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Screening Assessment

Selenium and its compounds

Environment and Climate Change Canada
Health Canada

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Synopsis

Pursuant to sections 68 and 74 of the Canadian Environmental Protection Act, 1999 (CEPA), the Minister of the Environment and the Minister of Health have conducted a screening assessment of selenium and its compounds as part of the Substance Groupings Initiative of Canada's Chemicals Management Plan (CMP). Substances in this grouping were identified as priorities for assessment as they met categorization criteria under subsection 73(1) of CEPA, or were included because a moiety-based assessment approach was taken.

This screening assessment focuses on the selenium moiety, and therefore includes substances containing selenium in all oxidation states (selenite, selenate, elemental, selenide), organic selenium, and all forms of selenium found in the environment. The selenium assessment encompasses all 29 selenium-containing substances on the Domestic Substances List (DSL), including those that met categorization criteria. All selenium compounds that have the potential to transform, dissolve, dissociate and/or degrade to release selenium through various transformation pathways can potentially contribute to the exposure of humans and other organisms to bioavailable forms of selenium. The assessment also considers exposure to relatively insoluble selenium-containing substances, because they can also be taken up by organisms through their diet. This assessment considers the combined exposure to the selenium moiety, from natural or anthropogenic sources, whether it is present in environmental media (e.g. water, sediment, soil and air), food or products. Selenium is an essential nutrient for human health; however, there are potential human health risks to certain sub-populations that have or are likely to have elevated selenium exposure levels. This assessment evaluates the potential for harm from elevated selenium exposure rather than deficiency or essentiality.

Natural sources of selenium include volcanic activity, sea salt spray, wildfires, weathering of selenium-rich soils and rocks, and volatilization from water bodies. Anthropogenic sources are also significant and include selenium production; the manufacture, import and use of selenium-containing substances, products and manufactured items; and the incidental production and subsequent release of selenium from activities such as fossil fuel combustion, mining, base metal refining operations, agricultural activities, and waste management. Once released to the environment, selenium may enter the air, water, and soil compartments, and eventually migrate to sediments and biota.

Selenium is an essential micronutrient taken up by aquatic, soil- and sediment-dwelling organisms, through diet and direct contact with the environment. Selenium bioavailability varies widely with environmental conditions, especially in aquatic ecosystems. Selenium is known to be bioaccumulative, and its effect on aquatic organisms can be related to their internal body concentrations. Tissue residues in fish, the most sensitive class of aquatic organisms, are used to characterize the exposures that may lead to harm in aquatic ecosystems.

The most severe effect resulting from long-term exposure to elevated concentrations of selenium in the food web is reproductive failure in egg-laying vertebrates (fish, waterbirds and amphibians). In fish, excess selenium may accumulate in fish eggs and affect developing embryos and larvae, while adults appear to be less affected. Reduced egg hatchability and increased embryonic deformities are the main selenium toxicity endpoints observed in birds, although causal evidence is sparse for oviparous reptiles and amphibians. Field studies conducted in Canada and other regions of North America have demonstrated the reproductive effects of selenium on birds and fish when present at sufficiently high concentrations in the food web, as well as potential impacts on fish populations and biodiversity, all of which affect the integrity of various ecosystems.

Ecological exposure to selenium was characterized for the following sectors based on their potential to release selenium as a by-product: metal mining, base metal smelting and refining, iron and steel production, electricity (power generation) co-located with coal mining, coal mining, oil sands extraction and processing, and pulp and paper mills. Scenarios for exposure to selenium from agricultural activities, the waste management of selenium-containing substances, products or manufactured items, and from selenium in the effluent of wastewater treatment systems were also developed.

Risk quotient analyses were performed by comparing selenium exposure concentrations to predicted no-effects concentrations (PNECs) for fish egg/ovary and fish whole-body tissues, and for the sediment and soil compartments. Based on these analyses, selenium may cause harm to aquatic, benthic and soil organisms in the vicinity of some facilities for a number of sectors, i.e., coal and metal mining, base metal smelting and refining, electricity generation (coal-fired power plants) co-located with coal mining, as well as near sensitive agricultural areas and publicly-owned wastewater treatment systems.

Considering all available lines of evidence presented in this screening assessment, there is risk of harm to organisms, but not to the broader integrity of the environment, from selenium and its compounds. It is concluded that selenium 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 concluded that selenium 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.

Selenium is an essential nutrient for human health and performs important functions in the body, including thyroid hormone metabolism, redox reactions and immune functions. When incorporated into proteins such as glutathione peroxidase, it is one of the most important antioxidants in the body. All Canadians are exposed to selenium through their diet, and intake levels in Canadians are considered adequate to meet nutritional requirements. When available, exposure to selenium was characterized using the measurement of total selenium concentrations in the whole blood of Canadians; total

selenium whole-blood concentrations are a measure of integrated exposure of all forms of selenium from all routes and sources, including environmental media, food and products. Cereals (breads, baked goods, grains and flours) are the main sources of selenium exposure for the general population, and traditional foods (such as marine mammals) can be the main sources of exposure for many Inuit in northern Canada who consume these food items. Some Inuit who eat traditional foods have been identified as a sub-population with elevated exposure. Subsistence fishers consuming fish with elevated selenium concentrations (e.g. around mining operations) and individuals consuming a subset of multi-vitamin/mineral supplements providing higher levels of selenium are two additional sub-populations in Canada with the potential for elevated selenium exposure. As there is a lack of biomonitoring data for these two sub-populations, other approaches were taken to characterize risk.

Although selenium is an essential element for humans, there are potential human health risks to certain sub-populations that have or are likely to have elevated selenium exposure levels. As such, guidance values exist to protect against insufficient and excessive exposures. Selenosis, or more specifically chronic selenium toxicity, was considered to be the critical health effect for selenium, characterized by hair loss, nail loss and deformities, garlic odour in breath, weakness, decreased cognitive function and gastrointestinal disorders. Selenosis is the basis for many international regulatory reference values, including the Tolerable Upper Intake Level (UL) established by the Institute of Medicine (IOM) for United States and Canadian populations. There are three sub-populations in Canada with exposures to selenium which exceed the UL. Total selenium in whole blood found in some Inuit exceed the whole blood equivalent of the UL and exceeds concentrations at which selenosis has been observed in humans. In addition, there are exceedances of a health-based screening value, based on the IOM UL, for high fish consumption (subsistence fishers including First Nations people) around point sources of selenium such as mines, smelting and refining facilities. Lastly, there are potential exceedances of the IOM UL for individuals taking a subset of multi-vitamin/mineral supplements providing higher levels of selenium.

On the basis of information presented in this screening assessment, it is concluded that selenium 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.

Overall Conclusion

Therefore, it is concluded that selenium and its compounds meet one or more of the criteria set out in section 64 of CEPA. The selenium moiety has been determined to meet the persistence and bioaccumulation criteria as set out in the Persistence and Bioaccumulation Regulations of CEPA. However, selenium is a naturally occurring element, with both natural and anthropogenic sources.

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Tables and Figures

1. Introduction

Pursuant to sections 68 and 74 of the Canadian Environmental Protection Act, 1999 (CEPA) (Canada 1999), the Minister of the Environment and the Minister of Health conduct screening assessments of substances to determine whether these substances present, or may present, a risk to the environment or human health.

The Substance Groupings Initiative is a key element of the Government of Canada's Chemicals Management Plan (CMP). The Selenium-containing Substance Grouping includes substances that were identified as priorities for assessment, as they met the categorization criteria under section 73 of CEPA. Four additional selenium-containing substances on the Domestic Substances List (DSL) were included, because a moiety-based assessment approach was taken.

This screening assessment focuses on the selenium moiety, and thereby considers selenium in all oxidation states (selenite, selenate, elemental, selenide), organic selenium, and any other form of selenium found in the environment. It considers all substances that have the potential to dissolve, dissociate and/or degrade to release selenium through various transformation pathways, and that can potentially contribute to the combined exposure of humans and ecological receptors to selenium. The existence of multiple pathways for selenium to enter organisms makes all forms of selenium of potential concern, whether they are soluble or not. As such, this screening assessment considers all selenium-containing substances on the DSL. Selenium is an essential nutrient for human health with an Estimated Average Requirement (EAR) of 45 µg/day; however, the Tolerable Upper Intake Level (UL) is only 400 µg/day. This assessment evaluates the potential for harm from elevated selenium exposure rather than deficiency or essentiality.

This screening 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 March 2014, and targeted literature searches were conducted up to March 2017. Empirical data from key studies and results from models were used to reach conclusions. When available and relevant, information presented in assessments from other jurisdictions was considered.

This screening 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 assessment have undergone external review and/or consultation. Comments on the technical portions relevant to the environment were received from Peter Chapman of Golder Associates Inc., David DeForest of Windward Environmental LLC, and David Janz of the University of Saskatchewan. Comments on the technical portions relevant to human health were received from Eric Hooker and Jennifer Flippin from Tetra Tech Inc. Additionally, the draft of this screening assessment

was subject to a 60-day public comment period. While external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Health Canada and Environment and Climate Change Canada.

This screening assessment focuses on information critical to determining whether substances meet the criteria as set out in section 64 of CEPA by examining scientific information and incorporating a weight of evidence approach and precaution[1]. The screening assessment presents the critical information and considerations upon which the conclusion is based.

[1] A determination of whether one or more of the criteria in section 64 of CEPA are met is based upon an assessment of risks to the environment and/or 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.

2. Assessment Scope and Identity of Substances

Selenium is either classified as a non-metal or as a metalloid element. Selenium-containing substances belong to various substance categories, including elemental selenium, inorganic metal compounds, organometallic compounds, and UVCBs (unknown or variable composition, complex reaction products, or biological materials). Identities of the 29 selenium-containing substances that are on the DSL are presented in Appendix A.

This screening assessment focuses on the selenium moiety and considers selenium in environmental media (e.g., water, sediment, soil and air), food, or products that may result from natural or anthropogenic sources. Anthropogenic sources include selenium production, incidental production and release of selenium-containing substances (i.e., as a by-product), and the manufacture, import and use of selenium-containing substances, products or manufactured items. Engineered nanomaterials containing selenium are not explicitly considered in exposure scenarios of this assessment, but measured total selenium concentrations in the environment or human biomonitoring could include engineered selenium-containing nanomaterials.

This assessment only considers effects associated with the selenium moiety, and does not address other elements that may be present in certain selenium-containing substances that may release these elements (such as cadmium, silver and copper). Some of these elements have already been addressed through previous assessments conducted as part of the Priority Substances List program under CEPA.

3. Physical and Chemical Properties

The physical and chemical properties of the selenium and selenium-containing substances listed on the DSL are provided in ECCC and HC (2017). Water solubility of selenium-containing substances ranges from sparingly soluble (e.g. metal selenides) to fully soluble (e.g. selenates and selenites). Under certain conditions, sparingly soluble selenium-containing substances may oxidize to form soluble oxyanions. Selenium occurs in the environment in various oxidation states, which differ in biological activity and physicochemical properties. Common selenium species include: selenate (SeO_4^{-2}); selenite (SeO_3^{-2}); elemental selenium (Se^0); and organic and inorganic selenides (Se^{-2}). Some selenium-containing substances are volatile. Once in the environment, selenium and selenium-containing substances may further transform depending on the properties of the receiving environment.

4. Sources, Uses and Releases to the Environment

4.1 Natural sources

Selenium is a naturally occurring element in the earth's crust. Typically, selenium is associated geochemically with sedimentary rocks, and more specifically with ferrous oxide formations and organic-rich marine shales. Selenium can be found in minerals such as pyrite, chalcopyrite, pyrrothite and sphalerite (Reimann and de Caritat 1998). Selenium is found naturally in crude oil, coal, and copper deposits. Natural releases of selenium include volcanic activity, wildfire, weathering of selenium-rich soils and rocks, sea-salt spray, and volatilization from plants and waterbodies (Mosher and Duce 1987; Nriagu 1989; Presser et al. 1994). Global natural selenium emissions to the atmosphere range between 660 and 19 000 tonnes per year (Mosher and Duce 1987; Nriagu 1989; Pacyna and Pacyna 2001).

Selenium in the upper continental crust worldwide has been estimated to vary between 0.05 and 0.30 mg/kg dry weight (dw) (Taylor and McLennan 1985, 1995; Wedepohl 1995; Reimann and de Caritat 1998; Rudnick and Gao 2003). In surface freshwater and salt water, Reimann and de Caritat (1998) estimated background selenium concentrations of approximately 0.2 µg/L, although they recognized that it is highly variable, depending on underlying geology.

Global selenium distribution is mainly determined by natural sources and transport processes, and is highly uneven (Winkel et al. 2012). Southeastern Alberta, southern Saskatchewan and southern Manitoba have naturally occurring elevated concentrations of selenium from the underlying cretaceous marine sedimentary rock. Conversely, east and north of the Great Lakes, and northern regions of the prairie provinces are selenium-deficient for animal nutrition (NRC 1983; Outridge et al. 1999). The high-selenium areas in Canada, in which selenium naturally accumulates in excess in soil, plants and groundwater, can mostly be attributed to selenium-rich local geology; however, anthropogenic factors can also have a significant influence on selenium concentrations.

