dated September 12, 2018; unreferenced. The average concentration of manganese in soil from 5 major geographical regions in Canada, 544 mg/kg (McKeague et al. 1979) and a bioaccessibility of 66% (personal communication, email from the EHSRB, Health Canada, to the ESRAB, Health Canada, dated September 12, 2018; unreferenced) were selected to characterize general population exposure in the background estimates of daily intake from environmental media, drinking water, and food.

8.2.2.4 Water

Sources of manganese in surface water and groundwater may be natural (rock and soil weathering) or anthropogenic (industrial discharges, mining activities, and landfill leaching). Physicochemical properties of the local environment (for example, organic carbon content, cation exchange capacity, pH, oxidation-reduction potential, mineral and particulate content) and the oxygen content of groundwater influence the manganese speciation and aqueous solubility, which in turn influence the concentration in ground and surface waters. Manganese may be added to drinking water as part of the treatment process; for example, permanganate ion (MnO_4^-) is used by drinking water treatment plants as an oxidizing agent to remove iron, manganese, and other contaminants (Health Canada 2019a).

In general, manganese is more prevalent in groundwater than in surface water because of the strong reducing conditions of the former (Health Canada 2019a). High manganese concentrations have been reported in the drinking water of many countries around the world where groundwater is used for human consumption (Frisbie et al. 2012), including Canada (Barbeau et al. 2011). The concentration in groundwater is influenced by the concentration of manganese in soils in contact with water and by conditions that favour manganese in solution. Overall, manganese concentrations in groundwater are less variable than in surface water. However, large variations in manganese concentrations have been observed between different wells located in close proximity to each other (Health Canada 2019a).

Manganese can accumulate in water distribution systems and later be released back into drinking water (Gerke et al. 2016; Health Canada 2019a). Manganese deposition can occur as a physical process (for example, particle settling) or through biological accumulation. It can also accumulate in loose deposits in the distribution system of pipes and in surface scale. Releases of manganese from deposits in the distribution system tend to be sporadic events associated with events such as hydraulic disturbances in the system or changes in water chemistry (Health Canada 2019a). It is also possible for manganese to accumulate in the plumbing of buildings. Therefore,

manganese concentrations measured at the tap can fluctuate depending on various factors such as water flow rate, changes in pH, chlorine residues, and temperature. Further information on the accumulation of manganese and its release in drinking water is presented in the Drinking Water Quality Guideline Technical Document for Manganese (Health Canada 2019a).

Health Canada has established a MAC of 120 µg/L for total manganese in drinking water (Health Canada 2019a). As part of a national drinking water survey conducted by Health Canada in 2009 and 2010, manganese concentrations in 65 drinking water treatment systems, including treatment facilities and distribution systems, were measured in all provinces and territories (Tugulea 2016). Up to 5 locations were sampled at each site: the source water, treated water, and 3 points within the distribution systems. Median concentrations of digested manganese in source water were 15 µg/L (n=86), decreasing to 3 µg/L (n=85) after treatment. Median concentrations in the distribution system closest to the treatment facility were 4 µg/L, declining slightly to 3 µg/L as distance from the treatment facility increased (Tugulea 2016).

Manganese concentrations were measured as part of general provincial drinking water monitoring programs. Provincial manganese concentration data for Alberta, British Columbia, Manitoba, New Brunswick, Newfoundland and Labrador, Ontario, Prince Edward Island, Quebec, Saskatchewan, and Yukon were originally provided to the WAQB, Health Canada (Health Canada 2019a). Overall, these manganese concentrations were reported for water sampled between 2000 and 2014. These data included manganese concentrations in surface water, ground water wells, treated water, and from distribution systems. Samples were analyzed for manganese in different laboratories using different methods, such as dissolved, total, or extractable.

The data described in Health Canada (2019a) were reanalyzed using a different approach. In particular, for any samples that were reported as below the detection limit, a value of half of the detection limit was assigned, consistent with standard risk assessment practices. Descriptive statistical analysis was conducted on provincial drinking water data to report manganese concentrations determined by total or extractable methods. Manganese in drinking water was measured in treated water and distribution system samples collected from British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Quebec, New Brunswick, Prince Edward Island, Newfoundland and Labrador, and Yukon. The median concentrations of the combined treated and distribution system samples ranged from 0.25 µg/L to 10 µg/L, while 95th percentile concentrations ranged from 1.3 µg/L to 820 µg/L. The median concentration of manganese in drinking water was highest in Saskatchewan (10 µg/L), followed by Manitoba (8.2 µg/L) and British Columbia (7.6 µg/L). The 95th percentile concentration of manganese in drinking water was highest in Saskatchewan (820 µg/L), followed by British Columbia (501 µg/L) and New Brunswick (380 µg/L) (Table D-1, Appendix D).

As part of the First Nations Food, Nutrition and Environment Study (FNFNES), concentrations of manganese were measured in tap water from First Nations

communities (Schwartz et al. 2021). Tap water samples were collected at first draw (that is, after water remained stagnant in the pipes for no less than 4 hours) and after running the water for 5 minutes at participants' homes, and tested for the presence of manganese. Median concentrations of manganese in tap water measured in samples collected from British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Quebec, and the Atlantic region ranged from 0.4 µg/L to 6.0 µg/L, while the 95th percentile concentrations ranged from 18.7 µg/L to 449 µg/L. In some households, manganese concentrations were higher after the 5-minute flush when compared to the first draw, indicating that plumbing may be a source of manganese in drinking water (Schwartz et al. 2021). The 95th percentile manganese concentrations in the drinking water of some First Nations communities, British Columbia, Saskatchewan, and Quebec were lower than in the provincial and territorial distribution systems (Table D-2, Appendix D).

Data on manganese concentrations in drinking water from public or private wells are available from Alberta, Saskatchewan, Manitoba, Quebec, New Brunswick, and Nova Scotia (Fitzgerald et al. 2001; Thompson 2003; MCC-MHSC 2021; NB DOE 2008; Bouchard et al. 2011; AG 2014; Montcoudiol et al. 2015; Ntihabose et al. 2018; Kullar et al. 2019; Kennedy 2021). Median concentrations of manganese in well water samples ranged from 2 µg/L to 500 µg/L. The highest median concentration of manganese in well water was found in Manitoba (500 µg/L). The average concentrations of manganese in well water are higher than in water from distribution systems in Alberta, Saskatchewan, Manitoba, Quebec, and New Brunswick (Table D-3, Appendix D, summarized in Table 8-2).

The median concentrations of manganese in drinking water measured in water treatment plants, distribution systems, tap water, and well water are highest in Saskatchewan and Manitoba. Median concentrations of manganese measured in well water were higher than the concentrations measured in treatment plants and distribution systems. Manganese concentrations in tap water measured in First Nations communities are similar to those from the provincial data. Median and 95th percentile concentrations of manganese in drinking water are presented in Table 8-2. The 95th percentile concentrations of manganese in drinking water in the provinces, territories, and First Nations Communities were selected for risk characterization. The highest 95th percentile manganese concentration in drinking water, measured at 820 µg/L in Saskatchewan, was selected to characterize exposure from background estimates of daily intake from environmental media, drinking water, and food.

Table 8-2. Median and P95 manganese concentrations (µg/L) in drinking water from provinces, First Nations communities, and well water

Province	Provincial[a] median (P95) (µg/L)	Well water[b] median (µg/L)	First Nations[c] median (P95) (µg/L)
British Columbia	7.6 (501)	NA	0.4 (24.9)
Alberta	0.25 (1.3)	2 to 135	3.0 (51.5)
Saskatchewan	10 (820)	240	2.2 (107)

Province	Provincial[a] median (P95) (µg/L)	Well water[b] median (µg/L)	First Nations[c] median (P95) (µg/L)
Manitoba	8.2 (235)	500	3.4 (278.8)
Ontario	1.4 (22)	NA	1.83 (39.1)
Quebec	2.9 (224)	8 to 55	0.8 (18.7)
New Brunswick	3 (380)	5 to <50	NA
Prince Edward Island[d]	0.9 (13)	NA	NA
Nova Scotia	NA	21	NA
Newfoundland and Labrador	7 (130)	NA	NA
Atlantic region	NA	NA	6.0 (449)
Yukon	4.3 (41)	NA	NA

Abbreviations: NA, not available; P95, 95th percentile.
[a] Calculated using data from Health Canada (2019a).
[b] References are listed in Table D-3, Appendix D.
[c] Tap water (Schwartz et al. 2021).
[d] Drinking water quality summary results (GOC [modified 2022]).

8.2.2.5 Food

Food is a major source of exposure to manganese for people in Canada. Manganese enters the food chain through natural uptake by plants from the soil. In addition, it is present in foods from manganese-containing food additives as well as from its use in food packaging, in the fortification of foods for special dietary use (for example, meal replacements, formulated liquid diets), and in infant formula, fertilizer and soil nutrient uses, and in pesticide uses (Health Canada [modified 2013], 2016, [modified 2016b], 2021, [modified 2022b]; personal communication, emails from the FND, Health Canada to the Existing Substances Risk Assessment Bureau [ESRAB], Health Canada, dated July 7, 2016, and August 9, 2021; unreferenced). The contribution of manganese from food packaging is less than 25 ng/kg bw/day (personal communication, email from the FND, Health Canada to the ESRAB, Health Canada, dated May 12, 2022; unreferenced). Some manganese compounds are permitted for use as food additives. For example, manganese sulfate is permitted as a pH-adjusting agent in bacterial cultures and as a yeast food in ale, beer, light beer, malt liquor, porter, and stout, in accordance with good manufacturing practices. Potassium permanganate is permitted to be used to modify starch, as long as the resulting modified starches contain no more than 50 ppm manganese (Health Canada [modified 2013], [modified 2016b], [modified 2022b]). Manganese may also enter the food chain from its use as a plant micronutrient in registered plant fertilizer and soil supplement products (CFIA [modified 2023]) or from the use of mancozeb, a pesticide with applications in food (Health Canada 2020c). Chronic exposure to mancozeb from food (not drinking water) was estimated to contribute less than 25 ng Mn/kg bw/day (calculated using information from Health Canada 2020c).

According to the Canadian Nutrient File (CNF; Health Canada [modified 2016a]), concentrations of manganese in various foods were as follows: breakfast cereal (34.72 µg/g), whole-wheat bread (19.87 µg/g), peanut butter (16.65 µg/g), spinach (8.97 µg/g), oatmeal (8.33 µg/g), crackers (6.86 µg/g), rice (4.72 µg/g), wheat flour (4.62 µg/g), strawberries (3.86 µg/g), pasta (3.22 µg/g), bananas (2.7 µg/g), brewed tea (2.19 µg/g), lettuce (1.55 µg/g), carrots (1.43 µg/g), and onions (1.29 µg/g) (personal communication, email from the FND, Health Canada to the ESRAB, Health Canada, dated October 13, 2022; unreferenced).

Dietary exposures to manganese for all individuals aged 1 year and older were estimated by Health Canada's FND using a 24-hour recall component of a full distribution of survey respondents from the Canadian Community Health Survey (CCHS 2015); these estimates were then statistically adjusted using the National Cancer Institute's (NCI's) method for the calculation of usual dietary intakes (NCI 2018) and manganese concentrations in individual foods from the CNF. The CNF database contains entries for thousands of individual foods, including raw, refined, and processed foods. Cooking and preparation water was included in the calculation of the dietary exposure estimates; however, drinking water was not (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated September 1, 2022; unreferenced). The 95th percentile of total dietary exposure to manganese in the general population (for all individuals aged 1 year and up) ranged from 0.078 mg/kg bw/day in males aged 71 or older to 0.255 mg/kg bw/day in children 1 to 3 years of age (Table D-4, Appendix D). The 95th percentile dietary exposure estimates for manganese in females of reproductive age (14 to 50 years) ranged from 0.090 mg/kg bw/day to 0.116 mg/kg bw/day. The dietary intake estimate of 0.089 mg/kg bw/day for 6 to 11 month-old infants was estimated on the basis of the 5-year average dietary intakes from the Canadian Total Diet Study (TDS) from 2003 to 2007 (Health Canada [modified 2011]). These dietary intake estimates capture naturally occurring manganese in food as well as contribution from food additives, food packaging, fertilizer, and pesticide uses. Dietary intake estimates for infants 6 to 11 months, children 1 to 8 years (both sexes), and adolescent males 14 to 18 years all exceed the IOM UL for those respective age groups (IOM 2001).

The primary contributor of manganese to the diet is whole-grain cereals. For all age groups combined, the food groups that contribute most significantly to total dietary exposure include grain and grain products (51%), vegetables (8%), fruit and tea (each 7%), and nuts, seeds, and nut butters (6%). For 1-year-olds, the foods contributing most significantly to total dietary manganese exposure were grains and grain products (62%), fruit (13%), and vegetables (6%) (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated May 12, 2022; unreferenced). Bioaccessibility values for manganese from various food items are highly variable, ranging from 0.2% to 100% (Powell et al. 1998; Vitali et al. 2008; Khouzam et al. 2011; Laird and Chan 2013; Kumari and Platel 2017; Pereira et al. 2018). The differences in bioaccessibility may be due to factors such as the chemical form (organic versus inorganic), oxidation state (Mn^{2+} versus Mn^{7+}), and the extent of the formation of insoluble manganese complexes in the studied food (Martins et al. 2020).

Manganese concentrations in traditional foods consumed by Indigenous peoples in Canada have been reported in studies conducted in Canada (Laird and Chan 2013; Larter et al. 2016; Chan et al. 2021). Exposures from traditional, subsistence, or country foods is highly dependant on the local conditions and consumption patterns of individual subpopulations. Concentrations of manganese in over 370 varieties of traditional foods from each province and ecozone were reported in the FNFNES (Chan et al. 2021). The average concentration of manganese in country foods categories for all regions in Canada ranged from 1.54 µg/g wet weight in fish, seafood, and marine mammals to 64.6 µg/g wet weight in trees and tree products (for example, bark, sap) (Chan et al. 2021). In a previous study, concentrations of manganese in organ meat (muscle and kidney) were reported in land mammals (moose, mountain caribou, Dall's sheep, and mountain goat) from the Mackenzie Mountain region of Northwest Territories. Concentrations in land mammal organ meats ranged from 0.22 µg/g to 0.46 µg/g and from 0.84 µg/g to 1.17 µg/g in organ meats (Larter et al. 2016).

Human milk

Manganese is present in human milk and infant formula in Canada, which are sources of exposure for infants. The concentration of manganese in human milk varies considerably. According to the IOM (2001) and Klein (2002), the mean human milk concentration of manganese ranges from 1.9 µg/L to 6.6 µg/L. A literature review, conducted by Mitchell et al. (2020), of studies published between 1980 and 2017 that measured manganese concentrations in human reported a concentration range of 0.17 µg/L to 30.27 µg/L. This review included a Canadian study conducted by Friel et al. (1999) from 1988 to 1993 in Newfoundland, which reported levels of manganese in the human milk of 43 nursing mothers. The median manganese concentration in human milk from mothers of full-term gestation during the first 3 months ranged from 10 µg/L to 17 µg/L (Friel et al. 1999). Later, as part of the MIREC project conducted from 2008 to 2011, manganese was measured in human milk collected from women who were between 2 weeks and 10 weeks postpartum, living in 10 Canadian cities across Canada. Manganese was detected in approximately 87% of the 835 samples analyzed (limit of detection [LOD] = 1.1 ng/g). Median, average, and 95th percentile manganese concentrations in human milk samples were 2 ng/g (2.1 µg/L), 2.41 ng/g (2.5 µg/L), and 5.0 ng/g (5.2 µg/L), respectively (assuming a human milk density of 1.030 g/mL) (personal communication, email from the EHSRB, Health Canada, to the ESRAB, Health Canada, dated January 10, 2022; unreferenced).

The upper-bounding daily intake of manganese for exclusively human milk-fed infants 0 to 5 months old from human milk was estimated to be 2.11×10^{-3} mg/kg bw/day (Table 8-3). This is based on the highest median manganese concentration in human milk of 17 µg/L (0.017 µg/g) measured in Canada (Friel et al. 1999) and the median consumption value of 127.95 g/kg bw/day (Arcus-Arth et al. 2005).