4.2 Anthropogenic sources, uses and releases

Nriagu (1989) estimated the median of anthropogenic emissions of selenium to the atmosphere at 6300 tonnes per year, and the median of natural emissions of selenium to the atmosphere at 9300 tonnes per year. Mosher and Duce (1987) similarly estimated that approximately 40% of the selenium flux in the atmosphere was anthropogenic. This indicates that anthropogenic emissions are not negligible relative to natural sources.

Anthropogenic sources of selenium and selenium-containing substances include activities such as selenium production; the manufacture, import and use of selenium or selenium-containing substances, products or manufactured items; and the disposal and waste management of selenium-containing substances, products or manufactured

items. These stages in the life cycle of selenium-containing substances are presented in the following sections, with an explanation of potential releases to the environment. Sources related to the incidental manufacture of selenium-containing substances (i.e., as a by-product) in any form are also described, where applicable, with respect to releases to the environment.

4.2.1 Selenium production

Certain underground and open-pit mining activities have the potential to release selenium to the environment. Selenium can be present in metal ores or overlying material, generally considered as a contaminant, and may be released from metal ore mining to water and air (adsorbed on particles).

In Canada, selenium is recovered from anode slimes generated in the electrolytic refining of copper and from the roaster off-gases of zinc sulphide concentrates. Selenium dioxide is also produced during the roasting of zinc sulphide concentrate, where selenide is oxidized. Selenium is then recovered by precipitation from acid leach solutions (Fthenakis et al. 2007). Canadian selenium production fluctuated between 97 000 kg and 288 000 kg between 2005 and 2012 (Natural Resources Canada 2014).

4.2.2 Manufacture, import and uses of selenium and selenium-containing substances, products and manufactured items

A targeted survey was conducted in 2013 for the reporting year 2012 for 23 selenium-containing substances that belong to the Selenium-containing Substance Grouping (Canada 2013). The survey had a reporting threshold of 100 kg at a concentration equal to or above 0.001% by weight, whether in a product or mixture, and focused on selenium-containing substances used in a residence in polishes, paints, coatings, inks, adhesives, sealants, cleaning products, and toys for children less than six years of age. No uses within the survey's scope were identified. Information on other products and manufactured items that contain selenium and that are in commerce in Canada is limited. Information is also sparse on use pattern and on industrial activities for which selenium is used. A literature review and stakeholder engagement indicated the following uses for selenium-containing substances in other countries: plastics (as a component of pigments), rubber (an accelerator in rubber vulcanization), agriculture (a soil supplement, animal feed, pesticides), paints (as a component of pigments), ceramics and glass (as a component of pigments), electronic and electrical equipment, drugs, dietary supplements, cosmetics, consumer products, lubricants, and metallurgical applications (Cranston 1985; Hoffman and King 2007; Brown 2000).

In Canada, releases from most of these sectors result in relatively low quantities of selenium in the environment, based on the National Pollutant Release Inventory (NPRI 2016); these data are presented in Section 4.2.4. For the purposes of the ecological portion of the screening assessment, only the largest selenium releases reported to the NPRI are further considered, and therefore, the aforementioned sectors are not

considered further with the exception of the agricultural and glass manufacturing sectors (see ECCC 2017k for additional details on sectors reporting low release volumes).

The use of selenium in food, natural health products, drugs, cosmetics, pest control products, animal feed, soil supplements, and surface coatings of toys is regulated in Canada. Selenium can be present in food packaging materials, including as a component or residual in glass jars, as an impurity in inks with no food contact, and in polyethylene materials (2013 email from Food Directorate to Risk Management Bureau, Health Canada, unreferenced). The addition of selenium as a mineral nutrient to infant formulas and formulated liquid diets, foods in low-energy diets, meal replacements and nutritional supplements is regulated under the Food and Drug Regulations of the Food and Drugs Act (Canada 1978; Canada 1985a). Since 2010, Health Canada has been working with food manufacturers to safely transition products previously marketed as natural health products to the food regulatory framework. In order to inform potential regulatory requirements under the Food and Drug Regulations for these products, Health Canada has concluded that a number of data and information gaps must be addressed to support its efforts to regulate these types of foods and to appropriately manage any potential health risks associated with consumption of these products. As a result, Temporary Marketing Authorizations (TMAs) have been used to allow market access to safe products for the purposes of gathering in-market data to inform appropriate regulatory amendments. In order to be eligible for a TMA, products must not exceed the proposed maximum levels (including naturally occurring and added sources) per serving for certain vitamins, mineral nutrients and amino acids. Health Canada proposed these maximum levels to help ensure their addition to foods does not contribute to excessive intakes; the levels are not related to nutritional requirements and are not recommended levels for addition. In the case of selenium, Health Canada has proposed a general maximum level of selenium per serving of supplemented foods of 6 µg/serving. For supplemented foods intended for consumption only by adults, those products may contain up to 23 µg/serving provided they carry a label statement to that effect (i.e., for adults only) (2014 email from Food Directorate to Existing Substances Risk Assessment Bureau, Health Canada, unreferenced).

Health Canada has, upon request, reviewed information and supported an assessment of chemical data in fish in Canadian waterbodies that contain elevated concentrations of chemicals. This review supports decisions by the appropriate authority(ies) regarding risk management strategies, such as fish consumption advisories (2014 email from the Bureau of Chemical Safety, Food Directorate, to the Existing Substances Risk Assessment Bureau, Safe Environments Directorate, Health Canada, unreferenced).

As indicated above, the use of selenium in natural health products is regulated under the Natural Health Products Regulations of the Food and Drugs Act (Canada 2003; Canada 1985a). The Natural and Non-prescription Health Products Directorate's (NNHPD's) Multi-Vitamin/Mineral Supplements Monograph and the Selenium Monograph outline the following source materials for selenium in natural health products: monohydrated selenium dioxide, selenium citrate, selenium hydrolyzed animal protein (HAP) chelate, selenium hydrolyzed vegetable protein (HVP) chelate, selenium

yeast, selenocysteine, selenomethionine, sodium selenate and sodium selenite (Health Canada 201607, 2016b). These are also identified, along with methylselenocysteine, selenious acid, monosodium salt, selenium aspartate, selenium fumarate, selenium glycinate, selenium malate, selenium proteinate and selenium succinate, in the Natural Health Products Ingredients Database (NHPID) as source ingredients for selenium (NHPID 2014). Selenium compounds are present as medicinal ingredients in currently licensed natural health products, with the most common products being multi-vitamin/mineral supplements, anti-dandruff shampoos, and homeopathic medicines (LNHPD 2014). Selenium is permitted in multi-vitamin/mineral supplements for adults only, to a maximum daily dose of 400 µg/day (d), based on the UL for selenium established by the Institute of Medicine (IOM) for intake from food, water and supplements (Health Canada 2016a, 2016b)[2]. Selenium compounds are also listed in the Drug Products Database as an active ingredient in human and veterinary drugs, primarily trace-element supplements (DPD 2014).

Selenium and its compounds are described as prohibited for use in cosmetic products, with the exception of selenium sulfide (Chemical Abstracts Service Registry Number [CAS RN]. 7488-56-4)[3], on the List of Prohibited and Restricted Cosmetic Ingredients (more commonly referred to as the Cosmetic Ingredient Hotlist or simply The Hotlist). This is an administrative tool that Health Canada uses to communicate to manufacturers and others that products containing certain substances are unlikely to be classified as a cosmetic under the Food and Drugs Act (FDA), and in addition, that certain substances, when present in a cosmetic at certain concentrations, may contravene the general prohibition found in section 16 of the Food and Drugs Act or a provision of the Cosmetic Regulations (Health Canada 2014b).

In Canada, selenium is a component of formulants in pest control products regulated under the Pest Control Products Act at concentrations below 0.0001% (1 part per million [ppm]) (2012 email from Pest Management Regulatory Agency to Existing Substances Risk Assessment Bureau, Health Canada; unreferenced). Product types include rodenticides and antifouling paints.

Selenium is an essential animal nutrient. Background levels of selenium in some Canadian regions are insufficient for the production of forage containing selenium concentrations adequate for livestock requirements; this can be addressed through the supplementation of selenium in animal feeds. Selenium is regulated in animal feeds under Schedule 1 of the Feeds Regulations under the Feeds Act (Canada 1983;

[2] A maximum dose of 200 µg/day for selenium is under consultation by Health Canada (Health Canada 2016b).

[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.

Canada 1985b)[4], and is permitted as a supplement or macro-premix, as a mineral feed, and as a micro-premix. Selenium, primarily selenite, can be added to feeds at concentrations of up to 0.3 mg/kg for chickens, turkeys, swine, dairy cattle, beef cattle, sheep, goats, ducks and geese, and at concentrations of 0.1 mg/kg for salmonid fish and rabbits (Canada 1983). This can also be addressed through the application of a selenium soil supplement, which can be applied directly to soil but is generally blended into fertilizers prior to application. When selenium soil supplements are blended into a fertilizer prior to import or sale, the product is regulated under the Fertilizers Act (Canada 1985c). Although the selenium content of fertilizers blended with selenium soil supplements exceeds the Standards for Metals in Fertilizers and Supplements set forth in Trade Memorandum T-4-93 (CFIA 1997), these products are deemed to be in compliance with the Fertilizers Act, since the selenium is being applied to address an identified soil deficiency.

Several selenium compounds are used as pigments in paints, plastics and glass, including cadmium selenide (CAS RN 1306-24-7), cadmium selenide sulfide (CAS RN 12214-12-9, 12626-36-7), C.I. Pigment Orange 20 (CAS RN 12656-57-4) and C.I. Pigment Red 108 (CAS RN 58339-34-7). The quantity of selenium in surface coatings of toys in Canada is regulated under Section 23 of the Toys Regulations under the Canada Consumer Product Safety Act (Canada 2011; Canada 2010). Toys that have a surface coating material applied to them containing selenium are prohibited if more than 0.1% of selenium dissolves in 5% hydrochloric acid after being stirred for 10 minutes at 20ºC. The quantity of selenium in surface coatings of baby gates, cribs, cradles and bassinets is subject to the same restrictions as specified under the Expansion Gates and Expandable Enclosures Regulations and the Cribs, Cradles and Bassinets Regulations under the Canada Consumer Product Safety Act (Canada 2010; 2016a; 2016b).

4.2.3 Incidental manufacture

The reporting threshold for “Selenium and its compounds” to the NPRI (2016) was lowered in 2011 from 10 000 kg[5] manufactured, processed or otherwise used (MPO) at a concentration of 1% or greater to 100 kg[3] MPO at a concentration of 0.000005% or greater. For the purpose of this assessment, the term “manufacture” includes the incidental production of a selenium-containing substance at any concentration as a

[4] The CFIA is in the pre-consultation phase of a complete modernization of the Feeds Regulations, which includes a review of maximum nutrient levels such as selenium allowed in livestock feeds. As part of this process, the CFIA is working with the Food Directorate of Health Canada to establish levels in feeds that are protective of Canadian foods.

[5] Total of the quantity of selenium manufactured, processed or otherwise used at a specified concentration or; incidentally manufactured, processed or otherwise used as a by-product at any concentration or; contained in tailings disposed of during the calendar year at any concentration or; contained in waste rock disposed of during the calendar year at any concentration.

result of the manufacturing, processing or other uses of other substances, mixtures or products. In other words, the unintentional production of a substance as a by-product is considered incidental. This definition is equivalent to the one used by Environment and Climate Change Canada's NPRI (NPRI 2013).

4.2.4 Releases to the environment

As a result of the lower NPRI reporting threshold, a greater number of sectors reported releasing selenium and its compounds after 2010. Analyses of available release data by sector, along with measured data in exposed areas which are used to describe the environmental concentrations, are presented in ECCC (2017a to j). Releases of selenium (and its compounds) reported to the NPRI to air, water and land are shown in Figure 4-1 for the reporting years 2010 to 2014. The large increase of selenium released to water in 2014 reflects the 32 970 kg of selenium released by the Mount Polley Mine tailings dam failure in August of that year. Releases to land and unspecified releases are very low compared to releases to water and air.

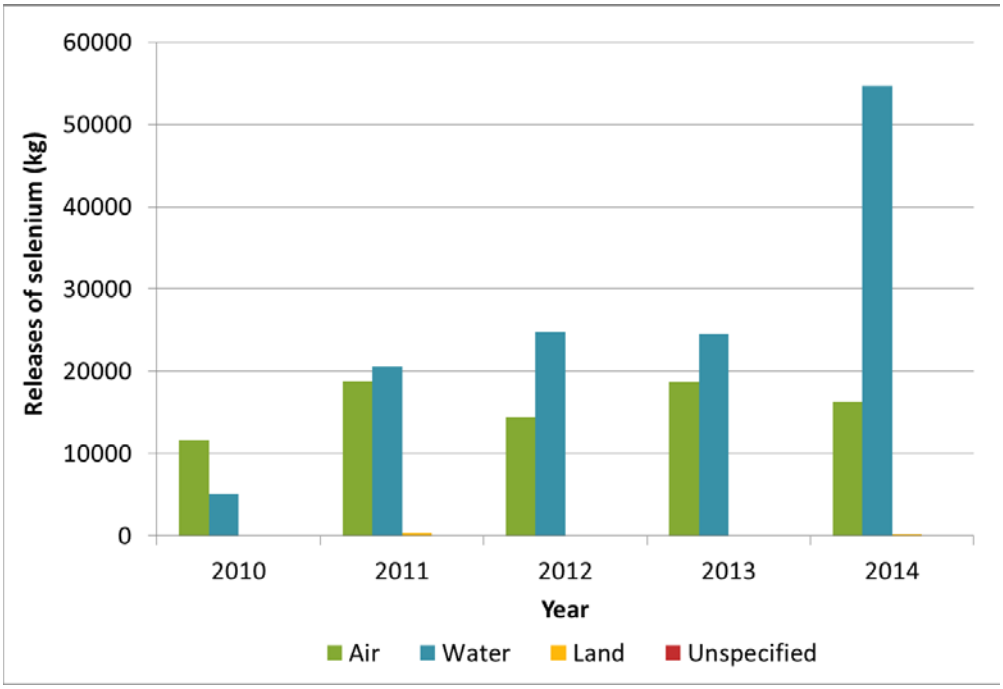

Figure 4-1: Total selenium released from 2010 to 2014 to air, water, and land

Summaries of the releases of selenium (and its compounds) reported to the NPRI by sector between 2005 and 2014 are presented in Figures 4-2 and 4-3. The five sectors that reported selenium releases of 1000 kg or more for at least one year are presented in Figure 4-2 and are the focus of this assessment. Figure 4-3 presents releases of selenium in a given year for sectors that reported lower releases of selenium (i.e., sectors for which combined releases to all compartments from all facilities were less than 1000 kg).

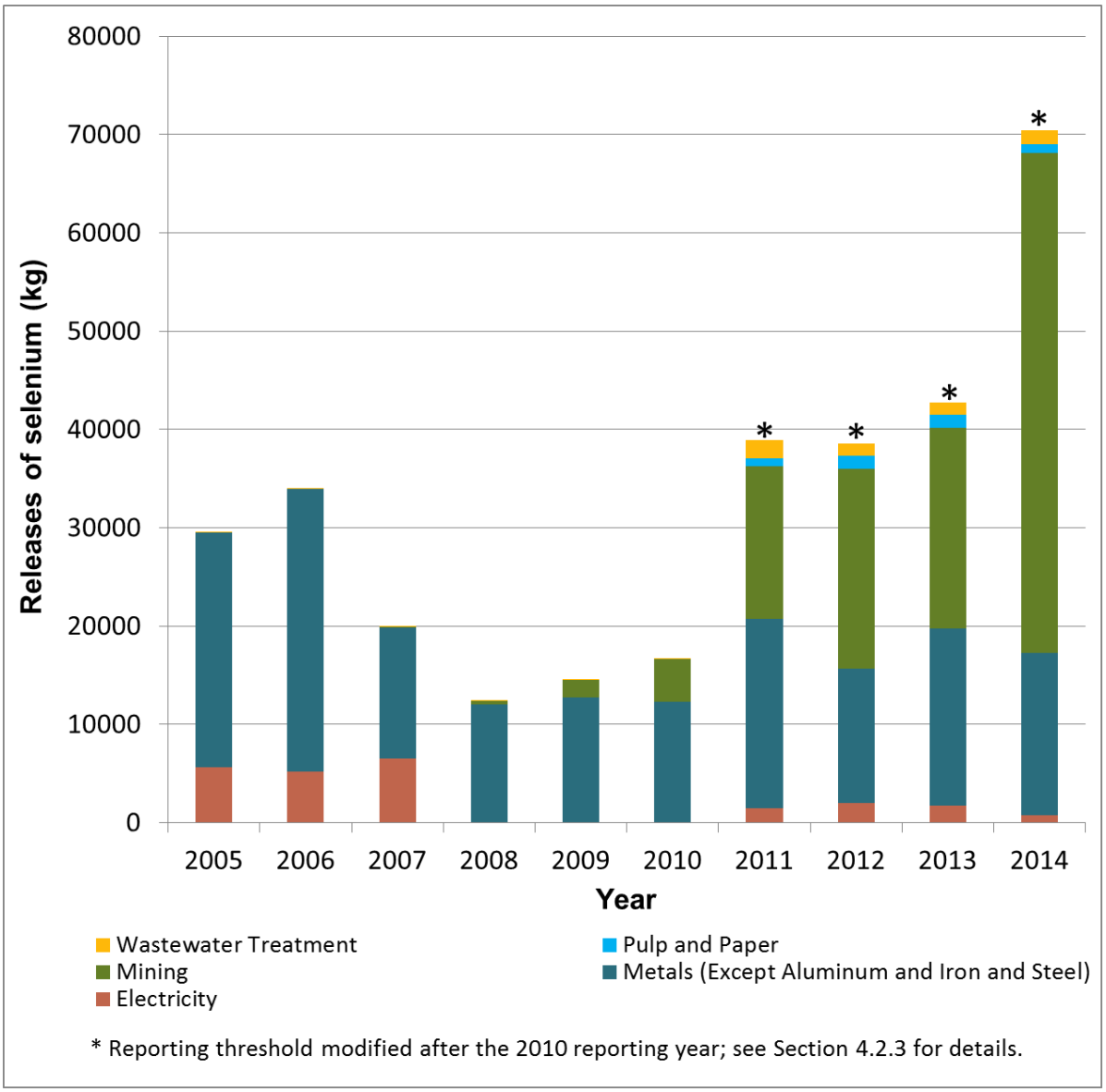

Figure 4-2: Total selenium releases from higher-emitting sectors, as reported to the NPRI between 2005 and 2014 (NPRI 2016)

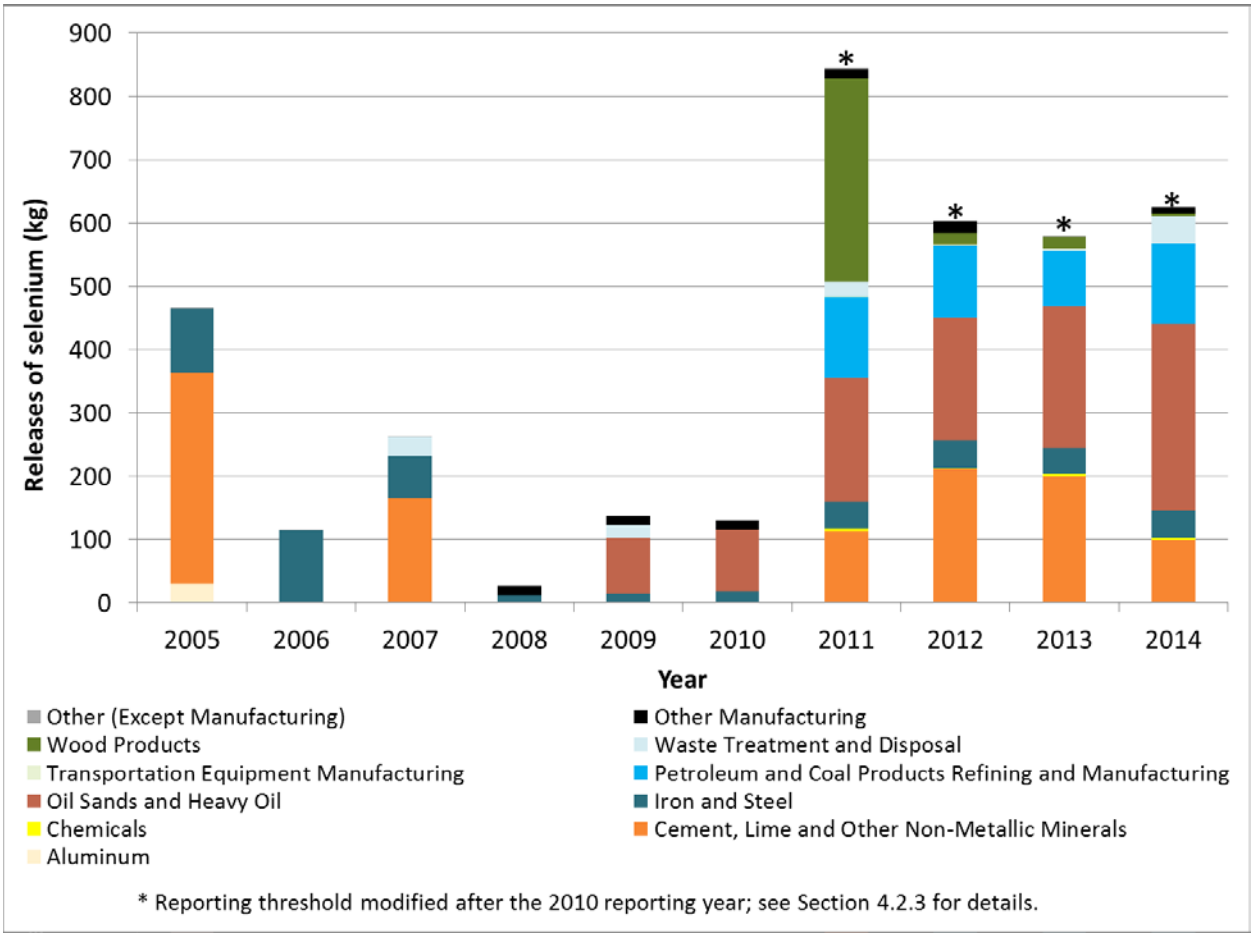

Figure 4-3: Total selenium releases from lower-emitting sectors, as reported to the NPRI between 2005 and 2014 (NPRI 2016)

Sectors reporting very low releases of selenium between 2011 and 2014 (Figure 4-3) were not characterized further in this assessment unless other indications were found that these sectors may impact the environment through releases of selenium. The iron and steel, oil sands extraction and processing, waste, and agricultural sectors were investigated further based on other indications of potential concern (as explained in ECCC 2017e, 2017g, 2017h and 2017i).

5. Environmental Fate and Behaviour

The environmental fate of inorganic substances is heavily dependent on the environmental characteristics of the receiving compartment. In the environment, selenium commonly exists in one of four oxidation states (Se^{0}, Se^{2-}, Se^{4+}, Se^{6+}). The oxyanions selenate and selenite are the dominant forms of selenium that are naturally found in freshwater and saltwater (Ralston et al. 2009). Biogeochemical cycling of organic forms of selenium is a determinant for selenium mobility between compartments

and in biota. Selenium is considered to be persistent because, although it can change its ionic state, it cannot be degraded any further in the environment.

Selenium is an essential micronutrient that can be incorporated into amino acids, proteins, and other biochemical intermediates (Maher et al. 2010). For this reason, most organisms accumulate, metabolize, transform and excrete selenium, which results in its complex speciation. Selenium is readily transformed by microbial activity to volatile and methylated species. Different inorganic and organic selenium species partition differently in the environment and have distinctive bioavailability and toxicity (Chapman et al. 2010). As such, predicting selenium behaviour in the environment requires an understanding of its speciation and other key ecosystem factors, such as productivity, residence time and food web structure.

5.1 Fate

5.1.1 Water

Selenium from natural and anthropogenic sources typically enters aquatic ecosystems as the oxidized inorganic anions, selenate (SeO_4^{2-}) or selenite (SeO_3^{2-}). The dominant form of selenium released industrially depends on the specific processes generating, and if applicable, treating the release (Maher et al. 2010). Representative selenium speciation patterns have been measured for several industrial sectors (Cutter and Cutter 2004; Maher et al. 2010). For example, selenite is typically present in larger proportions in the effluents of coal power plants and petroleum refineries, while selenate would most likely be found in mine effluents and run-off from agricultural areas (Maher et al. 2010; Young et al. 2010).

The cycling of selenium in aquatic systems is governed mainly by biologically mediated reactions (Maher et al. 2010). The oxyanions selenate and selenite are the predominant species present in the water column, although significant amounts of dissolved organic selenium compounds (Se^{2-}) can also be present in water due to biological activity (Ponton and Hare 2013). Contrary to typical cations, the solubility of oxyanions generally increases with pH. In the environmentally relevant pH range of 6–8, only elemental selenium, selenite, biselenite and selenate are present in water (Milne 1998). At these pH values, selenate and selenite are the predominant forms of dissolved selenium in well-oxygenated freshwater (Brookins 1998; Belzile et al. 2000; Ralston et al. 2009). At pH values of < 7 and under mildly reducing conditions, selenite species are reduced to elemental selenium (ATSDR 2003).

Although selenite oxidation occurs in oxic water, the sole presence of dissolved oxygen is not enough to appreciably transform selenite into selenate. Selenite oxidation is enhanced by strong oxidants in the water column, such as redox-active transition metals (iron and manganese), and by the presence of selenite-oxidizing bacteria (Maher et al. 2010).

Selenate does not form strong complexes in solution, considering its high geochemical mobility in oxic waters (Garrett 2004; Smith and Martell 2004). Selenate forms soluble minerals, but selenite salts tend to be more bioavailable due to their tendency to adsorb on biological material (Ihnat 1989; Yang et al. 2011). In lentic ecosystems such as lakes or wetlands, where the water flow is low, selenite predominates due to microbial enhanced transformations of selenate, lower redox potential, and abundant vegetation (Dungan and Frankenberger 1999; Martin et al. 2011).