Formula

Manganese is present in cow's milk or soy-based infant formula and soy or rice-based beverages, which are consumed by infants and children up to 3 years of age. In Canada, infant formula is available as ready-to-feed (RTF), which requires no reconstitution prior to being fed to an infant, and as both liquid and powdered concentrates, which require reconstitution with water prior to being fed to an infant (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated October 13, 2022; unreferenced). As manganese is an essential element for human health, the *Food and Drug Regulations* require a minimum level of 5 µg of manganese/100 kcal in infant formula. No maximum limit is specified (Canada 1978); however, the maximum release limits (that is, overages) are considered as part of the premarket evaluation process, and the CODEX/LSRO maximum is applied (100 µg/100 kcal). Overages are supposed to be reasonable to ensure that the labelled quantity of the nutrient is present throughout the expected shelf-life of the food (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated May 12, 2022; unreferenced). Based on the labels of infant formula currently sold on the Canadian market, reported concentrations of manganese in cow's milk-based formula ranged from 7 µg/100kcal to 15 µg/100kcal (47 µg/L to 100 µg/L), and in soy-based formula from 15 µg/100kcal to 59 µg/100 kcal (100 µg/L to 393 µg/L); only 1 product had a label concentration of 59 µg/100 kcal, whereas the rest of the soy-based formula products had label concentrations ranging from 15 µg/100kcal to 24 µg/100 kcal (100 µg/L to 160 µg/L) (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated May 12, 2022; unreferenced). Concentrations of manganese measured in formulas in the Canadian TDS were higher than the range of concentrations reported on product labels. According to the Canadian Food Inspection Agency (CFIA) guidelines on labelling requirements for foods for special dietary use (CFIA [modified 2025]), mineral nutrients are permitted to vary above label claims but not below. In a study conducted by Scher et al. (2021) in the United States, measured concentrations of Mn in formula were reported to be approximately 2- to 3-fold higher than the label specifications for cow's milk-based infant formula and 2- to 5-fold higher than the label specifications for soy-based infant formula (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated May 12, 2022; unreferenced).

Soy and rice are naturally rich in manganese, since they accumulate manganese from the soil. In particular, soy protein infant formula preparations (including soy protein isolate) can contain relatively high concentrations of manganese compared to human milk (Cockell et al. 2004). Manganese concentrations ranged from 42.4 µg/L to 2,800 µg/L in samples of cow's milk-based and soy-based infant formulas in studies conducted in Canada, the United States, France, and the United Kingdom (Cockell et al. 2004; FSA 2014; Frisbie et al. 2019; Committee on Toxicity 2020; Mitchell et al. 2020, 2021; Scher et al. 2021), which is far higher than the 0.17 µg/L to 30.27 µg/L range in human milk (Mitchell et al. 2020). Soy-based formulas tend to have higher concentrations of manganese than cow's milk-based formula.

For formulas that require reconstitution with drinking water, the drinking water used to reconstitute infant formula may be an additional significant source of exposure to

manganese for infants (Frisbie et al. 2019; Mitchell et al. 2020, 2021; Scher et al. 2021). The mean concentration of manganese in soy-based infant formula (reconstituted as prepared for consumption) measured as part of the Canadian TDS from 2008 to 2018 was 377.7 µg/L (range: 289.1 µg/L to 459.8 µg/L), while the mean concentration in cow's milk-based infant formula was 130.2 µg/L (range: 98.2 µg/L to 155.8 µg/L) (CANLINE [modified 2020]). Manganese concentrations of soy-based or cow's milk-based infant formula (sold as powdered formula, liquid concentrate, and ready-to-feed) are available from the CFIA's targeted surveys on trace elements (2011–12, 2012–13, 2017–18, and 2018–19) and as part of the CFIA's Children's Food Project (2012–13 and 2018–19) (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated December 8, 2022; unreferenced). Intake estimates of manganese for exclusively formula-fed 0- to 5- month-old infants (Table 8-3) were derived using the maximum manganese concentrations in soy-based and cow's milk-based powdered infant formula measured in CFIA data (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated December 8, 2022; unreferenced) and an upper-bounding drinking water concentration of 820 µg/L (the highest 95th percentile manganese concentration in drinking water, measured in Saskatchewan [personal communication, emails from the WAQB, Health Canada, to the ESRAB, Health Canada, dated April 18, 2018, and April 24, 2018; unreferenced]). Further details on the upper-bounding daily intake of manganese for infants consuming soy-based or cow's milk-based infant formula, sold as powdered formula, liquid concentrate, and ready-to-feed, are available in Table D-6, Appendix D.

For comparison purposes, daily intake estimates generated using the health-based MAC for drinking water concentration (120 µg/L) (Health Canada 2019a) are presented in Table D-7, Appendix D, to demonstrate the contribution of manganese from formula.

The upper-bounding daily intakes for infants consuming human milk and infant formula are presented in Table 8-3 below. The daily intake of manganese for infants consuming soy-based infant formula is more than 100 times higher than for infants consuming human milk. The source of drinking water can also have a significant impact on the quantity of manganese consumed per day.

Table 8-3. Estimated daily intake (mg/kg bw/day) of manganese from consumption of human milk and infant formula

Exposure estimate	Mn conc. (µg/g)	Intake from human milk/ infant formula (mg/kg bw/day)	Intake from drinking water (mg/kg bw/day)	Total exposure (mg/kg bw/day)
0 to 5 months, human milk	0.017	2.11×10^{-3}	N/A	2.11×10^{-3}
0 to 5 months, soy-based infant formula	5.73	1.13×10^{-1}	1.08×10^{-1}	2.20×10^{-1}

Exposure estimate	Mn conc. (µg/g)	Intake from human milk/ infant formula (mg/kg bw/day)	Intake from drinking water (mg/kg bw/day)	Total exposure (mg/kg bw/day)
0 to 5 months, cow's milk-based infant formula	3.32	6.53×10^{-2}	1.08×10^{-1}	1.73×10^{-1}

Abbreviations: BW, bodyweight; conc., concentration; Mn, manganese; N/A, not applicable

Daily dietary intake estimates were highest for exclusively human milk-fed and formula-fed infants (aged 0 to 5 months), infants 6 to 11 months old, children 1 to 3 years old, and females of reproductive age.

8.2.2.6 Background intake estimates of manganese from environmental media, drinking water, and food

In Canada, manganese in food, from natural and anthropogenic sources, is the primary contributor to daily background exposure from environmental media (air, soil, and dust), drinking water, and food. Upper-bounding estimates of background manganese exposure range from 2.6×10^{-3} mg/kg bw/day for exclusively human milk-fed infants aged 0 to 5 months to 2.9×10^{-1} mg/kg bw/day for 1-year-olds. In addition to food, drinking water is an important source of exposure for the general population. Generally, air, soil, and dust are minor contributors to background exposure, accounting for less than 1% of exposure for all age groups, except for exclusively human milk-fed infants aged 0 to 5 months. For infants aged 0 to 5 months, the use of human milk versus infant formula as a food source has a significant impact on exposure. The estimated daily intake of manganese for formula-fed infants can be up to 80 times higher than for human milk-fed infants, depending on the concentration of manganese in the drinking water used to reconstitute the formula. These estimates do not account for potential differences in the bioavailability of manganese between human milk and infant formula. Details on intake from environmental media, drinking water, and food, and the percent contribution for the aggregate exposure for all age groups are presented in Table D-8, Appendix D.

8.2.3 Products available to consumers

Exposure estimates were derived from the use of products available to consumers via the oral, dermal, and inhalation routes. Estimates of dermal and oral exposure were quantified in mg/kg bw/day. while estimates of inhalation exposure were quantified as $PM_{3.5}$ or PM_4 in µg/m^3, when possible, to align with the inhalation reference dose.

Information submitted to Environment and Climate Change Canada and Health Canada pursuant to a CEPA section 71 notice (Environment Canada 2013) and a voluntary data submission (ECCC, HC 2017); notifications submitted under the *Cosmetic Regulations* to Health Canada for manganese; the Licensed Natural Health Products Database

(LNHPD); the internal Drug Product Database (DPD); publicly available databases and websites (for example, CPCat 2021; CPID [modified 2021]); and material safety and technical datasheets were considered in order to identify products available to consumers where there is: (a) potential for oral exposure from the ingestion or mouthing of products containing manganese; (b) potential dermal exposure from the use of products containing manganese; and (c) potential for the inhalation of manganese from spray products, including aerosols, or particulates, including powders. As manganese is not volatile, the potential for off-gassing and emissions from products is not applicable. Dermal exposure estimates were not derived for manganese-containing pigments, including manganese violet, C.I. Pigment Red 48:4, C.I. Pigment Red 52:2, and C.I. Pigment Black 26 (CAS RNs 10101-66-3, 5280-66-0, 12238-31-2, and 68186-94-7, respectively). Pigments have very low solubility and are not expected to readily penetrate intact skin; therefore, systemic exposure via the dermal route is not anticipated for pigments.

Manganese is present in thousands of products available to consumers, including arts and crafts materials, children's jewellery and toys, as a fuel additive (gasoline octane enhancer) in a do-it-yourself (DIY) automobile product, odour eliminator household products, paints, textiles, and self-care products (that is, cosmetics, natural health products, and non-prescription drugs) (Environment Canada 2013; Guney et al. 2014; ECCC, HC 2017; CPCat 2021; CPID [modified 2021]; internal DPD [modified 2022]; LNHPD [modified 2021]; NHPID [modified 2021]; personal communication, email from the Consumer and Hazardous Products Safety Directorate [CHPSD], Health Canada, to the ESRAB, Health Canada, dated March 12, 2021; unreferenced; personal communication, email from the NNHPD, Health Canada, to the ESRAB, Health Canada, dated July 5, 2021; unreferenced; personal communication, email from the Pharmaceutical Drugs Directorate [PDD], Health Canada, to the ESRAB, Health Canada, dated August 3, 2021; unreferenced). Products such as arts and crafts materials, children's jewellery and toys, automotive products, paints, self-care products, and textiles can all result in the direct exposure of consumers during use. Other uses of manganese, including in building materials, are more likely to result in indirect exposure via ingestion of house dust or inhalation of indoor air; these exposures are captured in the intake estimates from environmental media.

Exposure scenarios were developed for children's products (for example, arts and crafts materials, jewellery, and toys), automotive products, household products (odour eliminator), paints, textiles, and self-care products (Table 8-4, Table 8-5). Exposure estimates were derived for all age groups and incorporate age-specific physiological parameters, such as body weight and skin surface area (Health Canada [modified 2022c]). The age group with the highest estimated exposure, based on product amount and frequency of use, is presented in Table 8-4 and Table 8-5 unless otherwise noted. Dermal and oral exposure estimates were combined and are based on an exposure frequency of once per day or more. To match the critical health effect via the inhalation route, which is a RfC characterized for continuous exposure, inhalation exposure estimates are representative of continuous exposure, incorporating frequencies of use of less than once per day. The US EPA guidance (2009) was applied to further refine

the per event inhalation exposure estimates for manganese in order to adjust for continuous exposure based on the duration of exposure and frequency of use.

Further details on the algorithms and model inputs used to derive these exposure estimates are presented in Appendix F.

Children's products: Manganese is present in a variety of products used by children, including arts and crafts materials, jewellery, and toys. Manganese compounds present in children's products include elemental manganese, manganese dioxide, potassium permanganate, manganese violet, manganese octoate, C.I. Pigment Red 48:4, and C.I. Pigment Red 52:2 (CAS RNs 7439-96-5, 1313-13-9, 7722-64-7, 10101-66-3, 15956-58-8, 5280-66-0, and 12238-31-2, respectively). Manganese is also present as a dye or a pigment in various arts and crafts materials, such as children's paint, crayons, and oil paint (Guney et al. 2014; Health Canada 2019b). Children may thus be exposed to manganese while playing with these materials. Several studies have examined concentrations of manganese in children's jewellery and toys available in North America, using techniques such as Inductively Coupled Plasma Mass Spectrometry (ICP-MS) and X-Ray Fluorescence (XRF) (Korfali et al. 2013; Guney et al. 2014; Stone 2014). Guney and colleagues (2014) measured total and bioaccessible (via simulated saliva) manganese in metallic toys, jewellery, plastic toys, toys with paints or coatings, and brittle or pliable toys purchased in North America. Total manganese concentrations ranged from 1.2 ppm to 4,320 ppm (1.2×10^{-4} to 0.43%). Bioaccessible manganese concentrations measured in simulated saliva over 120 minutes were below the limit of detection of 0.06 µg (Guney et al. 2014; personal communication, email from Guney, to the ESRAB, Health Canada, dated April 16, 2018; unreferenced). The highest potential oral exposures of 4.2×10^{-2} and 2.0×10^{-2} mg/kg bw/day were derived from the incidental ingestion of paint and modelling clay (Table 8-4). Uses of other arts and crafts materials, jewellery, and toys result in lower exposure than modelling clay.

Automobile products: Manganese in the form of MMT (CAS RN 12108-13-3) is present in a gasoline octane enhancer DIY automobile maintenance product. A dermal exposure estimate of 1.5×10^{-3} mg/kg bw/day was derived to characterize exposure from pouring the product into the automobile using a thin film approach (Table 8-4).

Household products - cleaning products and home maintenance products: Manganese and its compounds, including elemental manganese and manganese nitrate (CAS RNs 7439-96-5 and 10377-66-9, respectively), are present in household products. Household product types that contain manganese include cleaning products and epoxy putties. Dermal and inhalation exposures to manganese were modelled using ConsExpo Web v1.1.0 (2021). The highest dermal exposure estimate was for the use of a trigger spray odour eliminator (1.7×10^{-5} mg/kg bw/day) (Table 8-4). The highest mean daily air concentration was estimated from the use of the trigger spray odour eliminator (4.0×10^{-2} µg/m^3) (Table 8-5). Dermal and inhalation exposures from the use of the odour eliminator spray are the sentinel household product exposure scenarios brought forward for risk characterization. Manganese may also be present in

chimney cleaning products, but more information on the concentration and use is required to estimate direct consumer exposure.

Paint: Manganese and its compounds, including elemental manganese, manganese dioxide, manganese oxide, manganese octoate, manganese neodecanoate, frits, chemicals, C.I. Pigment Red 52:2, and C.I. Pigment Black 26 (CAS RNs 7439-96-5, 1313-13-9, 1317-34-6, 15956-58-8, 27253-32-3, 65997-18-4, 12238-31-2, and 68186-94-7, respectively), are present in a variety of paint products. Product types include tints and colourants for wall paints, ready-to-use speciality paints such as liquid stainless steel or high-heat paints, and paint additives to improve drying time. Manganese and its compounds are also present in colourants for cement products, which are expected to result in exposure levels similar to those associated with paint colourant. There is potential for dermal and inhalation exposures during application. The US EPA Residential SOPs (US EPA 2012) and ConsExpo Web v1.1.0 (2021) were used to model dermal and inhalation exposures from the use of various paint products. There was no product-specific information on the amount of tint and colorant added to the final paint product. It is anticipated that this would vary depending on the desired final colour. Consequently, default values for the amount of tint and colorant were used in the exposure estimates. Applying wall paint with an airless sprayer yielded the highest dermal and inhalation exposure estimates, that is, 8.2×10^{-2} mg/kg bw/day (Table 8-4) and 9.2×10^{-2} µg/m^3 (Table 8-5), respectively.

Textiles: Manganese compounds are used in the textile industry. Manganese oxide is used in textile printing, manganese acetate in textile dyeing, and potassium permanganate in bleaching (Clark 2011; AG-DCCEEW 2018). Manganese may be present in textiles as a result of any or all of these uses. Measured concentrations of manganese in polyester, cotton, wool, viscose, and many other fabric types ranged from 0.07 mg/kg to 13.3 mg/kg (Tuzen 2008; Rovira et al. 2015, 2017; Sungur and Gulmez 2015). Rovira and colleagues (2017) also measured the sweat-mediated migration of many metals from textiles. Algorithms based on those presented in the US EPA Residential Standard Operating Procedures (SOPs; US EPA 2012) were used to derive estimates of combined dermal and oral mouthing exposure to manganese from clothing. Infants aged 0 to 5 months had the highest exposure of 2.5×10^{-3}mg/kg bw/day (Table 8-4).