Selenide and elemental selenium are often found in suspended particles in the water column, and may represent an important portion of the total selenium in the water column (Maher et al. 2010). Partitioning of selenium to particulate matter is particularly common in lentic systems (Young et al. 2010); this matter may then settle to sediment. Selenite precipitates on contact with ferric compounds (Maher et al. 2010) and may partition to sediment through adsorption to iron- or manganese-rich sediment surfaces. Certain bacteria in sediments can remove selenium from water via respiratory reduction and use selenite and selenate as a terminal electron receptor in respiration (Oremland et al. 1989). Organo-selenium compounds undergo photo-oxidation in water and their mineralization eventually yields inorganic selenium species (Chen et al. 2005).

5.1.2 Sediment

Selenium speciation in sediments is controlled by micro- and macro-scale chemical and physical properties of sediments as well as by biotic factors (Belzile et al. 2000; Stolz et al. 2006). Abiotic reduction of selenite to elemental selenium in the presence of iron oxides has been shown to occur in lake sediments (Chen et al. 2008). Many microbial organisms reduce selenate and selenite, as a tolerance mechanism, to more reduced selenium species such as elemental selenium and selenide compounds (Long et al. 1990; Dowdle and Oremland 1998; Herbel et al. 2003; Zhang et al. 2004).

Adsorption of both selenite and selenate to sediment weakens with increasing pH due to increased hydroxide competition and increasingly negative surface charge. However, decreased pH also promotes the dissolution of iron and manganese hydroxide minerals, providing fewer possible adsorption surfaces. The result of these competing trends is an optimal pH for adsorption in the neutral range (Maher et al 2010). Major competitive anions are carbonate, sulfate and phosphate; increasing competitive anion concentrations decreases the binding of both selenite and selenate to sediment (Dhillon and Dhillon 2003). Sediment-dwelling organisms and exudates present in the rhizosphere of aquatic plants can both enhance the formation of reduced inorganic and organic selenium species, and are thus an important part of the selenium biogeochemical cycle in aquatic ecosystems (Peters et al. 1999).

5.1.3 Soil

Selenium enters the soil through wet and dry deposition of natural and anthropogenic emissions, surface run-off, and soil amendment. As with aquatic sediments, the behaviour of selenium in soils is affected by redox conditions, pH, iron hydroxide

content, clay content, organic materials, and the presence of competing anions (CCME 2009). Where iron oxide reduction occurs, selenium adsorbs specifically to iron oxide hydroxides under oxic conditions (Basu et al. 2007).

Selenide compounds, which tend to be less soluble and less mobile than oxidized forms, can be found in acidic soils and soils with high amounts of organic matter (Harada and Takahashi 2009). Elemental selenium is formed in moist, anoxic soils (Tayfur et al. 2010). Selenite is soluble but adsorbs to soil minerals and organic material (Sharmasarkar and Vance 1994; Tayfur et al. 2010), whereas selenate compounds are mobile because of their high water solubility and low soil adsorption behaviour (ATSDR 2003). Selenite compounds dominate in neutral, well-drained mineral soils (Masscheleyn et al. 1991; Sharmasarkar and Vance 1994). In alkaline, well-oxygenated soil environments, selenate predominates (Tayfur et al. 2010). Selenite adsorption declines with increasing pH in the range of 4-9, and selenate adsorption is minimal under most pH conditions (Masscheleyn et al. 1991).

5.1.4 Air and long-range transport potential in air

Although the biogeochemical cycling of selenium occurs mainly in water, sediment and soil, the atmosphere remains an important environmental compartment for the fate of selenium. Selenium emitted to the atmosphere from natural and anthropogenic processes is generally assumed to be gaseous selenium dioxide and elemental selenium adsorbed to air-buoyant particles (Chapman et al. 2010). Selenium dioxide released to air from the combustion of fossil fuels may be largely reduced to elemental selenium when there is an excess of co-produced sulphur dioxide (ATSDR 2003). Particulate forms, emitted directly or produced by further atmospheric physical and chemical processes, can then be transported over varying distances inversely related to particle size (Bronikowski et al. 2000; Wen and Carignan 2007; Maher et al. 2010).

The extent of selenium partitioning into volatile fractions is less understood than water-sediment partitioning; however, a few studies have demonstrated that volatilization may be important in the environmental cycle of selenium (Thompson-Eagle et al. 1989; Fan et al. 1998; Fan and Higashi 1998; Hansen et al. 1998). A common mechanism through which elemental selenium and inorganic selenium compounds enter the atmosphere is biotransformation to volatile organic selenium species, principally dimethyl selenide ($(CH_3)_2Se$) and dimethyl diselenide ($(CH_3)_2Se_2$) (Terry et al. 2000; Guo et al. 2001). However, the residence times of volatile selenium species in the atmosphere are relatively short (Wen and Carignan 2007).

Long-range transport potential was not quantified for this screening assessment, as inorganic substances are outside the domain of typical models. However, it is believed that selenium has a certain potential to travel long-range distances by air, due to the volatility of some selenium substances and the mobility of particulate forms (Steinnes 1987; Ihnat 1989; Wen and Carignan 2007). Long-range transport may contribute to environmental concentrations of selenium in remote areas; measurements of selenium in the air in various minimally exposed areas, including remote areas such as the Arctic,

are presented in ECCC (2017l). However, the emission sources of selenium contributing to concentrations found in the Arctic, as well as the fraction of the measured selenium that may be naturally occurring, is uncertain. Therefore no conclusion can be reached on the potential for long-range transport of selenium from these data.

5.2 Bioavailability, uptake and transfer

Biologically mediated reactions dominate the geochemical behaviour of selenium in the environment. Selenate and selenite can be actively taken up by microbes, algae and plants from low trophic levels (i.e., primary producers) and converted to organo-selenium compounds, creating the base from which selenium enters the aquatic food web (Stewart et al. 2010; Janz 2012). Compounds such as selenocysteine and selenomethionine are readily formed by plants and algae (Yan et al. 2004; Yang et al. 2011). In aquatic systems, the absorption of selenium by organisms through contact with water is low compared to absorption through diet (Besser et al. 1993; Presser and Luoma 2010). Selenite generally exhibits higher uptake-rate constants than selenate in consumer organisms (Orr et al. 2006). Selenium found in suspended particulate matter, regardless of its speciation, is available for uptake and may enter the food web through the ingestion of particles (Young et al. 2010).

Environmental characteristics (such as pH, temperature and the presence and identity of major ions) that affect the partitioning of selenium betwen the dissolved phase and particulate material (containing for example sediment, detritus, and primary producers) are reflected in the Enrichment Function (EF) of the system (Stewart et al. 2010; Chapman et al. 2010). The EF, also referred to as K_d in the terminology of Presser and Luoma (2010), is the ratio of the concentration of selenium in particulate material to the concentration dissolved in water. The EF is generally higher in lentic (standing water) systems than lotic (flowing water) systems, because of higher biological activity and the somewhat higher proportion of selenite in these environments. However, it should also be noted that EFs can be highly variable among lentic and lotic systems, and thus the potential ranges in EFs for lentic and lotic systems can overlap substantially (Presser and Luoma 2010). Differences in bioavailability between trophic levels are illustrated by the magnitude of trophic transfer factors (TTFs)[6]. Data are available for TTFs of selenium for many aquatic species in Canada and around the world (Presser and Luoma 2010; Hatfield Consultants 2010; Teck 2011).

For terrestrial food webs, selenium exposure is possible through contact with selenium-containing soil, ingestion of soil, drinking water, consumption of terrestrial and aquatic prey, and inhalation of volatile selenium species. Selenium uptake through respiration is

[6] TTFs are the ratio of the concentration in an organism to the concentration in its food (Presser and Luoma 2010). TTFs are species-specific and can be determined from laboratory or field studies.

expected to be low for terrestrial organisms (see Section 7.2). In soil, several factors such as pH, speciation, organic matter, clay content, and the abundance of other ions affect selenium uptake by plants (MEND 2008; CCME 2009). Selenium phytoavailability is decreased by increasing amounts of clay, iron oxide, organic matter in soil, phosphate, sulphate, and low pH (MEND 2008; CCME 2009). Therefore, selenate is the dominant form absorbed by terrestrial higher plants (MEND 2008).

5.3 Potential for bioaccumulation

Several key factors affect selenium bioaccumulation: the physical and chemical properties of the environment (e.g. pH, redox potential, temperature and hydrology), the chemical form of selenium, the ambient selenium concentration, the exposure route and duration, and the species exposed and their trophic level (MEND 2008). These factors, reflected in EF and TTF values, affect the bioavailability and bioaccumulation potential of selenium.

Bioconcentration factor (BCF) is a measure of the direct uptake from water and is mainly derived from laboratory studies. Bioaccumulation factor (BAF) is a measure of the combined uptake from all exposure pathways and can be derived in the laboratory or in the field (MEND 2008). Given the importance of diet as an uptake route for selenium in all consumer organisms, BAFs are of greater relevance than BCFs to assess selenium bioaccumulation. Of course, for primary producers, BCFs are relevant indicators of bioaccumulation because water is the only uptake route for selenium (i.e., by definition, BCFs and EFs for primary consumers are the same measure).

Presser and Luoma (2010) proposed an ecosystem-scale model to assess the bioaccumulation potential of selenium and estimate the extent of selenium bioaccumulation in organisms of various aquatic food-web types. The model consists of multiple steps in an aquatic food chain that are characterized by an EF (presented as a K_d in Presser and Luoma (2010)) and one or more TTFs depending on the length of the food chain being modelled. Presser and Luoma validated their model for many locations in Canada and the United States (Orr et al. 2006; Presser and Luoma 2010). However, this approach was not used to characterize bioaccumulation and ecological exposure in this assessment because the required dataset (including EFs, TTFs and knowledge of the species present on-site) is incomplete for most of the sites selected for exposure characterization. No significant relationship could be found between measured and predicted internal concentrations of selenium in organisms, when using a default EF for sites with incomplete data, in the Canadian environment (Golder Associates 2013). An alternative approach was therefore used for this assessment, as described in Section 5.3.1.

Selenium concentration in the tissue of organisms represents an integrative measure of the bioavailability of selenium regardless of environmental conditions (Chapman et al. 2010; US EPA 2016; BC MOE 2014). As a result, a tissue residue approach is used in this assessment to characterize toxicity thresholds for selenium (see Section 6.3).

5.3.1 Aquatic organisms

5.3.1.1 Freshwater algae and aquatic plants

The greatest selenium bioaccumulation occurs in primary producers (Young et al. 2010). The importance of the primary producers for selenium entry into food webs is demonstrated by the fact that EFs are significantly higher than most TTFs between other trophic levels above algae (Stewart et al. 2010). Although selenite EFs are generally higher than selenate EFs in algae (Riedel et al. 1991; Stewart et al. 2010), selenate is the dominant form absorbed by aquatic higher plants (MEND 2008).

5.3.1.2 Freshwater invertebrates

The pathways for selenium uptake to invertebrates are passive absorption of selenium through the water column; ingestion of primary producers; uptake of the dissolved and particulate form by filter-feeding organisms; and uptake of the particulate form via incidental ingestion of sediment by filter-feeding organisms (MEND 2008). Of these pathways, diet is the primary uptake route for freshwater invertebrates (Besser et al. 1993; Stewart et al. 2010). BAFs for selenium in invertebrates range from 595–4685 L/Kg dw (Swift 2002) and TTFs range from 0.9–7.4 (Presser et al. 2010; Young et al. 2010). The large difference between BAFs and TTFs indicates that a large proportion of the selenium accumulated by invertebrates was first accumulated by their prey.

5.3.1.3 Freshwater fish

There are two exposure pathways through which fish can accumulate selenium: uptake via the water column and from the diet. The latter is the predominant uptake route, with studies showing that selenium concentrations in fish muscle are strongly correlated to dietary selenium and less so to waterborne selenium (Hamilton and Buhl 2004). As such, BAFs and TTFs are much more appropriate indicators of selenium bioaccumulation in fish under natural conditions compared to BCFs, since the latter does not consider dietary uptake. BAFs in fish tend to be lowest for selenate exposures and highest for selenomethionine exposures (MEND 2008). Some fish species such as the Bluegill (Lepomis macrochirus) absorb selenate and selenite equally well from the water column, but it is likely that the accumulation in fish is due to the biotransformation of selenate and selenite to organo-selenium by algae and bacteria (Besser et al. 1993).

At a given selenium water concentration, selenium concentrations in fish are generally higher in lentic (standing water) habitats versus lotic (flowing water) habitats, reflecting greater bioaccumulation potential in lentic systems (Brix et al. 2005; Orr et al. 2006). Selenite is the most common form of inorganic selenium generally found in lentic environments that can be reduced to more bioavailable organic forms; selenate is more common in lotic environments (Stewart et al. 2010). Other factors that may account for the greater bioaccumulation potential of selenium in lentic systems include enhanced formation of organo-selenium, greater uptake by primary producers and cycling via sediment-detrital pathways, and longer food chains. To account for these variations in

aquatic ecosystems, the BAFs presented in this section are assessed for the lotic and lentic environments separately (Figure 5-1).

An in-depth analysis of BAF data was conducted in order to use BAFs to generate tissue residue concentrations of selenium in fish that can be compared to critical tissue residue toxicity values. The data were trimmed to remove BAFs that were artificially high due to low concentrations of selenium in water (i.e., below essential requirements). Very low BAFs, involving exposures greater than acute toxicity water concentrations, were also trimmed from the data set. BAFs for selenium in fish range from 203–27 566 L/kg dw in lentic systems and from 107–15 320 L/kg dw in lotic systems (Figure 5-1).

SigmaPlot v.10.0.1 (Systat Software, Inc. 2007) was used to plot the distribution of BAFs. Several cumulative distribution functions were fit to the data using regression methods, and the model fit was assessed using statistical and graphical techniques. The distributions of BAFs in lotic and lentic systems are significantly different (Student's T-test, $p<0.001$). A sigmoid model provided the best fit of the models tested for BAFs in lentic systems ($R^2=0.99$); the median of the distribution model corresponded to a BAF of 2363 L/kg (Figure 5-1). The logistic model provided the best fit for the distribution of BAFs in lotic systems ($R^2=0.99$); the median of the distribution model was 1281 L/kg (Figure 5-1). These median values were selected as "generic" values for the purposes of calculating risk quotients (see Section 6.4). The selection of median values, along with the removal of studies at very high or very low selenium water concentrations, further minimizes the potential for over- and under-estimation of bioaccumulation to produce appropriate reasonable cases for risk characterization in lentic and lotic environments. BAFs for selenium in fish range from 107 to 27 566 L/kg dw, and therefore selenium meets the bioaccumulation criterion (BAF > 5000) of the Persistence and Bioaccumulation Regulations.

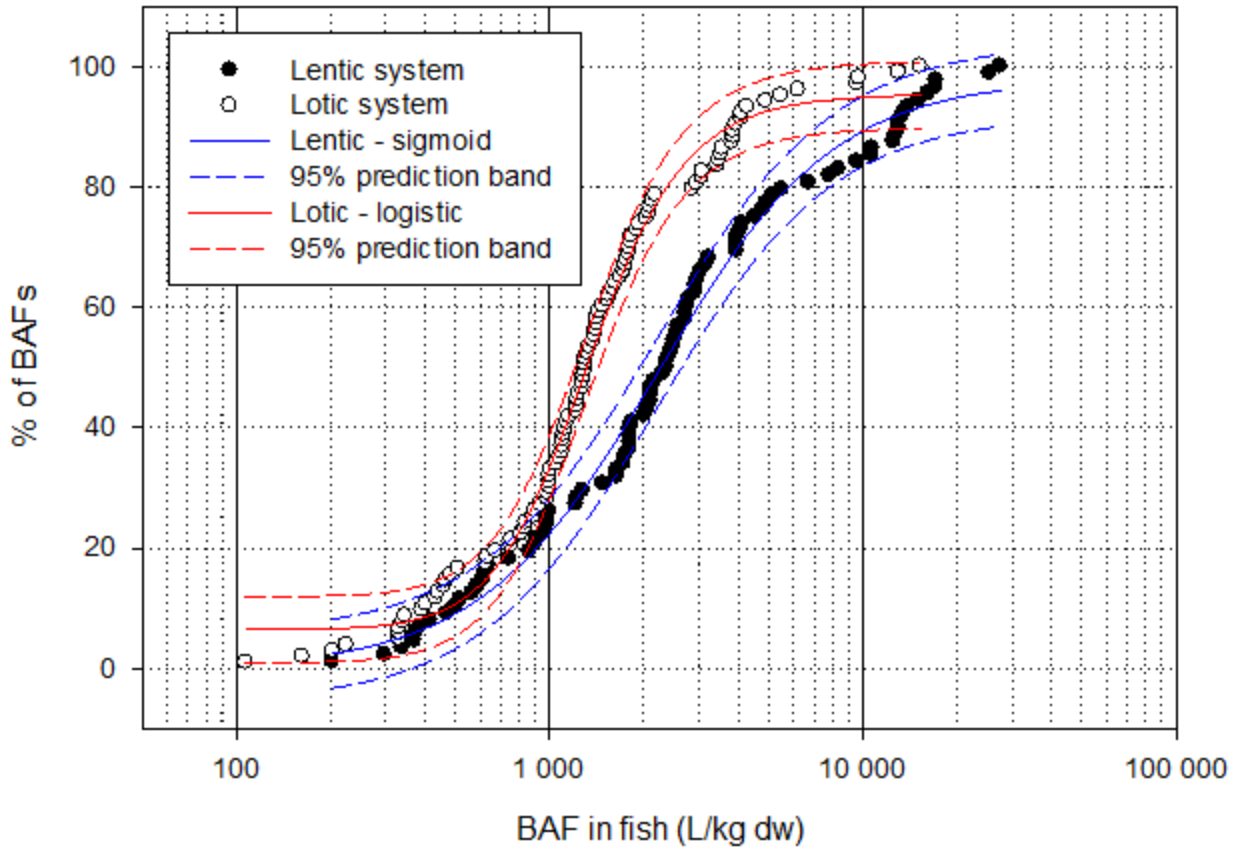

Figure 5-1: Distributions of fish BAFs for selenium in lentic and lotic freshwater environments

5.3.1.4 Marine water

Some marine organisms have much higher BAFs and BCFs than freshwater organisms (Janz et al. 2010). In marine diatoms, Zhang et al. (2010) found BCFs (EFs) between 5000–337 000 L/kg dw. TTFs for marine fish, barnacles and bivalves range from 0.52–0.89, 15.8–20.3 and 2.8–23, respectively, indicating the potential of selenium transfer from dietary exposure (Presser and Luoma 2010).

Campbell (2005) reported that the concentration of selenium in liver and kidney of ringed seal averaged 0.4 and 10.2 micrograms per gram (µg/g) wet weight (ww), respectively. Laird et al. (2013) reported a higher concentration of selenium in the liver of ringed seal (7.9 µg/g ww). Beluga Whales in the Canadian Arctic accumulated between 3.8 and 39.5 µg/g ww of selenium in their liver (mean concentration of 13.8 µg/g ww), while the concentration of selenium in Beluga Whale kidney was between 3.1 and 4.3 µg/g ww (Stern and Loseto 2013). These elevated selenium concentrations in the tissues of marine mammals indicate a certain potential for bioaccumulation.

5.3.2 Benthic organisms

The partitioning of selenium to sediments is an intermediate step leading to its accumulation in food webs and exposure to organisms at higher trophic levels (MEND 2008). Sources of food for epibenthic and endobenthic organisms may include detritus/particles, decaying organic matter, biofilm and periphyton.

Biota-to-sediment accumulation factors (BSAFs) are the ratio of selenium internal-body concentration in benthic organisms to selenium concentration in sediment. Sediment-dwelling and epibenthic species were considered in an analysis of available BSAF data, but filter-feeders were excluded because their main route of uptake is overlying water rather than sediment. BSAFs found in the literature ranged from 0.05 –16.3 dw with a geometric mean of 2.5 dw. Most of the BSAFs were for lentic systems, one was for a lotic environment, and one was for a mixed lotic/lentic zone.

5.3.3 Terrestrial organisms

5.3.3.1 Terrestrial plants

Selenium may have positive effects on plant processes, but it has not been confirmed to be essential to plants (CCME 2009; Germ et al. 2007). Some species of higher plants, such as bulrush and cattail (Typha), prince's plumes (Stanleya), Haplopappus and woodyasters (Xylorhiza), have shown a high tolerance to selenium. They can hyper-accumulate high concentrations of selenium (in excess of 5000 µg/g [dw]) and may cause toxicity in livestock and other animals that consume them (Terry et al. 2000; MEND 2008; CCME 2009).

5.3.3.2 Invertebrates

There are limited studies on selenium bioaccumulation in terrestrial invertebrates. Biota-to-soil accumulation factors for sodium selenite in earthworms range from 0.97–5.27 dw, and increase with decreasing selenium concentrations in soil (Fischer and Koszorus 1992). Beyer et al. (1987) observed that worms accumulated selenium more easily when the selenium concentration in soil was very low (<0.1 µg/g [dw]), compared to a higher selenium concentration (6.6 µg/g [dw]). Wu et al. (1995) studied the transfer of selenium from soil to plant to grasshopper to praying mantis, and calculated biota-to-soil accumulation factors of 43.6 for grass, 44.4 for grasshoppers and 75.1 for praying mantises. Wu et al. (1995) reported that selenium biomagnifies from soil to plant and from grasshopper to praying mantis, but observed no consistent increase in selenium concentration between plant and grasshopper.

5.3.4 Reptiles, amphibians and mammals

There are very few studies on the bioaccumulation potential of selenium in terrestrial vertebrates. Hopkins et al. (2005) studied the trophic transfer of selenomethionine in a laboratory food chain consisting of the House Cricket (Acheta domestica) and Western

Fence Lizard (Sceloporus occidentalis). Crickets were fed pellets laced with selenomethionine, and fed to lizards. Lizards fed with selenium-contaminated prey accumulated significantly higher selenium concentrations than controls, and concentrations differed between tissue-type and sex of the lizard.

Hopkins et al. (2006) studied the accumulation of selenium in Eastern Narrow-mouthed Toad (Gastrophryne Carolinensis) females and maternal transfer in their eggs, in an aquatic environment contaminated by the wastes of a coal power plant. The BAFs in the contaminated area and the reference area were, respectively, 10 789 and 9737 L/kg dw in adult females. The concentration of selenium in the females and eggs was significantly correlated, confirming the maternal transfer of selenium to the eggs.

Several studies acknowledge the presence of selenium in the tissues of wild mammals, with higher concentrations in organs such as the liver and kidneys (Driskell et al. 1997; Campbell et al. 2005; Gamberg et al. 2005; Pollock 2005). The reported mean concentration of selenium in these animals varies between 0.22 and 4.9 µg/g ww in the liver, and between 0.92 and 10.2 µg/g ww[7] in kidneys (Salisbury et al. 1991; Gamberg et al. 2005; Pollock 2005; Laird et al. 2013). Selenium concentrations in the tissues of terrestrial organisms that belong to upper-trophic levels tend to correlate with selenium concentration in their diet (NRC 1980; Heinz et al. 1989).

6. Potential to Cause Ecological Harm

6.1 Essentiality

Like many elements, selenium is essential for the health and survival of some organisms, and is also known for its narrow window between essentiality and adverse effects (NAS 1980; CCME 2009; Chapman et al. 2010). Selenium is required for bone metabolism, iodine metabolism, immune function, reproductive success and many other essential functions (Flueck et al. 2012). At the molecular level, a total of 25–30 selenoproteins are known to have enzymatic, antioxidant and cellular transport functions in animals (Stewart et al. 2010).

Selenium deficiency may cause adverse effects in fish, poultry, livestock and wild mammals (Schubert et al. 1961, as reported in Flueck et al. 2012). Examples of effects include muscle and heart disease, exudative diathesis, increased embryonic mortality in birds, heart diseases in pigs, and retained placenta for labouring cows (Mayland 1994). Very few occurrences of selenium deficiency in wildlife have been reported in Canada.

[7] Pollock (2005) reported the concentration of selenium in the organs of Moose and White-tailed Deer on a dw basis. The values were converted to a ww basis by estimating the moisture content at 71.5% and using a multiplying factor of 3.5.

Hebert and Cowan (1971) (as reported in Flueck et al. 2012) reported white muscle disease in wild goats from British Columbia that were experimentally fed with less than 0.05 mg/kg of selenium in their diet. Although not specified in that report, these are probably wet weight values, and this study suggests that the animals were acclimated to higher selenium concentrations in their natural diet. In Alberta, Samson et al. (1989) observed low selenium blood levels (5–45 µg/L) in Bighorn Sheep and Mountain Goats, but no signs of adverse effects on the animals were discernible. In fish, selenium is an essential element when absorbed in quantities resulting in concentrations between 0.1 and 0.5 µg/g dw in the fish tissues (Lemly 1997). A review of selenium essentiality to various organisms is available in ECCC (2017n).

The level of selenium that is tolerable to organisms can be assessed based on background concentrations of selenium in water or soil. In some areas naturally rich in metals (or naturally occurring substances), some organism populations can acclimate or adapt to high concentrations of metals by mechanisms of detoxification and by the storage of contaminants in tissues (Campbell et al. 2006). Although occurrences of this phenomenon have rarely been reported in the literature for selenium specifically (Kennedy et al. 2000; Janz et al. 2010), it may still be occurring in some regions of Canada.

6.2 Mechanisms of toxic action

Teratogenic effects at the molecular level in egg-laying vertebrates are believed to occur when selenium substitutes for sulphur in methionine amino acid in the female liver during protein synthesis (Janz 2012). The female transfers selenomethionine-enriched proteins to oocytes, which has been known to cause malformations in the developing embryo or in the juvenile organism (Janz et al. 2010). Another hypothesis for the mechanism of action of selenium toxicity at the molecular level is the appearance of oxygen radicals resulting from an enzymatic pathway activated by high levels of selenium (Palace et al. 2004). The two hypotheses may be complementary, as many possible pathways can occur simultaneously and lead to different effects observed at the organism level.

Deficiency or exceedance of selenoproteins could also be involved in non-reproductive effects such as muscle metabolism and thyroid hormones regulation, through the iodothyronine deiodinase enzymes (Brown and Arthur 2001). A malfunction of the thyroid-mediated hormonal system may lead to impairments of the immune system function and the metabolic breakdown of nutrients (Janz et al. 2010). There are various effects at the organism scale.