Self-care products - cosmetics, natural health products, and non-prescription drugs: Manganese and its compounds are present in approximately 11,600 self-care products (personal communication, email from the CHPSD, Health Canada, to the ESRAB, Health Canada, dated March 12, 2021; unreferenced; DPD [modified 2021]; LNHPD [modified 2021]; personal communication, email from the PDD, Health Canada, to the ESRAB, Health Canada, dated August 3, 2021; unreferenced; personal communication, email from the NNHPD, Health Canada, to the ESRAB, Health Canada, dated July 5, 2021; unreferenced). Manganese (CAS RN 7439-96-5) and manganese-containing compounds, manganese aspartate (CAS RN 16351-10-3), manganese chloride (CAS RN 7773-01-5), manganese gluconate (CAS RN 6485-39-8), manganese oxide (CAS RNs 1313-13-6 and 1344-43-0), manganese PCA (CAS RN 369630-79-5),

manganese sulfate (CAS RN 10034-06-5), manganese violet (CAS RN 10101-66-3), and ethylbisiminomethylguaiacol manganese chloride (CAS RN 81065-76-1) have been reported as ingredients in cosmetics in Canada (personal communication, email from the CHPSD, Health Canada, to the ESRAB, Health Canada, dated March 12, 2021; unreferenced). Of these manganese compounds, manganese oxide and manganese violet were identified as priorities for assessment (Appendix A). Manganese-containing ingredients reported to be in natural health products and non-prescription drugs in Canada can be found in the Natural Health Products Ingredients Database, the LNHPD, and the DPD (DPD [modified 2021]; LNHPD [modified 2021]; NHPID [modified 2021]).

Manganese is present in bath products, fragrances, hair care and styling products, hair colour, lip care products, makeup, nail polish, massage oil, mouthwash, skin care products (for example, moisturizer, cleanser), sunscreen, sunless tanning products, and tooth whitener. The most common cosmetics containing manganese include moisturizer, cleanser, bath products, hairstyling products, shampoo, conditioner, face makeup, lipstick, lip balm, and nail polish. Reported manganese concentrations in cosmetics range from less than 0.1% to 22%.

A large portion of the approximately 11,600 self-care products containing manganese are natural health products that have manganese as a medicinal ingredient (LNHPD [modified 2021]). Manganese is present as a medicinal ingredient in multivitamin/mineral supplements, workout supplements, and joint health products. According to Statistics Canada, 46% of people in Canada aged 1 year and older reported taking at least 1 nutritional supplement, most commonly multivitamins (Statistics Canada 2017). A maximum daily dose of 9 mg/day for adults only is associated with manganese in the NNHPD's Multi-Vitamin/Mineral Supplements, Workout Supplements and Multiple Ingredient Joint Health Products monographs (Health Canada 2018a, 2024a, 2024b). However, products for children and providing higher daily doses of manganese have also been licensed by the NNHPD (LNHPD [modified 2021]; personal communication, email from the NNHPD, Health Canada, to the ESRAB, Health Canada, dated July 5, 2021; unreferenced).

To characterize exposure from the use of self-care products, exposure estimates were derived using ConsExpo Web v1.1.0 (2021) or product- and route-specific exposure algorithms incorporating information on the product amount used and manganese concentration. Information on the product type and concentration was obtained from notifications submitted under the *Cosmetic Regulations* to Health Canada (personal communication, email from the CHPSD, Health Canada, to the ESRAB, Health Canada, dated March 12, 2021; unreferenced) and information from the LNHPD ([modified 2021]; personal communication, email from the NNHPD, Health Canada, to the ESRAB, Health Canada, dated July 5, 2021; unreferenced).

Given the number of products containing manganese that are available in the Canadian market, it is possible that exposure from several different types of products (that is, cosmetics, NHPs, and non-prescription drugs) and routes of exposure may occur on the same day (that is, aggregate exposure).

Sentinel dermal and oral exposure estimates for self-care products ranged from 5.1 × 10^{-3} mg/kg bw/day for pump hairspray to 2.0 mg/kg bw/day for mineral supplements and are presented in Table 8-4. A dermal absorption value of 8.3%, based on an *in vitro* dermal absorption study using human skin, was used in the estimates (IMnI 2010, REACH dossier [modified 2020]). Further details of this study are provided in section 8.1.2. Body lotion, permanent hair colour, face moisturizer, leave-on hair conditioner, liquid body soap, lipstick, and multivitamin/mineral supplements will be brought forward to characterize risk from oral and dermal exposures to self-care products.

Table 8-4. Summary of dermal and oral exposures to manganese from the use of products available to consumers

Product scenario	Age group[a] (years)	Dermal exposure (mg/kg bw/day)	Oral exposure (mg/kg bw/day)	Combined exposure (mg/kg bw/day)
Children's products, paint	1	Negligible	4.2×10^{-2}	4.2×10^{-2}
Children's products, modelling clay	1	Negligible	2.0×10^{-2}	2.0×10^{-2}
Automotive DIY product, fuel additive	Adult	1.5×10^{-3}	N/A	1.5×10^{-3}
Household products, odour eliminator spray	Adult	1.7×10^{-5}	N/A	1.7×10^{-5}
Paint, airless sprayer application	Adult	8.2×10^{-2}	N/A	8.2×10^{-2}
Paint, brush application	Adult	3.5×10^{-2}	N/A	3.5×10^{-2}
Paint, spot use with applicator stick	Adult	2.0×10^{-3}	N/A	2.0×10^{-3}
Textiles, clothing	0 to 5 months	2.4×10^{-3}	1.1×10^{-4}	2.5×10^{-3}
Self-care, body lotion (cosmetic)	14 to 18	1.0×10^{-1}	N/A	1.0×10^{-1}
Self-care, permanent hair colour (cosmetic)	Adult	5.4×10^{-2}	N/A	5.4×10^{-2}
Self-care, face moisturizer (cosmetic)	Adult	3.7×10^{-2}	N/A	3.7×10^{-2}
Self-care, leave-on hair conditioner (cosmetic)	Adult	2.9×10^{-2}	N/A	2.9×10^{-2}
Self-care, liquid body soap (cosmetic)	0 to 5 months	2.1×10^{-2}	N/A	2.1×10^{-2}
Self-care, face mask (cosmetic)	14 to 18	1.4×10^{-2}	N/A	1.4×10^{-2}
Self-care, pump hairspray (cosmetic)	Adult	5.1×10^{-3}	N/A	5.1×10^{-3}

Product scenario	Age group[a] (years)	Dermal exposure (mg/kg bw/day)	Oral exposure (mg/kg bw/day)	Combined exposure (mg/kg bw/day)
Self-care, lipstick/lip balm (cosmetic)	2 to 3	N/A	9.8×10^{-2}	9.8×10^{-2}
Self-care, tooth whitener (cosmetic)	Adult	N/A	2.1×10^{-3}	2.1×10^{-3}
Self-care, mineral supplement (NHP - MI)	Adult	N/A	2.0	2.0
Self-care, multivitamin/mineral supplement – Health Canada Monograph maximum dose (NHP - MI)	Adult	N/A	1.2×10^{-1}	1.2×10^{-1}
Self-care, multivitamin/mineral supplement (NHP - MI)	1	N/A	9.1×10^{-2}	9.1×10^{-2}

Abbreviations: DIY, do-it-yourself; MI, medicinal ingredient; N/A, not applicable; NHP, natural health product
Dermal exposure from products containing pigments were not quantified, since dermal absorption of solid pigments is anticipated to be minimal.
[a] Age group with the highest potential exposure was determined based on product amount and frequency of use.

Sentinel inhalation exposure estimates ranged from 3.2×10^{-2} µg/m^3 for loose body powder makeup and aerosol hairspray to 4.1×10^{-1} µg/m^3 for loose face powder makeup (Table 8-5). Aerosol hairspray, loose face powder makeup, and loose body powder makeup will be brought forward for risk characterization.

Table 8-5. Estimated potential air concentrations of manganese from the use of products available to consumers

Exposure scenario	Age group (years)	Average daily air concentrations (µg/m^3)
Household products, odour eliminator spray, $PM_{3.5}$	Adult	4.0×10^{-2}
Paint, spray can, $PM_{3.5}$[a]	Adult	8.4×10^{-2}
Paint, airless sprayer, respirable	Adult	9.2×10^{-2}
Self-care, aerosol hairspray, $PM_{3.5}$ (cosmetic)	Adult	3.2×10^{-2}
Self-care, loose face powder, PM_4 makeup (cosmetic)[a]	4 to adult	4.1×10^{-1}
Self-care, loose face powder, PM_4 makeup with SPF (NHP - NMI)[a]	4 to adult	5.3×10^{-2}

Exposure scenario	Age group (years)	Average daily air concentrations ($\mu g/m^3$)
Self-care, loose body powder, PM_4 makeup (cosmetic)[a]	4 to adult	3.2×10^{-2}

Abbreviations: DIY, do-it-yourself; N/A, not applicable; NHP, natural health product; NMI, non-medicinal ingredient; $PM_{3.5}$, particulate matter with a median aerodynamic diameter of less than 3.5 µm; PM_4, particulate matter with a median aerodynamic diameter of less than 4 µm; SPF, sun protection factor.
[a] Dermal exposure from products containing pigments were not quantified, since dermal absorption of solid pigments is anticipated to be minimal.

8.2.4 Consideration of subpopulations who may have greater exposure

Within Canada, there are groups of individuals who, due to greater exposure, may be more vulnerable to experiencing adverse health effects. The potential for elevated exposure within the Canadian population was examined. Exposure estimates are routinely assessed by age to take into consideration physical and behavioural differences during different stages of life. In the assessment of background exposure from environmental media, food, and drinking water, young children had higher levels of exposure than adults. Formula-fed infants had higher levels of exposure than human milk-fed infants and adults. Drinking water concentrations were also examined; manganese concentrations in drinking water from First Nation communities were similar to those from provincial and territorial drinking water data. Individuals who rely on private wells as a source of drinking water may have higher levels of exposure than those who rely on municipal water supply. Manganese concentrations in the drinking water of some provincial systems and some First Nations communities exceeded the drinking water guideline. In addition, people living near point sources of release of manganese from facilities have the potential for elevated exposure to manganese in air. Air concentrations of manganese around some of these facilities, as predicted using models, demonstrated higher concentrations compared to ambient outdoor air. As part of the assessment of exposure to manganese from products, products targeted for children were assessed, including craft paint, modelling clay, jewellery, and toys.

8.3 Characterization of risk to human health

The potential for cumulative effects was considered in this assessment by examining cumulative exposures to the manganese moiety. Considering the available information, the critical endpoint identified for risk characterization of oral manganese exposures is the LOAEL of 25 mg Mn/kg bw/day for neurotoxic effects (impairments in learning and arousal regulation) in the young, as described in the Kern et al. (2010), Kern and Smith (2011), Beaudin et al. (2013), and Conley et al. (2020) studies. Neurotoxic effects were noted to occur following a short duration of dosing; however, the exact timing and duration required for a neurotoxic effect to develop is not clear. In addition, studies suggest that children exposed to elevated levels of manganese as infants may be at an increased risk for neurodevelopmental deficits that may persist into adulthood. The selection of the developing fetus, infants, and children (based on studies in neonate rats) as a susceptible subpopulation for manganese oral exposure, together with the

selection of neurodevelopmental effects as the critical health effects, are considered protective against other adverse effects of oral exposure to manganese across the entire population. This POD was used by Health Canada (2019a) to calculate the drinking water MAC, which was established to be protective of infants consuming formula reconstituted with drinking water. A tolerable daily intake (TDI) of 0.025 mg/kg bw/day was calculated by incorporating a total UF of 1,000 (10x for interspecies extrapolation, 10x for intraspecies variability, and 10x for the use of a LOAEL).

The available data that examined health effects associated with manganese exposure through diet are not sufficient to derive a POD for risk assessment. There are no dietary studies that have examined neurotoxicity in the young. In the absence of appropriate toxicity endpoints via dietary exposure from food to manganese, the LOAEL of 25 mg Mn/kg bw/day from drinking water, along with a total uncertainty factor of 1,000, was also selected as the most sensitive endpoint for oral exposure. Although differences have been noted in the bioavailability of manganese in food versus in drinking water for adult individuals in a fasted state, manganese bioavailability was similar under other (non-fasted) conditions, and it is unknown whether these differences also apply to or exist in the subpopulation of interest, that is, the young.

No dermal toxicity studies that assessed the critical effect, that is, neurotoxicity, were identified. As neurotoxicity has not been evaluated via the dermal route, it is considered appropriate to compare dermal exposure to the oral endpoint (systemic dose; LOAEL of 25 mg Mn/kg bw/day), as outlined above, while taking into account a dermal absorption value of 8.3%.

Manganese is ubiquitous in environmental media (air, soil, and dust), drinking water, and food and is present in thousands of products available to consumers. Food is the primary source of exposure for the general public, followed by drinking water. Children 1 year of age have the highest background exposure, followed by formula-fed infants. Infants, children up to 3 years of age, and women of reproductive age (to be protective of the developing fetus) were considered the most sensitive subpopulations and were therefore brought forward to characterize risk for the general population in Canada. Since the neurological effects from oral exposure to manganese can occur after a short duration of exposure, although the exact timing and duration required for the development of a neurotoxic effect is not clear, it was considered appropriate to bring forward conservative upper-bounding exposure estimates in order to be protective of periods of short-term elevated exposure. Upper-bounding aggregate intake estimates of manganese from environmental media, drinking water, and food for all age groups are presented in Table D-8, Appendix D. The margins of exposure (MOEs) derived for aggregate exposure range from 33 to 9,493. Infants exclusively fed infant formula in the 0 to 5 month old age group have the highest aggregate exposure, followed by children 1 year of age.

Total manganese concentrations in drinking water from provinces and territories, as well as from First Nations communities (Schwartz et al. 2021), were compared with the MAC (120 µg/L) in order to characterize the risk to people in Canada from drinking water. The

upper bounding (95th percentile) manganese concentration in drinking water exceeded the MAC in provinces and territories other than Alberta, Ontario, Prince Edward Island, and Yukon, as presented in Table 8-6 below. The proportion of provincial and territorial drinking water samples that exceeded the MAC ranged from 0% to 21%. In First Nations communities, the upper-bounding manganese concentration in drinking water exceeded the MAC in Manitoba and the Atlantic region, and exceedances of the MAC ranged from 0% to 14.8% (Table 8-7).

Table 8-6. Comparison of manganese concentrations (µg/L) in drinking water from provinces and territories in Canada with the MAC (120 µg/L)

Province/ territory	P95 (µg/L)[a]	MAC (µg/L)[b]	% of values that exceed MAC
British Columbia	501	120	17
Alberta	1.3	120	0
Saskatchewan	820	120	21
Manitoba	235	120	8
Ontario	22	120	0.3
Quebec	224	120	12
New Brunswick	380	120	11
Prince Edward Island[c]	13	120	2
Newfoundland and Labrador	130	120	5
Yukon	41	120	0

Abbreviations: MAC, maximum acceptable concentration; P95, 95th percentile.
[a] Calculated using data from Health Canada (2019a).
[b] MAC = Health-based value based on tolerable daily intake of 0.025 mg/kg bw/day (25 mg/kg bw/day/total UF of 1,000) for a 7 kg infant consuming 0.75 L/day tap water, as used to reconstitute formula and a source allocation factor of 0.5 to account for the balance coming from the formula itself.
[c] Drinking water quality summary results (GOC [modified 2022]).

Table 8-7. Comparison of manganese concentrations (µg/L) in drinking water from communities of First Nations in Canada with the MAC (120 µg/L)

First Nations communities	P95 (µg/L)[a]	MAC (µg/L)[b]	% of values that exceed MAC
British Columbia	24.9	120	0.67
Alberta	51.5	120	0
Saskatchewan	107.0	120	5.8
Manitoba	278.8	120	14.8
Ontario	39.1	120	0
Quebec	18.7	120	1.2
Atlantic	449.0	120	10.2

Abbreviations: MAC, maximum acceptable concentration; P95, 95th percentile.
[a] Tap water (Schwartz et al. 2021).

[b] MAC = Health-based value based on tolerable daily intake of 0.025 mg/kg bw/day (25 mg/kg bw/day/total UF of 1,000) for a 7 kg infant consuming 0.75 L/day tap water, as used to reconstitute formula, and a source allocation factor of 0.5 to allow for the balance coming from the formula itself.

Dietary intake of manganese from natural sources in the diet is generally regarded as safe, and the risk and benefits of foods contributing most to dietary manganese exposure needs to be acknowledged (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated July 7, 2023; unreferenced).

The composition of infant formula is regulated in Division 25 Part B of the *Food and Drug Regulations*. Prior to selling their products on the Canadian market, manufacturers must submit a premarket notification providing evidence to demonstrate the safety and nutritional adequacy of their products, which is evaluated by Health Canada's FND. This includes growth and tolerance clinical trial data, adverse events, and product specifications. While Canada does not currently have a regulatory maximum level for manganese in infant formula, the FND internally applies the CODEX guidance upper limit (100 µg/100 kcal) in its premarket assessment. Canada is a contributor to CODEX, and this maximum level aligns with upper limits in other comparable jurisdictions, including the European Union. As part of its planned regulatory modernization of Division 25 of the *Food and Drug Regulations*, which provides compositional requirements for infant formulas, Health Canada will evaluate the incorporation of CODEX compositional requirements for many nutrients by reference into its regulations, including for manganese. Incorporation by reference will allow these values to be easily updated should the scientific consensus evolve (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated July 7, 2023; unreferenced).

Consequently, exposure estimates from dietary intake were not brought forward for risk characterization as part of this draft assessment. The development of product-specific compositional requirements or dietary guidance require consideration of minimum levels for nutritional adequacy at different life stages and the bioavailability of manganese in different matrices, which is outside the scope of this assessment.

Manganese is also present in products available to consumers, including infants, children, and females of reproductive age, that may result in oral and dermal exposures. Estimates of oral and dermal exposure to manganese from the use of arts and crafts products, automotive DIY products, household products, paints, textiles, and self-care products were derived. The MOEs between the critical health effect level and the highest oral or dermal exposure estimates derived from the exposure scenarios are presented in Table 8-8 below. The resultant MOEs from the use of modelling clay, automotive products, household odour eliminator spray, paint applicator stick, some self-care products (for example, liquid body soap), and textiles are adequate to address the uncertainties in the health effects and exposure data used to characterize risk. The MOEs derived for the use of children's paint, paint applied with an airless sprayer or a brush, and some self-care products (that is, body lotion, permanent hair colour, face moisturizer, leave-on hair conditioner, lipstick, and multivitamin/mineral supplement) are

potentially inadequate to address the uncertainties in the health effects and exposure data used to characterize risk.

Table 8-8. Sentinel oral and dermal exposures and risk estimates for manganese from the use of products available to consumers

Scenario	Age group (years)	Exposure (mg/kg bw/day)	Critical effect level (mg/kg bw/day)	MOE[a]
Children's products, paint	1	4.2×10^{-2}	25	592
Children's products, modelling clay	1	2.0×10^{-2}	25	1,260
Automotive product, fuel additive	Adult	1.5×10^{-3}	25	16,584
Household product, odour eliminator spray	Adult	1.7×10^{-5}	25	1.5×10^{6}
Paint, airless sprayer application	Adult	8.2×10^{-2}	25	303
Paint, brush application	Adult	3.5×10^{-2}	25	712
Paint, spot use with applicator stick	Adult	2.0×10^{-3}	25	12,810
Textiles, clothing	0 to 5 months	2.5×10^{-3}	25	9,833
Self-care, body lotion (cosmetic)	14 to 18	1.0×10^{-1}	25	241
Self-care, permanent hair colour (cosmetic)	Adult	5.4×10^{-2}	25	462
Self-care, face moisturizer (cosmetic)	Adult	3.7×10^{-2}	25	680
Self-care, leave-on hair conditioner (cosmetic)	Adult	2.9×10^{-2}	25	875
Self-care, liquid body soap (cosmetic)	0 to 5 months	2.1×10^{-2}	25	1,171
Self-care, lipstick (cosmetic)	2 to 3	9.8×10^{-2}	25	255
Self-care, mineral supplement (NHP - MI)	Adult	2.0	25	12
Self-care, multivitamin/mineral supplements – Health Canada monograph maximum dose (NHP - MI)	Adult	1.2×10^{-1}	25	206
Self-care, multivitamin/mineral supplement (NHP - MI)	1	9.1×10^{-2}	25	275

Abbreviations: MI, medicinal ingredient; MOE, margin of exposure; NHP, natural health product.
[a] MOE (MOE = Critical effect level / exposure) was rounded to the nearest whole number. Target MOE = 1,000 (x10 for interspecies extrapolation; x10 for intraspecies variation; x10 for use of a LOAEL, considering severity of effect).

The CNS is the primary target organ for inhalation exposure to manganese. Respiratory and lung effects associated with manganese exposure are not apparent at levels below those at which identifiable neurological changes can be detected. As a result, risk characterization based on a neurotoxic POD is expected to be protective of respiratory effects that would occur with higher doses.

The Health Canada (2010a) RfC of 0.05 µg/m^3 for the respirable fraction of manganese (as measured in $PM_{3.5}$) was selected to characterize the risk from inhalation exposure to manganese from air and products available to consumers that may result in inhalation exposure.

The RfC was established using a neurofunctional endpoint, which is considered to be the most sensitive marker associated with exposure to low concentrations of manganese via inhalation, in order to protect against impaired motor and cognitive functions. A $BMCL_{05}$ of 19.2 µg/m^3 for fine motor control (Luria Nebraska sum), was derived from the Lucchini et al. (1999) data set and converted from an occupational exposure regimen (8 hours/day, 5 days/week) to a continuous exposure scenario, with a UF of 100 (10x for inter-individual variation and 10x for database uncertainty) applied. An additional database UF was applied to account for variations in the solubility of manganese compounds, a lack of information on the impact of prenatal manganese exposure on the fetus, and unknowns associated with the significance of changes in prolactin values in the general population (Health Canada 2010a). For risk characterization, hazard quotients (HQs) were derived for manganese by calculating the ratio of continuous air concentrations to the RfC for the respirable fraction of inhaled manganese, a concentration at which health effects are not expected to occur. A HQ exceeding 1 was considered potentially inadequate to address uncertainties in the health effects and exposure data used to characterize risk.

HQs were calculated for continuous air concentration data in outdoor air, air concentrations with transit influence, and air concentrations in the vicinity of industrial facilities and are presented in Table 8-9 below. The HQs for manganese concentrations measured in outdoor air, adjacent to public transit (to account for a potential increase in exposure during commuting), are below 1 and are considered adequate to address uncertainties in the health effects and exposure data used to characterize risk.

HQs were derived to characterize the potential inhalation risk for people living in the vicinity of industrial facilities that release manganese to air. The HQs calculated for the airborne manganese concentrations in the vicinity of facilities from the electric power generation, transmission, and distribution sector and the pulp, paper, and paperboard mills sector are equal to or below 1 and are considered adequate to address uncertainties in the health effects and exposure data used to characterize risk. The HQs calculated for airborne manganese concentrations in the vicinity of facilities from the metal ore mining sector, the iron and steel mills and ferroalloy manufacturing sector, the agricultural, construction, and mining machinery manufacturing sector, the motor vehicle parts manufacturing sector, and the steel product manufacturing from purchased steel

sector exceeded 1 and are considered potentially inadequate to address uncertainties in the health effects and exposure data used to characterize risk.

Table 8-9. Inhalation exposure and risk estimates for manganese in air

Exposure scenario	Air concentration ($\mu g/m^3$)	Reference concentration ($\mu g/m^3$)	Hazard quotient[a]
Median outdoor manganese concentration (TSP) measured in Sarnia, Ontario	0.006	0.05	0.12
Mean daily air concentration ($PM_{2.5}$) with transit influence, in Toronto, Ontario	0.022	0.05	0.44
Metal ore mining sector: Mean daily air concentration ($PM_{2.5}$), in the vicinity of metal ore mining facility - modelled using SCREEN3	0.071	0.05	1.42
Iron and steel mills and ferroalloy manufacturing sector: Median manganese air concentration (TSP) in proximity to a steels mill in Hamilton, Ontario	0.136	0.05	2.72
Agricultural, construction, and mining machinery manufacturing sector: Mean daily air concentration ($PM_{2.5}$) in the vicinity of agricultural, construction, and mining machinery manufacturing industrial facility - modelled using SCREEN3	0.208	0.05	4.16
Electric power generation, transmission, and distribution sector: Maximum predicted air concentration in TSP (modelled using CALPUFF) released from an electric power generation, transmission, and distribution facility in Williams Lake, British Columbia	0.002	0.05	0.04

Exposure scenario	Air concentration (µg/m^3)	Reference concentration (µg/m^3)	Hazard quotient[a]
Motor vehicle parts manufacturing sector: Mean daily air concentration ($PM_{2.5}$) in the vicinity of motor vehicle parts manufacturing facility - modelled using SCREEN3	0.807	0.05	16.14
Pulp, paper, and paperboard mills Mean daily air concentration ($PM_{2.5}$) in the vicinity of pulp, paper, and paperboard mills - modelled using SCREEN3	0.051	0.05	1.02
Steel pipes and tubes manufacturing from purchased steel sector: Mean daily air concentration ($PM_{2.5}$) in the vicinity of iron and steel pipes and tubes manufacturing from purchased steel facility - modelled using SCREEN3	0.180	0.05	3.6

Abbreviations: PM, particulate matter; $PM_{2.5}$, particulate matter with a median aerodynamic diameter of less than 2.5 µm; TSP, total suspended particulate.
[a] Hazard quotient is defined as the ratio of the measured, estimated, or modelled air concentration to the RfC for the respirable fraction of inhaled manganese, at which health effects are not expected to occur.

In addition, HQs were calculated for continuous manganese air concentrations resulting from the use of products available to consumers (presented in Table 8-10). HQs calculated for air concentrations generated from the use of household products (that is, odour eliminator spray), aerosol hair spray, loose face powder (with 1.1% manganese concentration), and loose powder body makeup are equal to or below 1 and are considered adequate to address uncertainties in the health effects and exposure data used to characterize risk. The HQ calculated for air concentrations generated from the use of aerosol spray paint (can), paint applied using an airless sprayer, and loose face powder (with 8.7% manganese concentration) are above 1 and are considered potentially inadequate to address uncertainties in the health effects and exposure data used to characterize risk.

Table 8-10. Inhalation exposure and risk estimates for manganese in products

Exposure scenario	Air concentration (µg/m^3)	Reference concentration (µg/m^3)	Hazard quotient[a]
Household product, odour eliminator spray, $PM_{3.5}$	0.040	0.05	0.8
Paint, spray can, $PM_{3.5}$	0.084	0.05	1.68
Paint, airless sprayer (total inhalable)	0.092	0.05	1.8
Self-care, aerosol hairspray, $PM_{3.5}$ (cosmetic)	0.032	0.05	0.64
Self-care, loose body powder makeup, PM_4 (cosmetic)	0.032	0.05	0.63
Self-care, loose face powder, PM_4 makeup with SPF (NHP - NMI) (with 1.1% manganese concentration)	0.053	0.05	1.05
Self-care, loose face powder, PM_4 makeup (cosmetic) (with 8.7% manganese concentration)	0.41	0.05	8.2

Abbreviations: NHP, natural health product; NMI, non-medicinal ingredient; $PM_{3.5}$, particulate matter with a median aerodynamic diameter of less than 3.5 µm; PM_4, particulate matter with a median aerodynamic diameter of less than 4 µm; SPF, sun protection factor.

[a] Hazard quotient is defined as the ratio of the measured, estimated, or modelled air concentration to the reference concentration for the respirable fraction of inhaled manganese, at which health effects are not expected to occur.

8.4 Uncertainties in evaluation of risk to human health

There is uncertainty with respect to the oral bioavailability of manganese in diet and drinking water. It is widely accepted that the bioavailability of dietary manganese may be reduced by the presence of other dietary constituents; however, the degree to which this can occur has not been well established. In addition, in the context of a non-fasted state, absorption from food and drinking water appear to be similar. There is some uncertainty regarding the adequacy of the toxicity database and a lack of studies examining dietary sources of manganese and associated neurological outcomes.

The toxicokinetic and toxicodynamic profile for manganese in infants, who have been identified as a subpopulation of concern, has not been well established. It is unclear to

what extent homeostasis may be occurring and the amount of manganese that enters the brain following exposure in this subpopulation.

Both the oral and inhalation health effects data sets incorporate a fair amount of population-based studies, the majority of which are cross-sectional in study design. These studies do not provide a temporal component and often provide limited data on manganese exposure. While biomarkers can provide some insight into internal exposures, manganese is rapidly transferred out of circulation and minimally excreted in the urine, preventing these biomarker measures from being used to assess chronic exposure to low levels that would be expected in the general population. In addition, our current understanding does not allow for alternate biomarkers (hair, toenails, or teeth) to be used at a population level. There is uncertainty associated with the concentrations reported in ambient air and how these relate to past air concentrations and cumulative manganese exposures over time.

There is some uncertainty with regards to neurotoxic effects associated with dietary exposure in the subpopulation of concern, as no developmental neurotoxicity studies with manganese exposure through diet were available.

Manganese has been measured in traditional foods as part of several studies, including the FNFNES. However, no published estimates of manganese intake from the consumption of traditional foods are available.

Exposure estimates were derived from the use of products available to consumers via the oral, dermal, and inhalation routes. For some products available to consumers, such as chimney cleaners, there was a lack of information on manganese concentration and use pattern. Consequently, exposure and risk estimates could not be derived.

The potential use of more than 1 product by a single person in a day (that is, aggregate exposure) was not considered. This may potentially result in the underestimation of exposure for some individuals.

The 2010 Health Canada RfC was derived using manganese concentrations in $PM_{3.5}$, as that was the measurement used in Lucchini et al. (1999), the occupational study from which the POD was taken. Measured air concentration data were only available in $PM_{2.5}$ and PM_{10}; therefore, HQs were calculated using manganese concentrations in $PM_{2.5}$ for comparison to the RfC. Manganese concentrations in $PM_{2.5}$ would not have accounted for the potential increase in exposure that would occur if larger particle sizes ($PM_{3.5}$) were included, potentially resulting in an underestimation of exposure and risk.

Some of the publicly available air monitoring data reported manganese in TSP but lacked manganese concentrations in the respirable fraction. Where data were available, the concentration of manganese in the respirable fraction was predicted using the ratio between $PM_{2.5}$ and TSP at a specific location. However, these data were not available for all locations. Using the manganese concentrations in TSP may overestimate potential exposure and risk from the respirable fraction.

Publicly available manganese air concentration data from facilities that release manganese to air are limited. Predicted airborne concentrations of manganese around facilities may be refined using facility-specific information, including air monitoring data.

9. Conclusion

Considering all available lines of evidence presented in this draft assessment, there is risk of harm to the environment from manganese and its compounds. It is proposed to conclude that manganese and its compounds meet the criteria under paragraph 64(*a*) of CEPA as they are entering or may enter the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity. However, it is proposed to conclude that manganese and its compounds do not meet the criteria under paragraph 64(*b*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger to the environment on which life depends.

Considering all the information presented in this draft assessment, it is proposed to conclude that manganese and its compounds meet the criteria under paragraph 64(*c*) of CEPA as they are entering or may enter the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore proposed to conclude that manganese and its compounds meet one or more of the criteria set out in section 64 of CEPA.

It is also proposed that manganese and its compounds meet the persistence criteria but not the bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations* of CEPA.