6.3 Ecological effects assessment

6.3.1 Water

Empirical data are available in the literature on the acute and chronic toxicity of waterborne selenate, selenite, selenide, organo-selenium species, and mixtures of

different selenium species (BC MOE 2014; US EPA 2016). Selenium toxicity to aquatic organisms is modified by various factors, including temperature, hydrology and water chemistry (Lemly 1993; Maher et al. 2010). As discussed previously, the form of selenium that aquatic organisms are exposed to is of critical importance, as bioavailability varies between selenium species. For example, increases in sulphate concentrations reduce the toxicity of selenate to aquatic invertebrates and fish, but have no effect on selenite (Carlton 1998; US EPA 2016). Dietary organic selenium exposure has been widely examined by many authors, as this is generally considered the critical exposure pathway for assessing selenium toxicity at environmentally relevant concentrations.

There is experimental evidence that selenium causes harm to fish following longer-term (chronic) exposure at concentrations only slightly above essentiality (Hilton et al. 1980; Gatlin and Wilson 1984; Lemly 1997). Additionally, field studies report effects of selenium over the life cycle of multiple generations in fish, as well as reproductive and population-level effects in a few lentic sites (Chapman et al. 2010). Exposure to selenium during the larval stage occurs principally through maternal transfer to the eggs, then through yolk sac absorption at the larval stage. Reduced hatching, teratogenicity (deformities) and edema are among the most common effects observed in early life stages of fish, waterbirds and possibly amphibians (Janz et al. 2010; Janz 2012; US EPA 2016).

There is a general agreement that freshwater fish appear more sensitive to selenium than any other taxa of aquatic organisms (Hamilton et al. 1990; Hermanutz et al. 1992; Coyle et al. 1993; Janz et al. 2010; Young et al. 2010; BC MOE 2014; US EPA 2016). As such, this assessment of toxic effects of selenium in aquatic environments focuses on fish. A tissue-based approach was used because the concentration of selenium in tissues is an indicator of selenium bioavailability and also represents accumulation from all possible exposure pathways. Therefore, predicted no-effect concentrations (PNECs) in this assessment are based on selenium tissue residues in fish.

6.3.1.1 Fish eggs/ovaries (reproductive effects)

Reproductive impairments in fish are well-documented in cases of chronic selenium toxicity (BC MOE 2014). Through maternal transfer, dietary selenium is incorporated into egg yolk-proteins where it is metabolized by the developing embryo (Janz et al. 2010; Lemly 2002a). Teratogenicity, larval edema and larval mortality are the most sensitive endpoints for fish (Janz et al. 2010). Furthermore, the significant correlation of selenium concentration measured in fish ovaries and eggs with these endpoints make them accurate predictors of selenium toxicity to fish.

The relationship of selenium concentrations found in fish ovaries and eggs is positive and strong, with the slope of log-log regression equations varying between 0.57 and 0.97, depending on the species (Coyle et al. 1993; Kennedy et al. 2000; GEI Consultants et al. 2008; US EPA 2016). Consequently, toxicity values based on selenium residues in eggs and ovaries were assumed to be at a one-to-one ratio for this

assessment. Selenium concentration in eggs is the most useful indicator of fish early-life-stage effects (GEI Consultants et al. 2008). Chronic toxicity data for reproductive impairments of selenium in fish eggs were compiled and evaluated (ECCC 2017m). When more than one acceptable record was available for the preferred endpoint for an individual species, the geometric mean was calculated, in accordance with the preferred endpoint guidance of the CCME (2007) protocol. Selenium concentrations in eggs that were associated with toxic effects in larvae ranged from 16.2–54 µg/g dw (ECCC 2017m). The most sensitive species identified include the brown trout (Salmo trutta), white sturgeon (Acipenser transmontanus) and bluegill sunfish (Lemopis macrochirus). The most tolerant species was the Dolly Varden (Salvelinus malma). Given the number of data points available, and for the purposes of identifying a PNEC based on tissue residues, a species sensitivity distribution (SSD) was plotted using the software SSD Master version 3.0 (SSD Master 2013) (Figure 6-1).

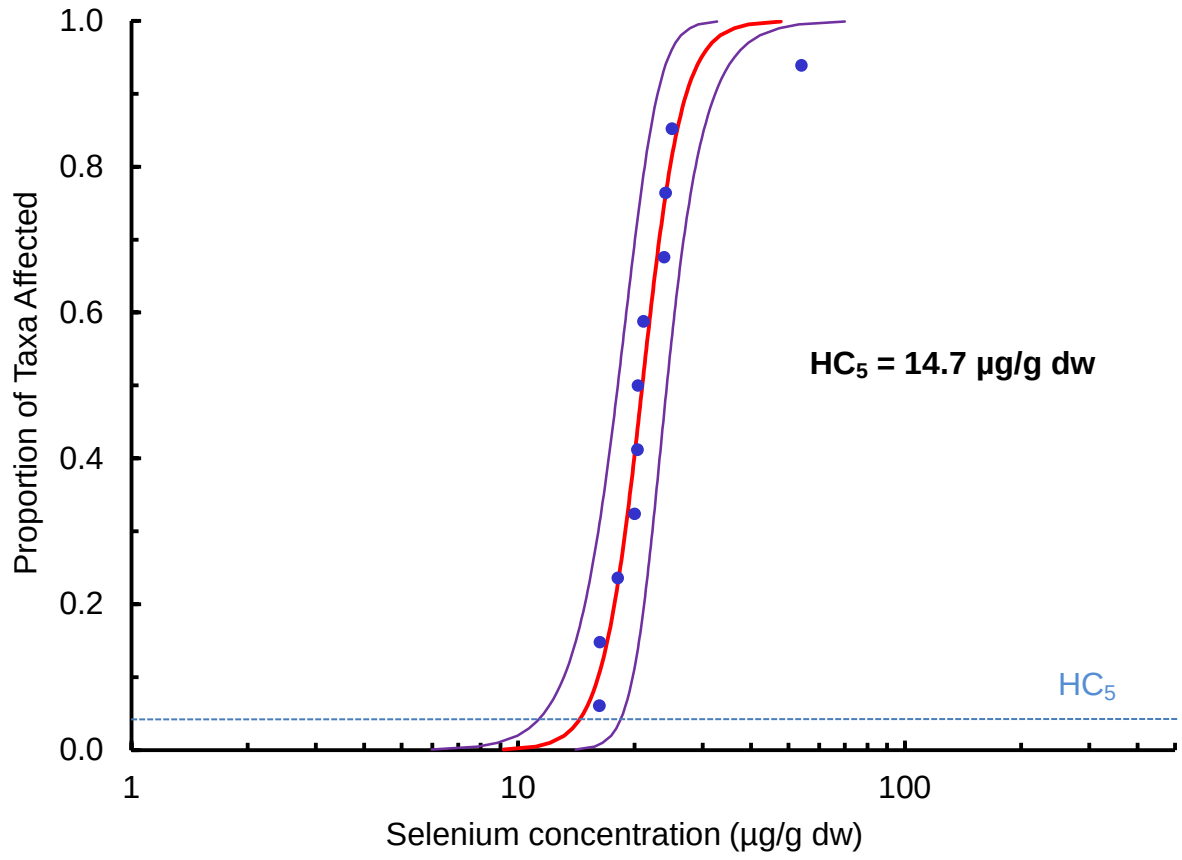

Figure 6-1: Species sensitivity distribution (SSD) for selenium based on residues in fish eggs/ovaries that lead to reproductive toxicity. The logistic model fit to data is shown on the graph, along with the 95% confidence interval and 5th percentile of the distribution (HC_5).

Model assumptions and fit were verified with statistical tests. The logistic model provided the best fit of the models tested. The 5th percentile (HC_5), i.e., hazardous concentration to 5% of fish species, of the SSD plot was 14.7 µg/g dw (Figure 6-1). The

HC_5 of 14.7 µg/g dw in fish eggs calculated from the SSD is selected as the PNEC for reproductive toxicity to freshwater fish. Since this value is based on a chronic SSD that covers multiple species, an assessment factor was not used to derive the egg-ovary tissue PNEC for the reproductive endpoints of freshwater fish. The confidence in the PNEC is high, based on the high reliability of studies underlying the SSD. The high representation of species present in Canada in the dataset and good fit of the logistic distribution also lead to high confidence.

The egg-ovary tissue PNEC for reproductive effects in fish is similar to the thresholds suggested by other authors/jurisdictions: 20 µg/g dw by DeForest et al. (2012), 10 µg/g dw from Lemly (1996), 11 µg/g dw by US DOI (1998), 11 µg/g dw in British Columbia (BC MOE 2014) and 15.1 µg/g dw by US EPA (2016).

6.3.1.2 Fish muscle and whole-body

The most sensitive life stage in fish is the egg-larval stage, where exposure is to maternally transferred selenium. However, pairing the egg-ovary PNEC to exposure concentrations is challenging, because measured concentrations of selenium in fish eggs are sparse, and their collection is limited by the period of the year. The concentration of selenium in adult fish muscle or whole-body is much more frequently available, and is a strong indicator of exposure to selenium in fish. Therefore, a fish whole-body PNEC was also developed. The more sensitive and significant reproductive-based endpoints from the egg-ovary SSD above were translated to whole-body values using species-specific egg-ovary to whole-body conversion factors developed by the US EPA (2016). The converted values (ECCC 2017m), were plotted using the software SSD Master version 3.0 (SSD Master 2013) (Figure 6-2). Toxicity-modifying factors that may affect the bioavailability of selenium were not separately taken into account, because the data used in the SSD are tissue residues and therefore inherently account for the influence of these factors on the toxicokinetics of selenium.

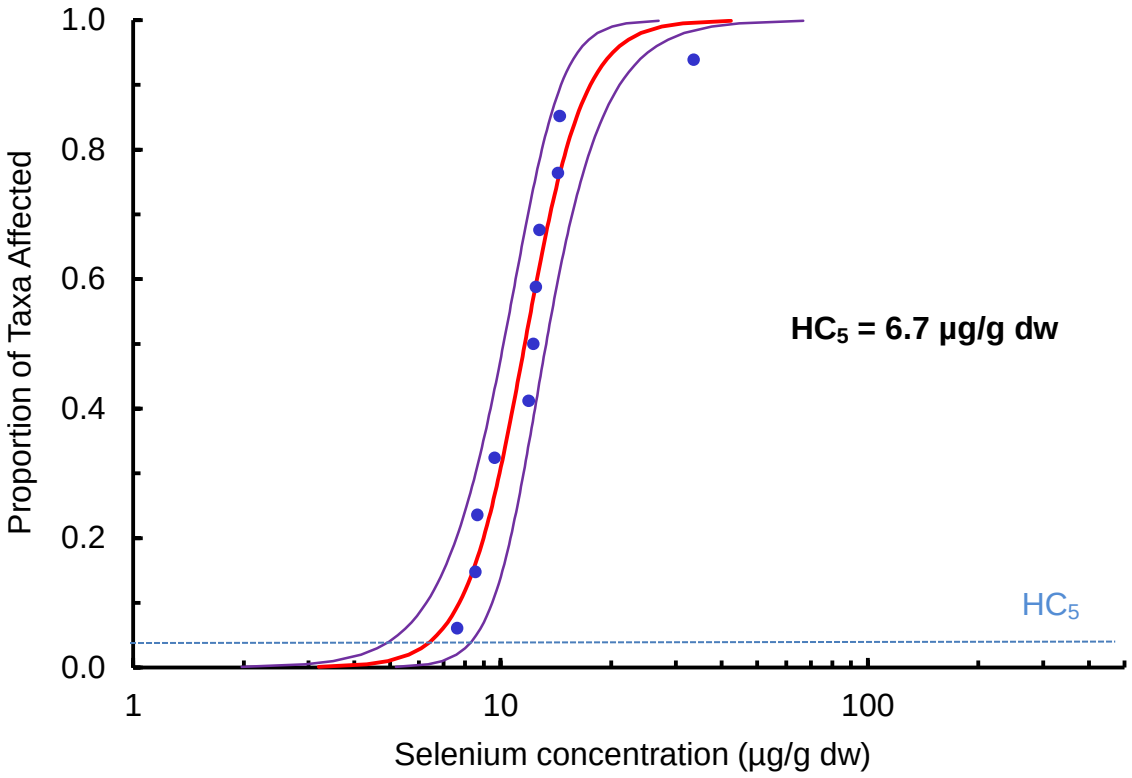

Figure 6-2: Species sensitivity distribution (SSD) for selenium based on residues in fish whole-body translated from egg-ovary reproductive endpoints using species-specific conversion factors. The logistic model fit to data is shown on the graph, along with the 95% confidence interval and the 5th percentile of the distribution.

The logistic model provided the best fit of the models tested, and the HC_5 of the SSD plot was 6.7 µg/g dw (Figure 6-2). The HC_5 of 6.7 µg/g dw calculated from the SSD is therefore selected as the whole-body PNEC for toxicity to freshwater fish. The value is not generally below essential requirements, considering that it is above the 50th percentile of concentrations of minimally exposed areas, ranging from 1.6–2.2 µg/g dw (ECCC 2017l). As for the egg-ovary tissue PNEC, based on the availability of data for multiple species an assessment factor was not used to derive the whole-body PNEC for reproductive endpoints of freshwater fish. The high confidence in the egg-ovary tissue PNEC similarly translates to the whole-body PNEC, based on the high reliability of underlying studies, high representation of Canadian species, and good fit of the logistic distribution.