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Appendix A. Physical and chemical properties of manganese substances identified as priorities for assessment in the Manganese and its compounds group

Table A-1. Physical and chemical properties of manganese substances identified as priorities for assessment

CAS RN	DSL or R-ICL name (common name, abbreviation)	List	Formula	Molecular weight (g/mol)	Water solubility (mg/L)	$logK_{ow}$	Vapour pressure (Pa)
1313-13-9	Manganese oxide (Manganese dioxide)	DSL	MnO_2	86.94	Insoluble	NA	NA
1335-36-0	1,2,3-Propanetriol, mono(dihydrogen phosphate), manganese salt (Manganese glycerophosphate)	R-ICL	$MnC_3H_9O_6P$; $MnC_3H_7O_6P$	225	NA	NA	NA
1344-43-0	Manganese oxide (Manganese oxide)	DSL	MnO	70.94	Insoluble[a,b]; 0.85 (20°C) estimated[c]	NA	NA
7439-96-5	Manganese (Elemental manganese)	DSL	Mn	54.94	Insoluble decomposes[d,e]; 0.7 (20°C)[c]	NA	1 (955°C)[b]
10101-66-3[l]	Diphosphoric acid, ammonium manganese (3++) salt (1:1:1) (Ammonium manganese pyrophosphate / Manganese violet)	DSL	$Mn(NH_4)P_2O_7$	246.92	7.8 (20°C)[c]; insoluble[j]	NA	NA

CAS RN	DSL or R-ICL name (common name, abbreviation)	List	Formula	Molecular weight (g/mol)	Water solubility (mg/L)	logK_{ow}	Vapour pressure (Pa)
12108-13-3	Manganese, tricarbonyl[(1,2,3,4,5-<C)-1-methyl-2,4-cyclopentadien-1-yl]-(Methylcyclopentadienyl manganese tricarbonyl) (MMT)	DSL	$MnC_9H_7O_3$	218.1	Insoluble[d]; 29 (25°C)[f]; 10 (22°C)[c]	3.7[f]; 3.4 (26°C)[c]	1066.6-48075.9 (100-200°C)[g]; 6.26 (20°C)[h]; 933 (100°C)
18820-29-6	Manganese sulfide	DSL	MnS	87	Slightly (cold)[e]; 6.16 (20°C)[c]	NA	NA
29193-02-0	L-Proline, 5-oxo-, manganese salt (1:?) (Manganese pyroglutamate)	R-ICL	$Mn_xC_5H_7NO_3$; $MnC_5H_6NO_3$	183.04	NA	NA	NA
35355-77-2[l]	C.I. Pigment Red 63:2	DSL	$C_{21}H_{12}MnN_2O_6S$	475.33	0.01[c]	2.5 (23°C)[c] [estimated]	NA
68551-42-8	Fatty acids, C6-19-branched, manganese salts (Manganous (C6-C19) branched alkanoate)	DSL	UVCB	Unspecified	NA	NA	NA

CAS RN	DSL or R-ICL name (common name, abbreviation)	List	Formula	Molecular weight (g/mol)	Water solubility (mg/L)	logK_{ow}	Vapour pressure (Pa)
105883-50-9	Manganese, bis[N-(acetyl-.K.O)-L-methioninato-.K.O]-(Manganese acetyl methionate)	R-ICL	$MnC_{14}H_{24}N_2O_6S_2$	435.41	NA	NA	NA

Abbreviations: CAS RN, Chemical Abstracts Service Registry Number; DSL, Domestic Substance List; log K_{ow}, octanol-water partition coefficient; NA, not available; R-ICL, Revised In Commerce List.
[a] HSDB 1983-
[b] Lide 2000
[c] ECHA c2007-2017a, c2007-2017b, c2007-2017c
[d] Sax and Lewis 1987
[e] ATSDR 2012
[f] Garrison et al. 1995
[g] O'Neil 2006
[h] Verschueren 1983
[i] NIOSH 2020
[j] Natural Sourcing 2018
[k] Weast and Selby 1974
[l] This substance did not meet categorization criteria but was prioritized through other mechanisms (ECCC, HC [modified 2017]).

Appendix B. Releases reported to the NPRI from 2015 to 2019 for manganese and its compounds

Sectors releasing greater than 1 tonne of manganese per year are listed in Table B-1 and appear in decreasing order in terms of total on-site releases. The sectors were identified by North American Industry Classification System (NAICS) 4-digit codes. The unit used is tonnes of manganese on an elemental basis. Yearly averages (± standard deviation) are presented, with the range in brackets, for releases reported for 2015 to 2019.

Table B-1. Average yearly releases[a] (in tonnes[b]) of manganese and its compounds from 2015 to 2019

Rank	Industrial sector (NAICS 4)	Air	Land	Water	All media <1 t	Total (per year)
1	Pulp, paper, and paperboard mills	10 ± 0.7 (9 to 11)	26 ± 4 (18 to 29)	895 ± 42 (861 to 974)	0[c]	932 ± 44 (888 to 1,013)
2	Metal ore mining	22 ± 6 (18 to 34)	95 ± 29 (66 to 144)[d]	91 ± 30 (48 to 136)	1 ± 0.6 (0.3 to 2)	210 ± 56 (133 to 282)
3	Water, sewage, and other systems	0.007 ± 0.004 (0.003 to 0.01)	0.0006 ± 0.0007 (NR to 0.002)	64 ± 3 (61 to 68)	0.6 ± 0.3 (NR to 1)	64 ± 3 (61 to 68)
4	Iron and steel mills and ferroalloy manufacturing	35 ± 6 (24 to 42)	0.03 ± 0.004 (NR to 0.03)	3 ± 0.6 (2 to 4)	1 ± 0.4 (0.7 to 2)	39 ± 5 (30 to 45)
5	Electric power generation, transmission, and distribution	6 ± 0.2 (6 to 7)	9 ± 3 (6 to 13)	0.6 ± 0.2 (0.4 to 0.8)	1 ± 0.08 (NR to 2)	17 ± 4 (13 to 22)
6	Basic chemical manufacturing	0.0004 ± 0.0003 (0.0001 to 0.0009)	NR	10 ± 4 (6 to 18)	0.002 (NR to 0.002)	10 ± 4 (6 to 18)
7	Foundries	2 ± 2 (0.05 to 5)	NR	3 ± 2 (NR to 5)	1 ± 0.4 (0.5 to 2)	5 ± 2 (1 to 6)

Rank	Industrial sector (NAICS 4)	Air	Land	Water	All media <1 t	Total (per year)
8	Motor vehicle parts manufacturing	3 ± 0.5 (3 to 4)	NR	0.0003 ± 0.00004 (0.0002 to 0.0003)	1 ± 0.5 (0.8 to 2)	5 ± 0.5 (4 to 5)
9	Cement and concrete product manufacturing	0.4 ± 0.04 (NR to 0.5)	5 ± 0.4 (NR to 6)	NR	0.2 ± 0.1 (0.1 to 0.4)	4 ± 3 (0.3 to 6)
10	Non-ferrous metal (except aluminum) production and processing	0.3 ± 0.2 (0.2 to 0.7)	NR	2 ± 2 (0.3 to 6)	0.6 ± 0.3 (NR to 1)	3 ± 2 (0.9 to 7)
11	Coal mining	0.6 ± 0.7 (NR to 2)	NR	0.7 ± 0.5 (NR to 1)	0.3 (NR to 3)	3 ± 1 (1 to 4)
12	Oil and gas extraction	0.7 ± 0.1 (0.5 to 0.8)	0.0007 ± 0.0003 (NR to 0.001)	2 ± 0.6 (0.8 to 2)	0.02 ± 0.002 (0.02)	2 ± 0.6 (2 to 3)
13	Coating, engraving, cold and heat treating, and allied activities	10 (NR to 10)	NR	NR	0.1 ± 0.06 (0.02 to 0.2)	2 ± 4 (0.2 to 10)
14	Architectural and structural metals manufacturing	0.07 ± 0.06 (NR to 0.1)	8	0.04	0.02 ± 0.004 (0.02 to 0.03)	2 ± 3 (0.02 to 8)
15	Steel product manufacturing from purchased steel	1 ± 0.7 (0.2 to 2)	NR	0.04 (NR to 0.04)	0.2 ± 0.09 (0.06 to 0.3)	1 ± 0.6 (0.3 to 2)
16	Non-metallic mineral mining and quarrying	0.01 ± 0.005 (0.003 to 0.02)	0.8 ± 1 (NR to 2)	0.4 ± 0.5 (0.00002 to 1)	0.3 ± 0.2 (0.001 to 0.5)	1 ± 0.9 (0.4 to 3)

Rank	Industrial sector (NAICS 4)	Air	Land	Water	All media <1 t	Total (per year)
17	Other non-metallic mineral product manufacturing	0.2 ± 0.08 (0.08 to 0.3)	NR	NR	0.9 ± 0.04 (0.8 to 0.9)	1 ± 0.1 (1)
18	Agricultural, construction, and mining machinery manufacturing	0.8 ± 2 (0 to 4)	NR	NR	0.04 ± 0.05 (NR to 0.1)	0.8 ± 2 (0 to 4)

Abbreviations: NAICS, North American Industry Classification System; NR, not reported.
[a] There is a degree of complexity surrounding NPRI data reporting, such as meeting reporting thresholds and the use of various acceptable methods and data sources to estimate release, disposal, and recycling quantities. Therefore, uncertainties exist in the reported quantities. Quantities for on-site and off-site disposal, as well as for off-site recycling, are not shown. See the NPRI reporting guidance document for more details (ECCC 2022).
[b] Values are rounded to 1 significant digit. Data used for this table are current as of March 30, 2022. Facilities can update their information reported to the NPRI at any time. As a result, similar analyses done using different versions of the data may produce different results.
[c] A 0 indicates a reported 0.
[d] The NPRI requires that manganese in tailings and by-products be included in the calculation of the reporting threshold, regardless of the concentration of manganese in these materials (including less than 1 percent). All releases, disposals, and transfers of manganese (except for quantities in waste rock at less than 1 percent) must then be reported to the NPRI if the threshold for reporting was met. The requirement to include all manganese in tailings in the calculation of the quantity manufactured, processed, or otherwise used threshold may contribute to more extensive reporting from the metal ore mining sector compared to other sectors. See ECCC (2022) for more details.

Table B-2. Total disposal quantities (in tonnes) of manganese and its compounds from 2015 to 2019

Year[a]	Land treatment	Landfill	Storage	Underground injection	Waste rock management	Tailings management	Annual total
2015	450	11,103	961	0.02	24,485	325,565	362,564
2016	456	11,280	921	0.02	38,381	334,977	386,015
2017	635	8,813	922	142	36,631	361,496	408,639
2018	664	4,749	826	112	49,165	303,050	362,567
2019	180	2,544	13	126	772	190,103	193,738
Mean ± standard deviation	477 ± 193	7,698 ± 3,903	729 ± 403	76 ± 70	29,887 ± 18,481	303,038 ± 66,519	342,705 ± 85,444

[a] Data used for this table are current as of September 2022. Facilities may periodically update their information reported to the NPRI. As a result, repeated analysis using data extracted at different times may produce different results. There is a degree of complexity surrounding NPRI data reporting, such as meeting reporting thresholds and

the use of various acceptable methods and data sources. Therefore, uncertainties exist in the reported quantities (see ECCC 2022 for further information).

Table B-3. Forty-three Canadian industrial sectors (NAICS-4) with reported releases of manganese to air between 2015 and 2019 (NPRI 2020; CIS 2022)

Industrial sectors	NAICS 4	Number of facilities
Oil and gas extraction	2111	3
Coal mining	2121	2
Metal ore mining	2122	49
Non-metallic mineral mining and quarrying	2123	4
Electric power generation, transmission, and distribution	2211	12
Water, sewage, and other systems	2213	5
Animal food manufacturing	3111	16
Sawmills and wood preservation	3211	4
Veneer, plywood, and engineered wood manufacturing	3212	2
Pulp, paper, and paperboard mills	3221	45[a]
Petroleum and coal product manufacturing	3241	3
Basic chemical manufacturing	3251	2
Resin, synthetic rubber, and artificial and synthetic fibres and filaments manufacturing	3252	1
Pesticide, fertilizer, and other agricultural chemical manufacturing	3253	1
Cement and concrete product manufacturing	3273	5
Other non-metallic mineral product manufacturing	3279	4
Iron and steel mills and ferroalloy manufacturing	3311	12
Steel product manufacturing from purchased steel	3312	7
Alumina and aluminium product and processing	3313	1
Non-ferrous metal (except aluminium) product and processing	3314	2
Foundries	3315	8[b]
Forging and stamping	3321	5
Architectural and structural metals manufacturing	3323	8
Boiler, tank, and shipping containing manufacturing	3324	1
Machine shops, turned product, and screw, nut, and bolt manufacturing	3327	2
Other fabricated metal product manufacturing	3329	9
Agricultural, construction, and mining machinery manufacturing	3331	2
Commercial and service industry machinery manufacturing	3333	1
Ventilation, heating air-conditioning, and commercial refrigeration equipment manufacturing	3334	1
Metalworking machinery manufacturing	3335	1
Engine, turbine, and power transmissions equipment manufacturing	3336	1
Other general purpose machinery manufacturing	3339	3
Electrical equipment manufacturing	3353	1

Industrial sectors	NAICS 4	Number of facilities
Motor vehicle manufacturing	3361	3
Motor vehicle body and trailer manufacturing	3362	1
Motor vehicle parts manufacturing	3363	16
Railroad rolling stock manufacturing	3365	1
Other transport equipment manufacturing	3369	4
Office furniture (including fixtures) manufacturing	3372	1
Other miscellaneous manufacturing	3399	1
Metal service centres	4162	9
Support activities for water transport	4189	1
Waste treatment and disposal	5622	7

Abbreviation: NAICS, North American Industry Classification System.
[a] One of the 45 facilities was closed down in 2018.
[b] One of the 8 facilities was closed down in 2018.

Appendix C. Background concentrations, toxicity modifying factors (TMFs), and site-specific predicted no-effect concentrations (PNECs) incorporating TMFs for manganese

Table C-1. Canadian ecozones and Great Lakes toxicity modifying factors for manganese

Region	Average pH	pH sample size	Geometric mean of water hardness (mg/L)	Water hardness sample size
Atlantic Maritime[a]	7.2	110	32[b]	5
Boreal Cordillera[a]	8.0	283	79	305
Boreal Plains[a]	8.0	656	130	643
Boreal Shield[a]	7.8	1,981	40	1,655
Hudson Plains[a]	7.8	5	50	5
Mixedwood Plains[a]	8.3	5,154	150	4,941
Montane Cordillera[a]	7.8	1,858	61	1,936
Pacific Maritime[a]	7.3	1,475	19	1,490
Prairies[a]	8.2	420	260	369
Taiga Cordillera[a]	8.0	22	110	22
Taiga Shield[a,c]	6.9	175	7.4	98
Lake Erie	8.03[d]	1,666	118[e]	362
Lake Huron	7.83[d]	1,960	93[e]	225
Lake Ontario	7.98[d]	1,990	125[e]	305
Lake Superior	7.60[d]	1,150	45[e]	46

[a] BQMA 2015; FQMS 2016; NLTWQM 2016; PWQMN [modified 2018]; RAMP 2016; personal communication, data prepared by the Water Stewardship Division, Province of Manitoba, for the Ecological Assessment Division, ECCC, dated February 24, 2016; unreferenced; personal communication, data prepared by the Environmental and Municipal Management Services, Saskatchewan Water Security Agency, for the Ecological Assessment Division, ECCC, dated February 25, 2016; unreferenced.
[b] Water hardness geometric mean was derived from all reference samples identified from the national equation, because there was only 1 sample in reference condition for the ecozone equation.
[c] Average pH and the geometric mean of water hardness were derived from all reference samples identified from the national equation, because an ecozone equation does not exist for the Taiga Shield.
[d] Personal communication, data provided by the Water Quality Monitoring and Surveillance Division, ECCC, for the Ecological Assessment Division, ECCC, dated June 20, 2017; unreferenced.
[e] Personal communication, data provided by the Water Quality Monitoring and Surveillance Division, ECCC, for the Ecological Assessment Division, ECCC, dated July 27, 2017; unreferenced.

Table C-2. Median background concentrations of total manganese for Canadian ecozones and Great Lakes

Region	Median (µg/L)	Sample size
Atlantic Maritime[a,b]	8.2	11
Boreal Cordillera[a]	12.3	304
Boreal Plains[a]	54.1	597
Boreal Shield[a]	24.6	1,922
Hudson Plains[a]	19.9	5
Mixedwood Plains[a]	20.6	4,492

Region	Median (µg/L)	Sample size
Montane Cordillera[a]	7.2	1,948
Pacific Maritime[a]	7.1	1,366
Prairies[a]	51.7	306
Taiga Cordillera[a]	36.6	21
Taiga Shield[c]	7.6	162
Lake Erie[d]	2.4	106
Lake Huron[d]	0.64	80
Lake Ontario[d]	0.80	165
Lake Superior[d]	0.51	83

[a] Kilgour & Associates Ltd. 2018. Data from BQMA 2015; FQMS 2016; PWQMN [modified 2018]; RAMP 2016; personal communication, data prepared by the Water Stewardship Division, Province of Manitoba, for the Ecological Assessment Division, ECCC, dated February 24, 2016; unreferenced; personal communication, data prepared by the Environmental and Municipal Management Services, Saskatchewan Water Security Agency, for the Ecological Assessment Division, ECCC, dated February 25, 2016; unreferenced.
[b] Median calculated using dissolved manganese concentrations (no total manganese concentrations were available for the Atlantic Maritime ecozone).
[c] NLTWQM 2016.
[d] Personal communication, data provided by the Water Quality Monitoring and Surveillance Division, ECCC for the Ecological Assessment Division, ECCC, dated June 20, 2017; unreferenced.