The whole-body PNEC is comparable to thresholds found in the literature for selenium concentration in fish whole-body tissues. For example, the US EPA (2016) provides a guideline of 8.5 µg/g dw and BC MOE (2014) provides a threshold value of 4 µg/g dw for selenium in whole-body fish tissues.

6.3.2 Sediment

6.3.2.1 Waterborne exposure to selenium

Experimental evidence suggests that selenium causes harm to freshwater benthic organisms following long-term (chronic) exposure at concentrations ranging from 100–100 000 µg/L in pore water (deBruyn and Chapman 2007). From these results, it is possible to estimate the concentration of selenium in sediment potentially causing harm, using the equilibrium partitioning approach considering selenium sediment to water (or pore water) partition coefficients. However, this approach would result in only very rough estimates, because partition coefficients for selenium species vary by orders of magnitude (Allison and Allison 2005). Moreover, the approach would reflect the exposure through water only, and the combination of diet and waterborne exposure pathways would be more appropriate. Consequently, a body residues approach was used to derive the PNEC, because the concentration of selenium in the body of benthic organisms is a representative indicator of all possible exposure pathways.

6.3.2.2 Whole-body selenium concentrations

Dietary and waterborne selenium represent possible exposure pathways of selenium to benthic invertebrates. No evidence of a specific detoxification mechanism for benthic invertebrates (such as the metallothionein enzyme pathway for metals) was found for selenium. Therefore, body concentrations in excess of essentiality or equilibrium with background selenium levels in sediments may be relevant for assessing harmful effects. Table 6-1 presents the lowest body concentrations found to cause effects to benthic organisms from exposure to selenium in diet and water. The table also presents the corresponding sediment concentrations, which are obtained by dividing the invertebrate body concentration causing low effects by the geometric mean of the BSAFs in benthic organisms, which is 2.5 (dw) (Section 5.3.2).

Table 6-1: Lowest selenium concentrations causing effects to benthic organisms due to exposure to selenium through diet and/or water

Test organism	Study type and duration	Food source and concentration	Endpoint (effect)	Invertebrate body concentration (µg/g dw[a])	Sediment effect concentration (µg/g dw[a])	Reference
Chironomus decorus	Laboratory (4 days)	Algae (Selenastrum capricornutum) (2.1 µg/g dw[b])	LOEC	2.55	1.02	Malchow et al. (1995)

Hyalella azteca	Laboratory (28 days)	Water exposure	LBC_{10} (lethality)[b]	5.8	BSAF not applicable to water exposure	Norwood and Milne (2014)
Chironomus decorus	Laboratory (14 days)	Plant (Ruppia maritima) (7.3 µg/g dw[b])	LOEC	10	4	Alaimo et al. (1994)
Centroptilum triangulifer	Laboratory	Periphyton (4.2 µg/g dw[b])	44% fecundity reduction (reproduction)	12.8	5.12	Conley et al. (2011)
Caecidotea sp.	Field (mesocosm) (>700 days)	Various (5–10 µg/g dw)	(lethality/ density reduction)	60	24	Swift (2002)[c]

[a] Dry weight
[b] LBC = Lethal body concentration (mean)
[c] Based on citation by author, reliability could not be verified.

Toxicity studies used to derive the PNEC were evaluated for reliability. The lowest reliable selenium body concentration (causing growth reduction) is a LOEC of 2.55 µg/g dw for Chironomus decorus (Malchow et al. 1995). This value is only marginally above the background concentration range of 0.5 to 2.0 µg/g dw for aquatic invertebrates cited by Malchow et al. (1995), and similarly the typical background of less than 2 µg/g dw cited by Skorupa (1998). This value is however below the maximum background of 4.5 µg/g dw identified by Skorupa (1998). The effects concentration estimated by Malchow et al. (1995) carries some uncertainty due to the relatively short exposure period compared to other studies. For example, Alaimo et al. (1994) also observed growth effects on Chironomus decorus in 4-day and 14-day feeding studies. Reduced weight was only observed in the 14-day study, with a LOEC of 10 µg/g dw. Production of organo-selenium by the greater amount of detrital microflora in the food source for the longer experiment may have contributed to the difference between the 4-day and 14-day results. All considered, the level of confidence in the LOEC values of Malchow et al. (1995) and Alaimo et al. (1994) is medium.

The geometric mean of the two lowest sediment effect concentrations for the most sensitive species, Chironomus decorus, is 2.0 µg/g dw, and this value is used as the PNEC in sediment to protect benthic organisms. Considering that Chironomus decorus is a sensitive species (the Chironomus genus is the most sensitive to selenium among the 13 genera for which toxicity data were found) and that the sediment low-effect concentrations are close to background values, no application factor was used to derive the PNEC.

This PNEC is within the same range as the one recommended by Thompson et al. (2005), suggesting thresholds of 0.9 µg/g dw in lentic systems and 1.9 µg/g dw in lotic systems to protect benthic communities. It is also consistent with the threshold of 2 µg/g dw obtained by BC MOE (2014). Given the scarcity of the data available for selenium effects on benthic organisms, and the variability of the BSAFs used to transform body concentrations, the level of confidence in the precision of this PNEC is low to medium. However, a relatively sensitive species was used to derive this PNEC, and therefore there is a medium to high level of confidence that the environment is protected when the concentration of selenium in sediment is lower than 2.0 µg/g dw.

Limited information is available to allow the correction of selenium toxicity with modifying factors for sediments, including consideration of the difference between lotic and lentic systems. While, the sediment effect concentration based on the most sensitive species may overlap with ambient concentration ranges, the median selenium concentration in sediment in Canada, based on an analysis of data from the CMP Monitoring and Surveillance program, is 0.51 µg/g dw (ECCC 2017l).

6.3.2.3 Selenium effects on benthic organism feeders in upper trophic levels

deBruyn and Chapman (2007) concluded, following a thorough review of data, that thresholds proposed to protect predators of benthic organisms may not be protective for their prey. To verify this assumption, key studies proposing selenium concentration thresholds for the protection of bentho-pelagic fish and their predators were evaluated and are presented in Table 6-2. These studies are identical to those presented in the water quality guidelines for selenium prepared by the BC MOE (2014).

Table 6-2: Selenium sediment concentration thresholds for benthic predators

Protected species	Type of system	Sediment threshold	Selenium conc. in sediment (µg/g dw[a])	Level of confidence	Reference
Fish and aquatic birds	Lentic	Toxic value	2.0	Medium-high	Lemly (2002b)
Fish and birds	Lotic	Predicted effects (10th percentile)	2.5 (2.27[b])	High	Van Derveer and Canton (1997)
Fish and birds	Lotic	Observed effects	> 4	High	Van Derveer and Canton (1997)
Fish and waterfowl	Lotic/lentic[c]	Level of concern	≥ 4	Medium-high	Lemly and Smith (1987)

[a] Dry weight
[b] 5th percentile of predicted effects
[c] Likely mixed systems

To protect bentho-pelagic fish and bird species feeding on benthic organisms, the lowest threshold is 2.0 µg/g dw. This value is supported and proposed as the sediment concentration for the protection of aquatic life by BC MOE (2014), and is consistent with the sediment PNEC of 2.0 µg/g dw calculated above.

6.3.3 Soil

Information on the acute and chronic toxicity of selenium in soil organisms was reviewed by the CCME (2009). The derivation of the Canadian soil quality guideline for soil contact (SQG_{SC}) is based on ecotoxicological data for vascular plants and soil invertebrates. The data indicate that selenium species found in soil generally have a moderate potential to cause harm to soil organisms. According to the guideline protocol for soil, there were insufficient data for the derivation of an SSD, but there were sufficient data for use in the LOEC method. The LOEC method states that the threshold effects concentration is calculated as the lowest LOEC of a dataset consisting of a minimum of three data points (one data point for each group of receptors: microbial community, plants and invertebrates), divided by an uncertainty factor.

The lowest LOEC reported in the literature was 1 µg/g (Carlson et al. 1991). The endpoint for this LOEC was reduced shoot growth (approximately 60%) in Broomcorn (Sorghum vulgare) over a 42-day exposure period. Singh and Singh (1979) also reported a LOEC of 1 µg/g for reduced dry matter yield in Cowpea (Vigna sinensis) over a 50-day exposure period. No uncertainty factor was applied, because the critical study was chronic, more than three studies were consulted, and three taxonomic groups were represented (CCME 2006). The reader should consult the CCME guidelines fact sheet (CCME 2009) for more detailed information. Therefore, the PNEC selected for soil is 1 µg/g soil.

6.3.4 Mammals, birds, amphibians and reptiles

Chronic effects of selenium were observed in domestic and farm animals, including loss of hair and hooves, reduced conception, increased fetal resorption, lameness, and liver cirrhosis (Clayton and Clayton 1994). These effects may occur at dietary concentrations of selenium between 1 and 44 µg/g dw (CCME 2009). Peterson and Nebeker (1992) estimated that chronic exposure to over 5 µg/g dw of selenium in the diet of mammals and birds may produce toxic effects or may cause reproductive adverse effects in the latter. The no-effects threshold of selenium on sensitive wildlife was estimated in the North American environment for shrews, bats, minks and otters, living in aquatic-dependent habitat and feeding on aquatic invertebrates or fish (Peterson and Nebeker 1992). Their calculations took into account the dietary and waterborne levels of selenium in the environment, as well as mammals' feeding habits. The toxicity threshold was based on a rat growth inhibition no observable adverse effect level (NOAEL). The estimated no-effect threshold for wildlife mammals corresponds to a dietary concentration of fish of 4.7–7.5 µg/g dw. This range captures the HC_5 of 6.7 µg/g dw proposed as the PNEC for whole-body fish tissues in section 6.3.1.2. Therefore, it is likely that piscivorous mammals would be protected using the fish HC_5 value.

A similar threshold of chronic selenium toxicity was obtained by Peterson and Nebeker (1992) on four sensitive aquatic birds (5.4–14.3 µg/g dw of selenium in fish). Lemly and Smith (1987), DuBowy (1989), Skorupa and Ohlendorf (1991) and BC MOE (2014) suggested that waterborne selenium concentrations between ~1 and 3 µg/L would result in a concentration of selenium in prey suitable for the aquatic bird predators.

Through maternal transfer, dietary selenium is incorporated into egg yolk-proteins where it is metabolized by the developing embryo of egg-laying vertebrates (Lemly 2002b; Janz et al. 2010). Hatchability is the most sensitive endpoint for birds (Janz et al. 2010). Selenium toxicity has also been linked to deformities in waterfowl (Luoma and Presser 2009). For instance, Heinz et al. (1989) observed parental transfer of selenium to mallard ducklings: parents fed with 8–10 µg/g dw selenomethionine in their diet had significantly reduced survival of progeny. They observed that, at a concentration of 16 µg/g dw of selenomethionine in the female diet, no young birds survived. Information regarding the reproductive impairments of dietary selenium to birds is presented in Table 6-3.

Table 6-3: Data for hatchability and reproductive effects in birds in relation to egg selenium concentrations

Test Organism	Common Name	Endpoint	Effect	Egg selenium conc. (µg/g dw[a])	Reference
Anas platyrhynchos	Mallard	EC10	Teratogenic effects	23	Skorupa (1998)
Anas platyrhynchos	Mallard	EC8.2	Impaired egg hatchability	9	Lam et al. (2005)
Anas platyrhynchos	Mallard	EC10	Reduced egg hatchability	7.7–16	Meta-analysis of Heinz et al. (1989); Adams et al. (2003); Ohlendorf (2003); Beckon et al. (2008)
Himantopus mexicanus	Black-necked stilt	EC11.8	Reduced clutch viability	14	Meta-analysis from Lam et al. (2005)
Himantopus mexicanus	Black-necked stilt	EC10	Teratogenic effects	37	Skorupa (1998)
Himantopus mexicanus	Black-necked stilt	EC10	Reduced Hatchability	21–31	Meta-analysis from Adams et al. (2003)
Recurvirostra	American	EC10	Teratogenic	74	Skorupa

americana	avocet		effects		(1998)
Actitis macularia	Spotted sandpiper	15% effects	Egg viability	7.3	Harding et al. (2005)

[a] Dry weight

Selenium concentrations in eggs corresponding to reduced hatchability ranged from 7.7–74 µg/g dw. Although the effects reported in Table 6-3 are presented in relation to selenium egg concentrations, mixture effects are also possible in the environment. For exposure characterization, measured concentration data for birds are sparse and modelling is less reliable when estimated mainly from the water concentration. Therefore, a PNEC protective of birds is not proposed in this assessment. Nevertheless, a description of the impacts of selenium on birds in North America is available in Section 6.5.

Little is known about the effects of maternal transfer of selenium to amphibians and reptiles (Hopkins et al. 2004; Hopkins et al. 2005). However, these type of effects were demonstrated for other egg-laying vertebrates (sections 6.3.1 and 6.3.4), indicating a potential for a similar mode of toxicity. Also, amphibians are believed to be an important species to assess selenium toxicity because of cumulative absorption via both dermal and dietary exposure pathways (Janz et al. 2010).