Table C-3. Toxicity modifying factors and predicted no-effect concentrations (PNECs) for the pulp and paper sector from 16 chemical (C) (kraft) and 14 mechanical (M) mills across Canada from 2018 to 2019

Mill	Mean pH[a,b]	Mean water hardness (mg/L as $CaCO_3$)[a,b]	Median PNEC (range) (µg Mn/L)
C-1	7.78	120	370 (130 to 1,100)
C-2	6.42	21	200 (86 to 660)
C-3	8.35	144	260 (76 to 1,000)
C-4	7.97	156	400 (130 to 1,300)
C-5	7.13	33	380 (170 to 990)
C-6	7.20	41	380 (170 to 970)
C-7	8.06	126	260 (76 to 1,000)
C-8	6.80	43	350 (140 to 1,000)
C-9	7.10	46	380 (170 to 990)
C-10	6.18	5.0[c]	200 (83 to 670)
C-11	7.82	72	320 (130 to 930)
C-12	8.22	159	260 (75 to 990)
C-13	7.28	87	490 (200 to 1,300)
C-14	7.80	83[d]	350 (130 to 1,000)
C-15	7.50	17	260 (110 to 660)
C-16	7.59	57	390 (170 to 1,000)
M-1	7.76	4,543.3	1,100 (427 to 2,973)
M-2	6.18	4,993.3	1,400 (562 to 3,957)
M-3	6.59	17	210 (84 to 660)
M-4	6.91	24	350 (140 to 1,000)
M-5	6.75	20	230 (96 to 690)

Mill	Mean pH[a,b]	Mean water hardness (mg/L as $CaCO_3$)[a,b]	Median PNEC (range) (µg Mn/L)
M-6	7.37	81	490 (200 to 1,300)
M-7	7.50	16	260 (110 to 660)
M-8	7.64	180[d]	540 (200 to 1,600)
M-9	6.58	5.0[c]	210 (84 to 660)
M-10	7.18	53	490 (220 to 1,200)
M-11	7.50	103	530 (220 to 1,400)
M-12	8.25	76	240 (85 to 900)
M-13	6.71	26	350 (140 to 1,000)
M-14	6.86	25[c]	350 (140 to 1,000)

Abbreviations: C, chemical mill; M, mechanical mill; NA, not available; PNEC, predicted no-effect concentration.
[a] n=3 measurements.
[b] TMFs measured in intake water unless otherwise specified.
[c] One-half of detection limit.
[d] Water hardness measured in receiving water.

Table C-4. Toxicity modifying factors and predicted no-effect concentrations (PNECs) for the metal ore mining sector

Facility	Median pH	Median water hardness (mg/L as $CaCO_3$)	Median PNEC (range) (µg Mn/L)
1-R	8.14	76	240 (220 to 590)
1-E[a]	7.60	170	720 (320 to 860)
2-R	7.59	31	320 (200 to 560)
2-E	7.85	160	420 (220 to 760)
3-R	6.54	14	210 (190 to 260)
3-E	6.53	21	240 (190 to 650)
4-R	7.30	13	240 (200 to 880)
4-E	6.70	92	490 (190 to 1,200)
5-R	7.15	20	260 (200 to 290)
5-E	6.10	29	330 (190 to 1,200)
6-R	6.92	14	230 (160 to 260)
6-E	7.33	36	350 (200 to 380)
7-R	7.30	21	260 (320 to 490)
7-E	7.82	150	400 (260 to 430)
8-R	6.56	20	240 (190 to 350)
8-E	6.21	820[c]	1,400 (660 to 1,400)
9-R	7.30	17	260 (210 to 710)
9-E	7.20	230	760 (230 to 1,200)
10-R	8.04	100	300 (240 to 590)
10-E	7.95	130	380 (250 to 650)
11-R[a]	7.54	35	270 (210 to 500)
11-E[a]	7.56	30	320 (240 to 350)
12-R[a]	7.65	43	350 (270 to 480)
12-E[a]	7.99	980[a]	480 (320 to 770)

Abbreviations: E, exposure area; Mn_T, total manganese concentration; PNEC, predicted no-effect concentration; R, reference area.

[a] The water hardness value exceeded the range valid for calculating manganese PNEC; therefore, the estimated PNEC should be used with caution.

Table C-5. Toxicity modifying factors and predicted no-effect concentrations (PNECs) for the wastewater sector from 30 WWS across Canada from 2009 to 2019 (ECCC 2020)

Facility (type)	Ecozone average pH	Ecozone geometric mean water hardness (mg/L as $CaCO_3$)	PNEC (range) (µg Mn_T/L)
1 (secondary)	7.3	19	260 (110 to 660)
2 (advanced)	8.2	260	270 (75 to 1,100)
3 (lagoon)	7.8	40	270 (110 to 770)
4 (advanced)	7.8	61	320 (130 to 930)
5 (secondary)	7.2	32	380 (170 to 970)
6 (lagoon)	8.3	150	260 (91 to 1,100)
7 (secondary)	7.6	45	320 (130 to 930)
8 (lagoon)	7.2	32	380 (170 to 970)
9 (primary)	8.3	150	260 (91 to 1,081)
10 (secondary)	7.98	125	390 (130 to 1,200)
11 (lagoon)	8.3	150	260 (91 to 1,100)
12 (secondary)	8.3	150	260 (91 to 1,100)
13 (secondary)	7.98	125	390 (130 to 1,200)
14 (secondary)	7.98	125	390 (130 to 1,200)
15 (lagoon)	8.2	260	270 (75 to 1,100)
16 (lagoon)	8.3	150	260 (91 to 1,100)
17 (secondary)	7.98	125	390 (130 to 1,200)
18 (lagoon)	7.8	40	270 (110 to 770)
19 (primary)	8.3	150	260 (91 to 1,100)
20 (secondary)	8.2	260	270 (75 to 1,100)
21 (lagoon)	8.0	79	350 (130 to 1,000)
22 (secondary)	8.3	150	260 (91 to 1,100)
23 (secondary)	8.3	150	260 (91 to 1,100)
24 (secondary)	8.3	150	260 (91 to 1,100)
25 (lagoon)	8.3	150	260 (91 to 1,100)
26 (lagoon)	8.3	150	260 (91 to 1,100)
27 (secondary)	8.3	150	260 (91 to 1,100)
28 (secondary)	8.3	150	260 (91 to 1,100)
29 (advanced)	7.8	61	320 (130 to 930)
30 (secondary)	7.8	61	320 (130 to 930)

Abbreviations: Mn_T, total manganese concentration; PNEC, predicted no-effect concentration; WWS, wastewater system.

Appendix D. Exposure to environmental media, drinking water, and food

Table D-1. Manganese concentrations (µg/L) in drinking water (treated water in treatment facilities, distribution systems, and tap water) from provinces and territories in Canada

Province (survey period)	Analytical method (µg/L)	Total # of samples	% Below LOD[a]	Median (µg/L)	P75 (µg/L)	P95 (µg/L)
All provinces and territories[b]	Digested µg/L	91	43	3	NA	82
British Columbia[c] (1991 to 2014)	Total	3,573	18.9	7.6	65.6	501
Alberta[c] (2003 to 2013)	Extracted + total	4,043	67.0	0.25	0.5	1.3
Saskatchewan[c] (2003 to 2014)	Extracted and total	4,016	29.7	10	74	820
Manitoba[c] (2002 to 2012)	Method not mentioned	1,612	3.8	8.2	21.7	235
Ontario[c] (2009 to 2014)	Method not mentioned	3,430	3.1	1.4	4.1	22
Quebec[c] (2010 to 2014)	Method not mentioned	127	7.9	2.9	14	224
New Brunswick[c] (2004 to 2014)	Method not mentioned	4,723	48.3	3	20	380
Prince Edward Island[d] (2014 to 2019)	Total	10,294	47	0.9	3	13
Newfoundland[c] (2000 to 2014)	Method not mentioned	10,285	25	7	20	130
Yukon[c] (2011 to 2014)	Method not mentioned	12	50	4.3	11.6	41

Abbreviations: NA, not available; P75, 75th percentile; P95, 95th percentile.
[a] Detection limits ranged from 0.05 µg/L to 10 µg/L.
[b] Sampled at distribution systems (Tugulea 2016).
[c] Calculated using data from Health Canada (2019a).
[d] Drinking water quality summary results (GOC [modified 2022]).

Table D-2. Manganese concentrations (µg/L) in tap water – first draw from First Nations communities in Canada[a]

First Nations community (survey period)	Total # of samples	Median (µg/L)	P75 (µg/L)	P95 (µg/L)
British Columbia (2008 to 2009)	300	0.4	1.0	24.9

First Nations community (survey period)	Total # of samples	Median (µg/L)	P75 (µg/L)	P95 (µg/L)
Alberta (2013)	106	3.0	16.9	51.5
Saskatchewan (2015)	224	2.2	4.7	107
Manitoba (2010)	142	3.4	21.3	278.8
Ontario (2011 to 2012)	322	1.83	6.4	39.1
Quebec (2016)	167	0.8	1.6	18.7
Atlantic (2014)	217	6.0	20.0	449

Abbreviations: P75, 75th percentile; P95, 95th percentile.
[a] Detection limits ranged from 0.2 µg/L to 1.0 µg/L.
Reference for the data, Schwartz et al. (2021).

Table D-3. Manganese concentrations (µg/L) in private or public wells in Canada

Province	Survey period	Number of wells sampled	Median (µg/L)	Reference
Alberta	2010 to 2011	397 (raw well water)	2	AG 2014
Alberta	2010 to 2011	217 (treated well water)	13	AG 2014
Alberta	1995 to 1996	816 (farm well water)	135 (mean)	Fitzgerald et al. 2001
Saskatchewan	2002	283	240	Thompson 2003
Manitoba	NA	NA	500 (mean)	MCC-MHSC 2021
Quebec (western)	2011 to 2012	139	11	Montcoudiol et al. 2015
Quebec (southern)	2007 to 2009	251 (tested home tap water)	8 (private well), 55 (public well)	Bouchard et al. 2011
New Brunswick	1994 to 2007	10,571	60% <50	NB DOE 2008
New Brunswick	2012 to 2014	274	5.2	Ntihabose et al. 2018
New Brunswick	2012 to 2014	259	5	Kullar et al. 2019

Province	Survey period	Number of wells sampled	Median (µg/L)	Reference
Nova Scotia	NA	4,713	21	Kennedy 2021

Abbreviations: NA, not available

Table D-4. P95 dietary intake of manganese for the general population in Canada

Age-sex group (years)	P95 dietary Mn exposure[a] (mg/kg bw/d)[b] (± SE)
1+ to 3 – M+F	0.255
4 to 8 – M+F	0.178
9 to 13 – M	0.122
9 to 13 – F	0.120
14 to 18 – M	0.150
14 to 18 – F	0.090
19 to 30 – M	0.135
19 to 30 – F	0.092
31 to 50 – M	0.100
31 to 50 – F	0.116
51 to 70 – M	0.093
51 to 70 – F	0.094
71 or more – M	0.078
71 or more – F	0.103

Abbreviations: F, females; M, males; P95, 95th percentile.

[a] Values represent usual intake estimates derived from the 24-hour recall component of the Canadian Community Health Survey (CCHS 2015) and statistically adjusted using the National Cancer Institute's method for the calculation of usual dietary intakes (NCI 2018). Cooking and preparation water was included in the dietary exposure estimates; drinking water was not included (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated September 1, 2022; unreferenced).

[b] Body weight basis calculated using each CCHS survey respondent's individual body weight, that is not calculated with a single overarching estimate per age-sex group.

Table D-5. Scenarios (Health Canada [modified 2022c])

Age group	Body weight (kg)	Inhalation rate (m^3/day)	Soil ingestion rate (mg/day)	Dust ingestion rate (mg/day)	Drinking water intake (L/day)
0 to 5 months	6.3	3.7	N/A[a]	21.6	0.83[b]
6 to 11 months	9.1	5.4	7.3	27.0	0.76[b]
1 year	11	8.0	8.8	35.0	0.36
2 to 3 years	15	9.2	6.2	21.4	0.43
4 to 8 years	23	11.1	8.7	24.4	0.53
9 to 13 years	42	13.9	6.9	23.8	0.74

Age group	Body weight (kg)	Inhalation rate (m^3/day)	Soil ingestion rate (mg/day)	Dust ingestion rate (mg/day)	Drinking water intake (L/day)
14 to 18 years	62	15.9	1.4	2.1	1.09
Adults (19+)	74	15.1	1.6	2.6	1.53

Abbreviation: N/A, not applicable.

[a] Given typical caregiver practices, it is assumed that no soil ingestion occurs.

[b] For ages less than 1 year old (infants 0 to 5 months old and 6 to 11 months old), it is assumed that the drinking water volume is equivalent to the volume of intake of reconstituted (or ready-made) infant formula.

Table D-6. Upper-bounding daily intake of 0- to 5-month-old infants (mg/kg bw/day) from consumption of different types of infant formula available on the Canadian market, using the highest 95th percentile manganese concentration in drinking water (820 µg/L)

Type of infant formula	Manganese concentration[a]	Daily consumption of formula[b]	Intake from infant formula (mg/kg bw/day)[c]	Daily consumption of water (L/day)[d]	Intake from drinking water (mg/kg bw/day)[e]	Total exposure (mg/kg bw/day)
Soy-based powdered infant formula	5.73 µg/g	124 g/day	1.13×10^{-1}	0.826	1.08×10^{-1}	2.20×10^{-1}
Cow's milk-based powdered infant formula	3.32 µg/g	124 g/day	6.53×10^{-2}	0.826	1.08×10^{-1}	1.73×10^{-1}
Soy-based liquid concentrate infant formula	630.7 µg/L	0.413 L/day	4.13×10^{-2}	0.413	5.38×10^{-2}	9.51×10^{-2}
Cow's milk-based liquid concentrate infant formula	305 µg/L	0.413 L/day	2.00×10^{-2}	0.413	5.38×10^{-2}	7.37×10^{-2}
Soy-based ready-to-feed infant formula	507.8 µg/L	0.826 L/day	6.66×10^{-2}	N/A	N/A	6.66×10^{-2}
Cow's milk-based ready-to-feed infant formula	272.3 µg/L	0 .826 L/day	3.57×10^{-2}	N/A	N/A	3.57×10^{-2}

Common footnotes for Tables D-6 and D-7 are located below Table D-7.

Table D-7. Daily intake of 0- to 5-month-old infants (mg/kg bw/day) from consumption of different types of infant formula available on the Canadian market, using the MAC for drinking water (120 µg/L) to demonstrate the manganese contributions from formula

Type of infant formula	Manganese concentration[a]	Daily consumption of formula [b]	Intake from infant formula (mg/kg bw/day)[c]	Daily consumption of water (L/day)[d]	Intake from drinking water (mg/kg bw/day)[e,g]	Total exposure (mg/kg bw/day)
Soy-based powdered infant formula	5.73 µg/g	124 g/day	1.13×10^{-1}	0.826	1.57×10^{-2}	1.29×10^{-1}
Cow's milk-based powdered infant formula	3.32 µg/g	124 g/day	6.53×10^{-2}	0.826	1.57×10^{-2}	8.11×10^{-2}
Soy-based liquid concentrate infant formula	630.7 µg/L	0.413 L/day	4.13×10^{-2}	0.413	7.87×10^{-3}	4.92×10^{-2}
Cow's milk-based liquid concentrate infant formula	305 µg/L	0.413 L/day	2.00×10^{-2}	0.413	7.87×10^{-3}	2.79×10^{-2}

Abbreviations: BW, body weight; N/A, not applicable

[a] Highest manganese concentration in formula consumed by 0- to 5-month-olds from CFIA's targeted surveys on trace elements (2011−12, 2012−13, 2017−18, and 2018−19) and CFIA's Children's Food Project (2012−13 and 2018−19 (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated December 8, 2022 and January 11, 2023; unreferenced).

[b] Formula-fed infants 0 to 5 months old are assumed to consume 0.826 L of infant formula per day, and formula is assumed to be the only dietary source for infants under 6 months of age (Health Canada [modified 2022c]). Daily intake of powdered formula was estimated assuming that 9 g of dry formula is reconstituted with 60 mL of water (Mead Johnson & Company, LLC [modified 2020a], 2020b). The daily intake of liquid concentrate formula of 0.413 L/day was estimated based on a 1:1 formula:water ratio, based on half of the daily water consumption used for reconstitution (personal communication, email from the FND, Health Canada, to the ESRAB, Health Canada, dated December 8, 2022; unreferenced; AHS 2017).

[c] Intake from infant formula = Concentration of manganese in formula * infant formula consumed/day / bw *1,000 µg/mg.

[d] Infants 0 to 5 months old are assumed to consume 0.826 L drinking water per day (Health Canada [modified 2022c]). Infants consuming liquid concentrate are assumed to consume 0.413 L drinking water per day (footnote b).

[e] Intake from drinking water = Concentration of manganese in drinking water * drinking water consumed/day / bw *1,000 µg/mg.

[f] Intake was estimated using the highest 95th percentile manganese concentration in drinking water of 820 µg/L, measured in Saskatchewan (personal communication, email from the WAQB, Health Canada, to the ESRAB, Health Canada, dated April 18, 2018 and April 24, 2018; unreferenced).

[g] Intake was estimated using the MAC for drinking water (120 µg/L) (Health Canada 2019a).

Table D-8. Upper-bounding background daily intake (mg/kg bw/day) and percentage contribution (%) of manganese from air, drinking water, food, soil, and dust for the general population in Canada.

Route of exposure[a]	0 to 5 months, exclusively human milk-fed[b]	0 to 5 months, exclusively formula-fed[c]	6 to 11 months[d]	1 yr	2 to 3 yrs	4 to 8 yrs	9 to 13 yrs	14 to 18 yrs	Adults
Air[e]	3.5E-06 (0.1%)	3.5E-06 (0.0016%)	3.6E-06 (0.002%)	4.4E-06 (0.002%)	3.7E-06 (0.001%)	2.9E-06 (0.001%)	2.0E-06 (0.001%)	1.5E-06 (0.001%)	1.2E-06 (0.001%)
Drinking water[f]	N/A	1.1E-01 (48.7%)	6.8E-02 (43%)	2.7E-02 (9%)	2.4E-02 (8%)	1.9E-02 (9%)	1.4E-02 (11%)	1.4E-02 (11%)	1.7E-02 (13%)
Food and beverages[g]	2.0E-03 (76%)	6.4E-01 (51%)	8.9E-02 (56%)	2.6E-01 (90%)	2.6E-01 (92%)	1.8E-01 (90%)	1.2E-01 (89%)	1.2E-01 (89%)	1.1E-01 (87%)
Soil[h]	N/A	N/A	2.9E-04 (0.2%)	2.9E-04 (0.1%)	1.5E-04 (0.1%)	1.4E-04 (0.1%)	5.9E-05 (0.04%)	8.1E-06 (0.01%)	7.8E-06 (0.01%)
Dust[i]	6.2E-04 (24%)	6.2E-04 (0.3%)	5.4E-04 (0.3%)	5.8E-04 (0.2%)	2.6E-04 (0.1%)	1.9E-04 (0.1%)	1.0E-04 (0.1%)	6.1E-06 (0.005%)	6.4E-06 (0.005%)
Total intake: (mg/kg bw/day)	2.6E-03	2.2E-01	1.6E-01	2.9E-01	2.8E-01	2.0E-01	1.3E-01	1.3E-01	1.3E-01

Abbreviations: BW, body weight; N/A, not applicable; yr, years.

[a] General exposure factors (for example, body weight) used to estimate intake for all age groups from environmental media, food, and drinking water are summarized in Table D-5, Appendix D.

[b] The highest median manganese concentration in human milk samples of 17 µg/L (0.017 µg/g) measured in Canada (Friel et al. 1999) and the median human milk consumption of 127.95 g/kg bw/day were used to derive the estimated daily intake of manganese in human milk (Arcus-Arth et al. 2005).

[c] Estimated using the maximum manganese concentration in soy-based powdered infant formula (5.73 µg/g) measured in CFIA's targeted surveys on trace elements (2011−13; 2017−19) and CFIA's Children's Food Project (2012−13; 2018−19) (personal communication, email from the FND to the ESRAB, Health Canada, December 8, 2022; unreferenced) and assuming that 9 g of dry formula is reconstituted with 60 mL of water (Mead Johnson & Company, LLC 2020a, 2020b). Formula-fed infants 0 to 5 months old are assumed to consume 826 mL of infant formula per day, and formula is assumed to be the only dietary source for infants under 6 months of age (Health Canada [modified 2022c]). Intake from infant formula (mg/kg bw/day) = [(Concentration of manganese in powdered formula (µg/g) * (infant formula consumed (124 g)] / bw *1,000 µg/mg.

[d] The dietary intake estimate for 6- to 11-month-old infants was estimated based on 5-year average dietary intakes from the Canadian TDS from 2003 to 2007 (Health Canada [modified 2011]).

[e] Intake estimates were derived using the highest average outdoor manganese air concentration of 0.006 µg/m^3 measured in TSP from Sarnia, Ontario (CASA [modified 2022]).

[f] Intake was estimated using the highest 95th percentile manganese concentration in drinking water of 820 µg/L, measured in Saskatchewan (personal communication, email from the WAQB, Health Canada, to the ESRAB, Health Canada, dated April 18, 2018 and April 24, 2018; unreferenced).

[g] Intake estimates were derived by the FND, Health Canada, and provided to the ESRAB, Health Canada; details in Table D-4, Appendix D. Where estimates exist for each sex, the average of the sexes was taken to estimate daily intake. When age groups were not comparable, the highest estimate was taken from the applicable age groups.

[h] Intake was estimated using the average concentration of manganese in soil of 544 mg/kg measured from 5 major geographical regions in Canada (McKeague et al. 1979) and the highest bioaccessibility of 66% (personal communication, email from the EHSRB, Health Canada, to the ESRAB, Health Canada, dated September 12, 2018; unreferenced).

[i] Intake was estimated using the median of the national baseline concentration of manganese (267 mg/kg) measured in 1,025 homes in the CHDS (personal communication, email from the EHSRB, Health Canada, to the ESRAB, Health Canada, dated July 20, 2016; unreferenced) and highest dust bioaccessibility of 68% (Reis et al. 2015).

Appendix E. SCREEN3 Model and parameters

SCREEN3 is a tier-one screening-level Gaussian air dispersion model that is based on the Industrial Source Complex (ISC) model (for assessing pollutant concentrations from various sources in an industry complex) (SCREEN3 2011). The driver for air dispersion in the SCREEN3 model is wind. The maximum calculated exposure concentration is selected based on a built-in meteorological data matrix of different combinations of meteorological conditions, including wind speed, turbulence, and humidity. This model can be used to predict air concentrations resulting from point, area, and volume source releases. SCREEN3 gives the maximum concentrations of a substance at chosen receptor heights and at various distances from a release source in the direction downwind from the prevalent wind 1 hour after a given release event. The highest predicted air concentration is presented in Table E-1 below, ensuring there was a residential receptor at that distance. An adjustment factor of 0.2 was used for the estimation of maximum manganese concentration annually based on the resultant SCREEN3 output (which is an estimate for a 1-hour period). This factor takes into account temporal variations in wind and meteorological conditions (US EPA 1992). In order to apportion total manganese emissions to manganese emissions with particle diameters of 2.5 micrometers or smaller, it was assumed that all manganese emissions reported in each facility's NPRI report have the same particle size distribution as their total particulate matter (TPM) and $PM_{2.5}$ emission estimates. The ratio of Mn ($PM_{2.5}$) to Mn (TPM) was used to estimate the quantity of manganese emissions with particle diameters of 2.5. The parameters used to estimate ambient air concentrations using the SCREEN3 model are presented in Table E-1 below. The manganese particulate concentrations determined are considered to be upper-bounding estimates, since SCREEN3 is a screening level air dispersion model and does not consider the dry deposition of particulates from the air to the ground, which can occur over longer distances.

Table E-1. Input parameters to SCREEN3

Common input parameters:
Ambient air temperature[a] (K) = 293
Receptor height[b] (m) = 1.74 (average adult height)
Urban-rural option[a] = U
Consider building downwash = N
Consider terrain above stack height = N
Consider terrain above stack base = N
Meteorology[a] = 1 (full meteorology)
Minimum and maximum distance to use = 10 to 3,000 (m)
Adjustment factor to annual air concentration[c] = 0.2 (takes into account temporal variations in wind and meteorological conditions)

Input parameter	Facility A - Metal ore mining (2122)	Facility B - Agricultural, construction, and mining machinery manufacturing (3331)	Facility C - Motor vehicle parts manufacturing (3363)	Facility D - Pulp, paper, and paperboard mills (3221)	Facility E - Iron and steel pipes and tubes manufacturing from purchased

					steel sector (3312)
NPRI 2015 to 2019 release to air (average tonnes/year)	16.5	3.9	3.0	2.5	1.2
Source type	Point	Area	Area	Point	Point
Emission rate[e] (g/s)	0.523	0.123	0.096	0.080	0.038
Source release height[f] (m)	30.4	N/A	N/A	22.86	9.75
Source height[d] (m)	N/A	6	6	N/A	N/A
Stack inside diameter[g] (m)	1.7	N/A	N/A	1.7	1.7
Stack gas exit velocity[f] (m/s)	8.37	N/A	N/A	9.41	8.23
Length of the larger side[h] (m)	N/A	308	270	N/A	N/A
Length of the smaller[h] side (m)	N/A	172	161	N/A	N/A
Emission temperature[g] (K)	352	N/A	N/A	352	352
Distance to the receptor- residence[h]	973	1270	352	2440	460
Ratio of Mn ($PM_{2.5}$) to Mn (TPM)	0.044	0.197	0.197	0.313	0.748
1-hour air concentration at the receptor, TPM ($\mu g/m^3$)	8.04	5.27	20.48	0.820	1.16
Annual air concentration at the receptor, TPM ($\mu g/m^3$)[c]	1.61	1.054	4.096	0.164	0.232
Annual air concentration at the receptor, $PM_{2.5}$ ($\mu g/m^3$)	0.071	0.208	0.807	0.051	0.180

Abbreviations: N/A, not applicable; $PM_{2.5}$, particulate matter with a median aerodynamic diameter of less than 2.5 µm.
[a] Default value in SCREEN3.
[b] Curry et al. 1993.
[C] US EPA 1992.
[d] Professional judgment.
[e] Based on an average emission rate given in NPRI in tonnes/year converted to g/s (364d × 24h × 3,600s)
[f] Estimated median values for stack heights and exit gas velocities by Standard Industrial Classification (SIC) codes (US EPA 1999).
[g] Assuming that stack diameter and exit temperature were identical to the known parameters from a stack at another facility.
[h] Measured using measurement tool on photomap.

Appendix F. Exposure estimates from the use of products available to consumers

Exposure estimates were derived for multiple age groups; however, only estimates for the age group with the highest exposure estimate are presented here. Details of age-specific physiological parameters such as body weight and skin surface area are available from the Canadian exposure factors used in human health risk assessments fact sheet and summarized in Table D-5, Appendix D (Health Canada [modified 2022c]). Dermal and oral exposure estimates were combined and are based on an exposure frequency of once per day or more. To match the inhalation reference dose, which is representative of continuous chronic exposure, inhalation exposure estimates are representative of continuous exposure incorporating frequencies of use of less than once per day. Air concentrations for inhalation estimates were adjusted to $PM_{3.5}$ or PM_4 when possible.

Exposure estimates were derived using the highest concentration (weight fraction) of manganese found per product type or scenario, unless otherwise noted. The concentration of manganese in products available to consumers was obtained through voluntary information submitted to Health Canada (ECCC, HC 2017; cosmetic notifications submitted to Health Canada; the LNHPD [modified 2021]; the internal DPD [modified 2021]; the NNHPD's Multi-Vitamin/Mineral Supplements (Health Canada 2018a), Workout Supplements (Health Canada 2024a), and Multiple Ingredient Joint Health Products (Health Canada 2024b) monographs; and publicly available information including published studies, the SDS Search Tool (Health Canada 2019b), and websites, as described in section 8.2.3. Concentrations of manganese compounds were adjusted to a manganese equivalent concentration on the basis of the composition and molecular weight of the substances as shown in Table A-1.

Product amount, retention factor, and frequency of use in self-care product estimates were assumed from internal defaults, unless otherwise noted (Health Canada 2020b). The values used for product amount, retention factors, exposure frequency (that is, frequency of use) and retention factors were developed through a process established for CMP assessments (Health Canada 2020b). This process includes a review of the data available on product amount, frequency of use, and retention factors of self-care products to assess the comprehensiveness of the study or survey, the relevance of the data collected, and the type of information collected. The highest central tendency value from the studies with the highest quality rating is selected for use in CMP assessments, and underlying studies are cited.

Dermal exposure from manganese-containing pigments, including manganese violet, was not quantified, since dermal absorption of solid pigments is anticipated to be minimal compared to other manganese compounds. A dermal absorption value of 8.3% was incorporated into dermal estimates based on data from an *in vitro* dermal absorption study conducted using $MnCl_2$ on human skin, as described in section 8.1.2 (IMnI 2010; REACH dossier [modified 2020]).

Table F-1. Dermal and oral exposures to manganese from products available to consumers

Scenario	Model and inputs	Exposure
Children's products, paint	Oral ingestion exposure (mg/kg bw/day) = ingestion amount (mg) * Concentration (%) / body weight (kg) Population: 1 year Body weight: 11 kg Oral ingestion amount: 400 mg (RIVM 2008) Concentration: 0.116% Mn	Oral – 1 year old: 4.2×10^{-2} mg/kg bw/day Dermal – negligible (pigment)
Children's products, modelling clay	Oral ingestion exposure (mg/kg bw/day) = ingestion amount (mg) * Concentration (%) / body weight (kg) Population: 1 year Body weight: 11 kg Oral ingestion amount: 100 mg (RIVM 2008) Concentration: 0.22% Mn	Oral – 1 year old: 2.0×10^{-2} mg/kg bw/day Dermal – negligible (pigment)
Automotive DIY product, fuel additive	Dermal exposure (mg/kg bw/day) = exposed area (cm^2) * thickness of film on skin (cm) * density (g/cm^3) * 1×10^3 (mg/g) * concentration (%) * dermal absorption (%) / body weight (kg) Population: Adult Body weight: 74 kg Exposed area: 12 cm^2 (based on area of 2 fingertips and 2 thumbs; RIVM 2007a) Film thickness: 1.187×10^{-2} cm (mineral oil, immersion, no wipe; US EPA 2011b) Density: 0.92 g/cm^3 (US EPA 2011b) Concentration: 1.0% Mn	Dermal – Adult: 1.5×10^{-3} mg/kg bw/day
Household product, odour eliminator spray	ConsExpo Web v1.1.0 (2021) Fact sheet: Air fresheners, fabric freshener, interior fabric spray trigger spray, spraying furniture with non-volatile substances – adult users	Dermal – Adult: 1.7×10^{-5} mg/kg bw/day

Scenario	Model and inputs	Exposure
	Model: Dermal, direct product contact – constant rate Population: Adult Body weight: 74 kg Contact rate: 46 mg/min Release duration: 0.333 minutes Concentration: 0.1% Mn	
Paint, airless sprayer application	Dermal exposure (mg/kg bw/day) = Dermal unit exposure value (mg/kg ai) * volume of paint (L) * density (kg/L) * concentration (%) * dermal absorption (%) / body weight (kg) (US EPA 2012): Treated paints and preservatives, residential handler dermal, and inhalation handler exposure algorithm (10.1) Population: Adult Body weight: 74 kg Volume of paint: 56.7 L (Health Canada 2020a) Density: 1.5 g/mL = 1.5 kg/L (RIVM 2007b) Concentration: 0.87% Mean unit exposure: (single layer, no gloves) 99.297 mg/kg ai (Health Canada 2020a)	Dermal – Adult: 8.2×10^{-2} mg/kg bw/day
Paint, brush application	ConsExpo Web v1.1.0 (2021) Fact sheet: Paint products, Brush / roller painting, waterborne wall paint Model: Dermal, direct product contact – constant rate Population: Adult Body weight: 74 kg Weight fraction: 0.87% Contact rate: 30 mg/min Application duration: 120 minutes	Dermal – Adult: 3.5×10^{-2} mg/kg bw/day
Paint, spot use with applicator stick	ConsExpo Web v1.1.0 (2021) Fact sheet: Do-it-yourself products, Filler, Filler/putty from tube Model: Dermal, instant application	Dermal – Adult: 2.0×10^{-3} mg/kg bw/day

Scenario	Model and inputs	Exposure
	Population: Adult Body weight: 74 kg Product amount: 0.05 g (RIVM 2007a) Concentration: 3.5% Mn Retention factor: 1	
Textiles, clothing	Population: 0 to 5 months Body weight: 6.3 kg Concentration: 1.33×10^{-3} % Mn (maximum measured value; Rovira et al. 2015) **Dermal exposure from wearing clothes** US EPA Residential SOPs (2012): Impregnated materials, textiles (algorithm 9.1, 9.2, 9.3) Dermal exposure (mg/kg bw/day) = concentration (%) * area weight of textile (mg/cm^2) * surface area of skin exposed (cm^2) * % migration * dermal absorption (%) / body weight (kg) Area weight of textile: 20 mg/cm^2 for cotton (US EPA 2012) Surface area of skin exposed: 2,670 cm^2 (total body minus head and hands) % migration: 26% (sweat mediated migration calculated from Rovira et al. 2017) **Oral exposure from mouthing clothes** Oral (mouthing) (mg/kg bw/day) = concentration (%) * area weight of textile (mg/cm^2) * surface area of textile mouthed (cm^2) * migration (%) / body weight (kg) Area weight of textile: 20 mg/cm^2 (US EPA 2012) Surface area of textile mouthed: 10 cm^2 (US EPA 2012)	Dermal – 0 to 5 months: 2.4×10^{-3} mg/kg bw/day Oral – 0 to 5 months: 1.1×10^{-4} mg/kg bw/day Combined – 0 to 5 months: 2.5×10^{-3} mg/kg bw/day

Scenario	Model and inputs	Exposure
	% migration: 26% (Rovira et al. 2017)	
Self-care, body lotion (cosmetic)	Dermal exposure (mg/kg bw/day) = product amount (mg) * concentration (%) * dermal absorption (%) * frequency of use (#/day) * retention factor / body weight (kg) Population: 14 to 18 years old (based on product-specific information) Body weight: 62 kg Concentration: 0.77% Mn Product amount: 10,000 mg Retention factor: 1 Frequency of use: 1/day	Dermal – 14 to 18 years old: 1.0×10^{-1} mg/kg bw/day
Self-care, permanent hair colour (cosmetic)	Dermal exposure (mg/kg bw/day) = product amount (mg) * concentration (%) * dermal absorption (%) * retention factor / body weight (kg) Population: Adult Body weight: 74 kg Concentration: 0.36% Mn Product amount: 132,600 mg Retention factor: 0.1	Dermal – Adult: 5.4×10^{-2} mg/kg bw/day
Self-care, face cream/moisturizer (cosmetic)	Dermal exposure (mg/kg bw/day) = product amount (mg) * concentration (%) * dermal absorption (%) * frequency of use (#/day) * retention factor / body weight (kg) Population: Adult Body weight: 74 kg Concentration: 1.09% Mn Product amount: 1,500 mg Retention factor: 1 Frequency of use: 2/day	Dermal – Adult: 3.7×10^{-2} mg/kg bw/day
Self-care, leave-on hair conditioner (cosmetic)	Dermal exposure (mg/kg bw/day) = product amount (mg) * Mn concentration (%) * dermal absorption (%) * frequency of use (#/day) * retention factor / body weight (kg) Population: Adult Body weight: 74 kg	Dermal – Adult: 2.9×10^{-2} mg/kg bw/day

Scenario	Model and inputs	Exposure
	Concentration: 1.77% Mn Product amount: 13,100 mg Retention factor: 0.1 Frequency of use: 1.1/day	
Self-care, liquid body soap (cosmetic) Sentinel scenario covering dermal exposure from solid body soap (cosmetic), bath foam/bubbles (cosmetic), bath salt (cosmetic), sunless tanning product (cosmetic), non-permanent body makeup (cosmetic), and sunscreen (NHP).	Dermal exposure (mg/kg bw/day) = product amount (mg) * concentration (%) * dermal absorption (%) * frequency of use (#/day) * retention factor / body weight (kg) Population: 0 to 5 months Body weight: 6.3 kg Concentration: 3.0% Mn Product amount: 4,500 mg Retention factor: 0.01 Frequency of use: 1.2/day	Dermal – 0 to 5 months: 2.1×10^{-2} mg/kg bw/day
Self-care, face mask (cosmetic) Sentinel scenario covering dermal exposure from liquid face makeup foundation (cosmetic), powder face makeup foundation (cosmetic), eyeshadow (cosmetic), makeup remover lotion (cosmetic), eye makeup remover (cosmetic), shaving cream (cosmetic), face exfoliation (cosmetic), eye cream (cosmetic), face makeup with SPF (NHP and NPD), face moisturizer with SPF (NPD), and face serum with SPF (NHP).	Dermal exposure (mg/kg bw/day) = product amount (mg) * concentration (%) * dermal absorption (%) * retention factor / body weight (g) Population: 14 to 18 years old Body weight: 62 kg Concentration: 1.09% Mn Product amount: 9,700 mg Retention factor: 0.1	Dermal – 14 to 18 years old: 1.4×10^{-2} mg/kg bw/day
Self-care, pump hairspray (cosmetic)	Exposure (mg/kg bw/day) = product amount (mg) * concentration (%) * fraction landing on hair * fraction	Dermal – Adult 19+: 5.1×10^{-3} mg/kg bw/day

Scenario	Model and inputs	Exposure
Sentinel scenario covering dermal exposure from rinse out hair conditioner (cosmetic), rinse out shampoo (cosmetic), hair oil (cosmetic), aerosol dry shampoo (cosmetic), aerosol hairspray (cosmetic), hair mousse (cosmetic), hair gel (cosmetic), hair perm/ straightener (cosmetic), and temporary hair colour (cosmetic).	migrating from hair to scalp * dermal absorption (%) * frequency of use (#/day) / body weight (kg) Population: Adult Body weight: 74 kg Concentration: 1.00% Mn Product amount: 3,600 mg Fraction landing on hair: 0.85 (RIVM 2006) Fraction migrating from hair to scalp: 0.1 (RIVM 2006) Frequency: 1.5/day	
Self-care, lipstick, or lip moisturizer (cosmetic)	Oral exposure (mg/kg bw/day) = product amount (mg) * concentration (%) * frequency of use (#/day) / body weight (kg) Population: 2 to 3 years old Body weight: 15 kg Concentration: 6.68% Mn Product amount: 22 mg Frequency of use: 1/day	Oral – 2 to 3 years old: 9.8×10^{-2} mg/kg bw/day
Self-care, tooth whitener (cosmetic) Sentinel scenario covering toothpaste (NHP) and NMI in mineral supplements (NHP)	Oral exposure (mg/kg bw/day) = product amount (mg) * concentration (%) * frequency of use (#/day) / body weight (kg) Population: Adult Body weight: 74 kg Concentration: 0.077% Mn Product amount: 80 mg Frequency of use: 2.5/day	Oral – Adult 19+: 2.1×10^{-3} mg/kg bw/day
Self-care, mineral supplement (NHP - MI)	Oral exposure (mg/kg bw/day) = dosage (mg) * frequency of use (#/day) / body weight (kg) Population: Adult Body weight: 74 kg Dosage: 25 mg Mn (per tablet)	Oral – Adult 19+: 2.0 mg/kg bw/day

Scenario	Model and inputs	Exposure
	Frequency of use: 6 tablets/day (2 tablets, 3 times daily)	
Self-care, multivitamin/mineral supplements – Health Canada Monograph maximum dose (NHP - MI)	Oral exposure (mg/kg bw/day) = dosage (mg) * frequency of use (#/day) / body weight (kg) Population: Adult Body weight: 74 kg Dosage: 9 mg Mn Frequency of use: 1 per day	Oral – Adult 19+: 1.2×10^{-1} mg/kg bw/day
Self-care, multivitamin/mineral supplement (NHP - MI)	Oral exposure (mg/kg bw/day) = dosage (mg) * frequency of use (#/day) / body weight (kg) Population: 1 year old Body weight: 11 kg Dosage: 1 mg Mn Frequency of use: 1 tablet/day	Oral – 1 year old: 9.1×10^{-2} mg/kg bw/day

Abbreviations: ai, active ingredient; BW, body weight; Mn, manganese; MI, medicinal ingredient; NHP, natural health product; NMI, non-medicinal ingredient; NPD, non-prescription drug; SPF, sun protection factor.

Table F-2. Inhalation exposure to manganese from products available to consumers

Scenario	Model and inputs	Exposure
Household product, odour eliminator trigger spray	ConsExpo Web v1.1.0 (2021) Fact sheet: Air fresheners, fabric freshener, interior fabric spray trigger spray, spraying furniture with non-volatile substances – adult users Model: Inhalation, exposure to spray, spraying Concentration: 0.1% Mn Exposure frequency: 0.14/day (52/year) Mass generation rate: 1.7 g/s Spray duration: 0.167 minutes Exposure duration: 240 minutes Room volume: 58 m^3 Room height: 2.5 m Ventilation rate: 0.5 per hour Airborne fraction: 0.018 Density non-volatile: 1.13 g/cm^3 Inhalation cut-off diameter: 3.5 µm Aerosol diameter: Log-normal Median diameter: 2 µm	Adult: Air concentration (continuous exposure) $PM_{3.5}$: 4.0×10^{-2} µg/m^3

Scenario	Model and inputs	Exposure
	Arithmetic coefficient of variation: 0.39 Maximum size: 50 µm Spraying towards person: No	
Paint, spray can	ConsExpo Web v1.1.0 (2021) Fact sheet: Painting products, Spray painting, spray can Model: Spray model, exposure to spray, spraying Population: Adult Concentration: 1.2% Mn Exposure frequency: 2/year Product amount: 340 g Spray duration: 13 minutes (adjusted for size of can, 340 g) Exposure duration: 20 minutes Room volume: 90 m^3 (adjusted for 2-car garage) Room height: 2.25 m Cloud volume: N/A Ventilation rate: 1.5 per hour Mass generation rate: 0.45 g/s Airborne fraction: 0.7 Density non-volatile: 1.5 g/cm^3 Inhalation cut-off diameter: 3.5 µm Aerosol diameter: Log-normal Median diameter: 15.1 µm Arithmetic coefficient of variation: 1.2 Maximum size: 50 µm Spraying towards person: No	Adult: Air concentration (continuous exposure) $PM_{3.5}$: 8.4×10^{-2} µg/m^3
Paint, airless sprayer	Population: Adult Air concentration (µg/m^3) = inhalation unit exposure value (8-hr TWA mg / m^3/lb ai) * conversion 1,000 µg/mg * volume of paint (mL/day) * density (g/mL) * conversion factor (0.0022 lbs/g) * concentration (%) * (8hr/24hr) * frequency (#/year) Unit exposure: inhalation 8-hr TWA 0.0154 mg/m^3/lb ai (using Parallel Particle Impactor [PPI] - respirable (US EPA 2019) Volume of paint: 56.7 L = 56,700 mL (Health Canada 2020a)	Adult: Air concentration (continuous exposure) respirable: 9.2×10^{-2} µg/m^3

Scenario	Model and inputs	Exposure
	Density: 1.5 g/mL (RIVM 2007b) Conversion factor: 0.0022 lbs/g Concentration: 0.87% Mn Frequency: 4 day/365 day (mean) (US EPA 2011b; Health Canada 2020a)	
Self-care, aerosol hairspray (cosmetic) Sentinel scenario covering inhalation exposure from hair fragrance spray (cosmetic), aerosol temporary hair colour (cosmetic), and aerosol nail polish (cosmetic).	ConsExpo Web v1.1.0 (2021) Fact sheet: Cosmetics, Hair care cosmetics, Hair spray Model: Spray model, exposure to spray, spraying Population: Adult Exposure frequency: 1.49/day (Loretz et al. 2008; Health Canada 2020b) Product amount: 2.58 g (Health Canada 2020b) Spray duration: 6.45 seconds (adjusted for product amount of 2.58 g hairspray from Health Canada 2020b) Concentration: 0.364% Mn Exposure duration: 5 minutes Room volume: 10 m^3 Room height: 2.5 m Cloud volume: 0.0625 m^3 Ventilation rate: 2 per hour Mass generation rate: 0.4 g/s Airborne fraction: 0.2 Density non-volatile: 1.5 g/cm^3 Inhalation cut-off diameter: 3.5 µm Aerosol diameter: Log-normal Median diameter: 46.5 µm Arithmetic coefficient of variation: 2.1 Maximum size: 50 µm Spraying towards person: Yes	Adult: Air concentration (continuous exposure) $PM_{3.5}$: 3.2×10^{-2} µg/m^3
Self-care, loose powder - face makeup (cosmetic)	Population: 4 years old to adult Algorithm: Manganese event air concentration (µg/m^3) = airborne PM_4 concentration (µg/m^3) * Mn concentration in product (%) Mean daily air concentration (µg/m^3) = event air concentration (µg/m^3) * exposure	4 years to adult: Air concentration (continuous exposure) PM_4: 4.1×10^{-1} µg/m^3

Scenario	Model and inputs	Exposure
	duration (min) * frequency (/day) / 1,440 minutes/day Average airborne PM_4 concentration: 1.36 × 10^3 µg/m^3 (Anderson et al. 2017; Rasmussen et al. 2019) Concentration: 8.68% Mn Exposure duration: 5 minutes[a] (RIVM 2006; US EPA 2011b) Frequency: 1/day	
Self-care, loose powder - face makeup with SPF (NHP - NMI)	Population: 4 years old to adult Algorithm: Manganese event air concentration (µg/m^3) = airborne PM_4 concentration (µg/m^3) * Mn concentration in product (%) Mean daily air concentration (µg/m^3) = event air concentration (µg/m^3) * exposure duration (min) * frequency (/day) / 1,440 minutes/day Average airborne PM_4 concentration: 1.36 × 10^3 µg/m^3 (Anderson et al. 2017; Rasmussen et al. 2019) Concentration: 1.11% Mn Frequency of use: 1/day	4 years to adult: Air concentration (continuous exposure) PM_4: 5.3 × 10^{-2} µg/m^3
Self-care, loose powder - body makeup (cosmetic) Sentinel scenario covering inhalation exposure from loose powder dry shampoo (cosmetic), loose powder eye shadow (cosmetic), loose powder nail polish (cosmetic), and pouring powdered bath products (cosmetic).	Population: 4 years old to adult Algorithm: Manganese event air concentration (µg/m^3) = average airborne PM_4 concentration (µg/m^3) * Mn concentration in product (%) Mean daily air concentration (µg/m^3) = event air concentration (µg/m^3) * exposure duration (min) * frequency (/day) / 1,440 minutes/day Average airborne PM_4 concentration: 1.36 × 10^3 µg/m^3 (Anderson et al. 2017; Rasmussen et al. 2019) Concentration: 0.67% Mn Exposure duration: 5 minutes[a] (RIVM 2006; US EPA 2011b) Frequency of use: 1/day	4 years to adult: Air concentration (continuous exposure) PM_4: 3.2 × 10^{-2} µg/m^3

Abbreviations: NHP, natural health product; NMI, non-medicinal ingredient; PM_4, particulate matter with a median aerodynamic diameter of less than 4 µm; SPF, sun protection factor.
[a] An exposure time of 5 minutes/application as time spent in bathroom (RIVM 2006; US EPA 2011b). This accounts for the duration of the particle cloud measured in Rasmussen et al. (2019) (approximately 1 minute), the average sampling duration of 6 minutes from Anderson et al. (2017), and the formation of secondary particle clouds while the user is in the bathroom.