Metts et al. (2012) conducted a mesocosm study on toads captured in a coal combustion waste-contaminated area: 7.2 µg/L of selenium was measured in the ash basin's water and 21.2 µg/g dw of selenium was measured in sediment. Following exposure in the laboratory to the ash basin conditions, the mean selenium body concentration was 9.4 µg/g dw in post-ovipositional female toads and 60.8 µg/g dw in the metamorphs. This study indicated that the female toads efficiently transfer selenium to their progeny. Larval survival and the metamorphs' growth rate were reduced and metamorphosis length increased in ash basin water and sediments, compared to the reference conditions.

Lockard et al. (2013) investigated the effects of dietary selenium on Cope's Gray Tree Frogs (Hyla chrysoscelis) from the larval stage to the end of metamorphosis (maximum 78 days). Three doses of selenium in the diet were tested: control, low exposure and high exposure. No deformities were observed in the control group exposed to a selenium dose of 1.4 µg/g dw in the diet, but only 49% of the metamorphs survived the 78 days of observation. Seventy percent of the frogs exposed to the low-dose ration of 47.4 µg/g dw of selenium in the diet developed rear-limb deformities during metamorphic climax, and these deformities were strongly associated with mortality before metamorphic completion. The overall survival of frogs exposed to a low-dose ration of selenium in their diet was 28%. All frogs from the high-dose treatment (528 µg/g dw of selenium in the diet) were dead after 22 days of exposure.

A PNEC protective of amphibians is not proposed in the assessment, due to sparse effects data and the general lack of measured environmental concentrations in

amphibian tissues in Canada. However, a description of the impacts of selenium on amphibians in North America is available in Section 6.5.

6.3.5 Ecological effects summary

The PNECs developed in this assessment for fish and benthic invertebrates were compared with the estimated range of essential selenium concentrations (ECCC 2017n) and concentrations from minimally impacted areas (ECCC 2017l). The PNECs developed are above essential requirementsand generally exceed ambient concentration ranges in the Canadian environment. It is possible that background concentration ranges in some regions exceed the PNECs, and that resident species may have acclimated in regions where selenium concentrations are naturally high. As a result, resident species may also have naturally elevated levels of selenium.

Based on species sensitivity distributions (Figures 6.1, 6.2), the PNEC for selenium concentration in fish eggs or ovaries ($PNEC_{fish\ eggs/ovaries}$) was established at 14.7 µg/g dw, and the PNEC in whole-body fish tissues ($PNEC_{fish\ WB}$) selenium concentration is 6.7 µg/g dw. The PNEC in sediment ($PNEC_{sed}$) was established from the lowest body residues endpoints reported in the literature: 2.0 µg/g dw for sediment where benthic organisms reside. The PNEC in soil ($PNEC_{soil}$) is based on the Canadian soil quality guideline (CCME 2009), where the threshold effects concentration of selenium, protective of soil contact by plants, invertebrates and micro-organisms, was calculated to be 1 µg/g dw.

6.4 Ecological exposure assessment

Anthropogenic releases of selenium to the environment result from activities such as selenium production, incidental production and release of selenium-containing substances, as well as the manufacture, import and use of selenium-containing substances, products and manufactured items. Selenium releases may also occur following the disposal and waste management of these substances, products and manufactured items.

Exposure scenarios were developed for the various activities that have been reported or that may represent significant sources of release of selenium to the environment, and are presented in this section, divided by industrial/commercial sectors: mining, metal processing facilities, fossil fuel power plants, agriculture, oil sands extraction and

processing, wastewater treatment systems[8], pulp and paper mills, waste management, and glass manufacturing. Monitoring studies were selected on the basis that sampling campaigns were conducted close to the point source (e.g., < 10 km from the source) for each of the sectors (ECCC 2017a to 2017j). In some cases, the proximity of two or more sectors made it impossible to attribute exposure solely to one specific industrial activity. Monitoring studies include national-, provincial- and municipal-led monitoring campaigns, as well as site-specific information and peer-reviewed scientific journal articles.

To estimate the concentrations of selenium in the Canadian environment in the vicinity of point sources, a tiered approach was applied depending on data availability. Although fish and aquatic bird eggs are preferred media for estimating the impact of selenium contamination on the aquatic environment, the availability of measured selenium concentrations in eggs is poor and may not be sufficient to assess all sectors of activity in Canada. For the aquatic environment, if no measured concentration data for selenium in fish eggs and ovaries are available, whole-body fish tissue concentration data are used instead. Alternatively, if measured fish tissue data ($PEC_{measured}$) are not available for a given sector of activity, fish tissue concentrations are estimated ($PEC_{estimated}$) using the total selenium concentration in surface water and the median lotic or lentic BAF calculated in Section 5.3.1.3.

A summary of the measured concentrations of selenium in fish eggs/ovaries reported near two of the highest-emitting sectors, coal mining and metal (including uranium) mining (ECCC 2017a, 2017b, 2017c), is presented in Figure 6-3. Measured concentrations of selenium in fish whole-body tissue are presented in Figure 6-4 for each sector for which data were found (ECCC 2017a to 2017g, and ECCC 2017i). Figures 6-5 and 6-6 summarize the fish whole-body tissue concentrations estimated by multiplying surface water concentrations for each sector by the appropriate lotic or lentic BAF (ECCC 2017a to 2017h, and ECCC 2017j). The similarity between the measured fish tissue concentrations in Figure 6-4 and the estimated fish tissue concentrations for sectors which have both, particularly for lentic environments in Figure 6-6, supports the validity of the approach for those sectors for which fish tissue concentrations could only be estimated. Figure 6-7 summarizes the selenium concentrations measured in sediments near key industrial activities. For Figures 6-3 to 6-7, the solid bars represent the range of average or median concentrations reported in the studies described in ECCC (2017a to 2017j). The error bars are used to indicate the minimum and maximum

[8] In this assessment, the term “wastewater treatment 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 treatment 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 treatment systems” and/or “industrial wastewater treatment systems”.

concentrations reported across all reports at sites downstream of releases from sectors, where N is the number of reports. The PNEC values discussed above are also included for comparison.

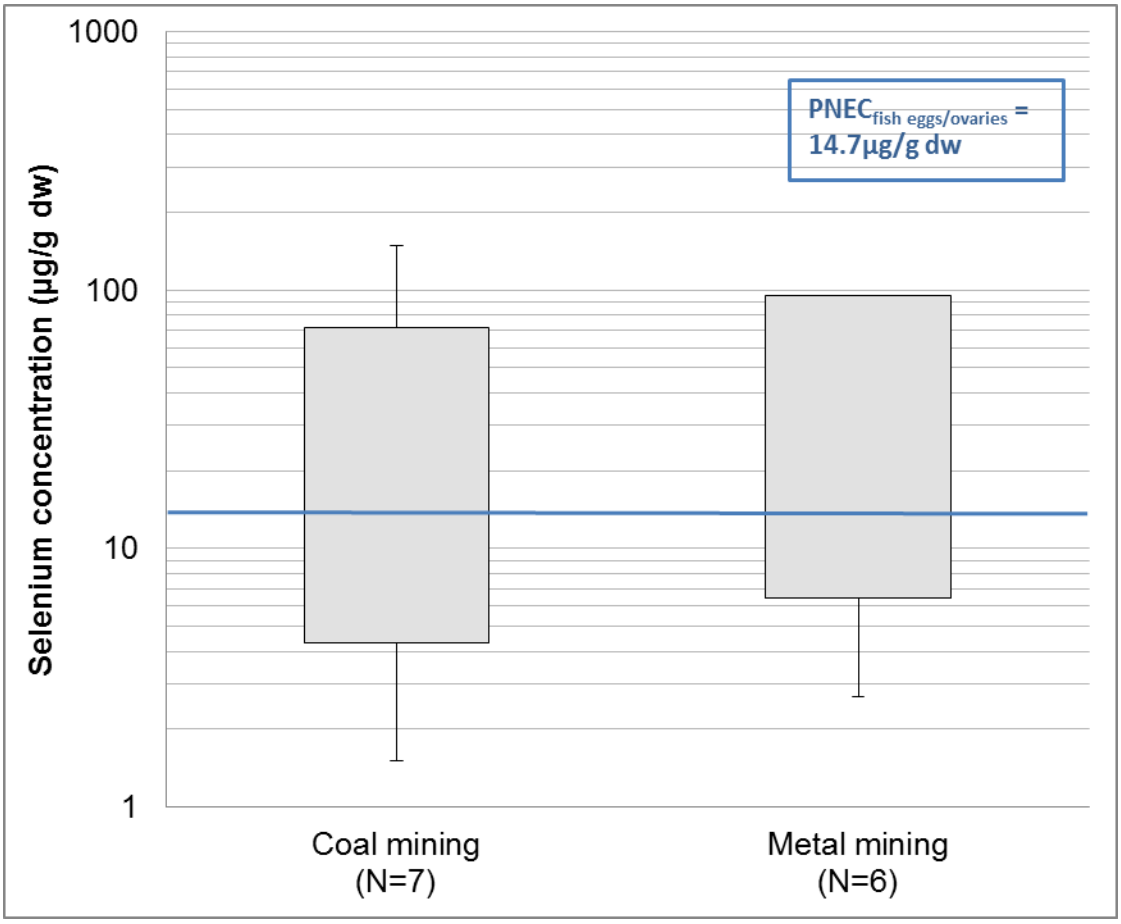

Figure 6-3: Selenium concentration in fish eggs and ovaries collected in the vicinity of coal mines and metal mines, in comparison to the $PNEC_{fish\ eggs/ovaries}$

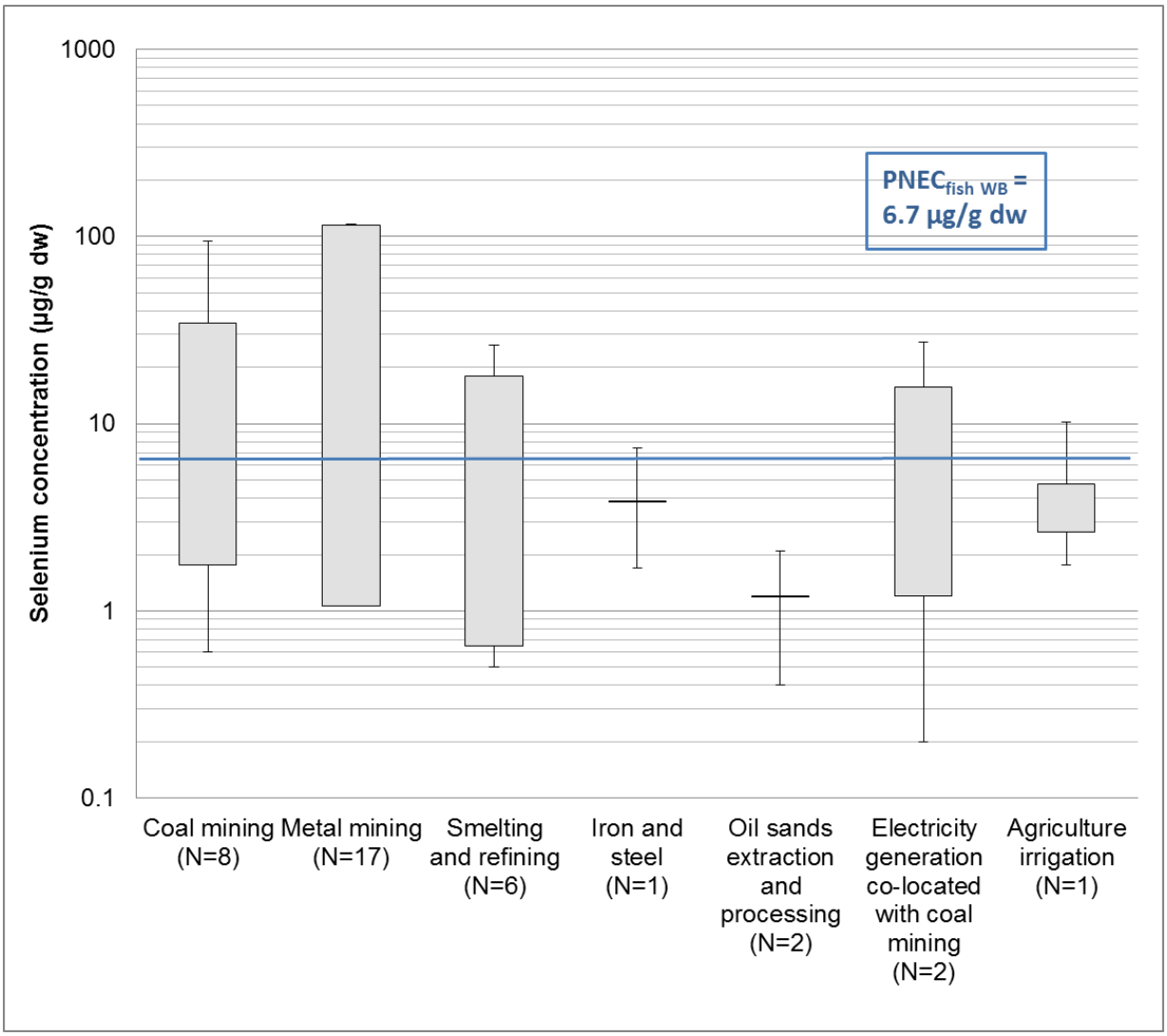

Figure 6-4: Selenium concentration in fish tissues collected in the vicinity of sectors of interest, in comparison to the $PNEC_{fish\ WB}$

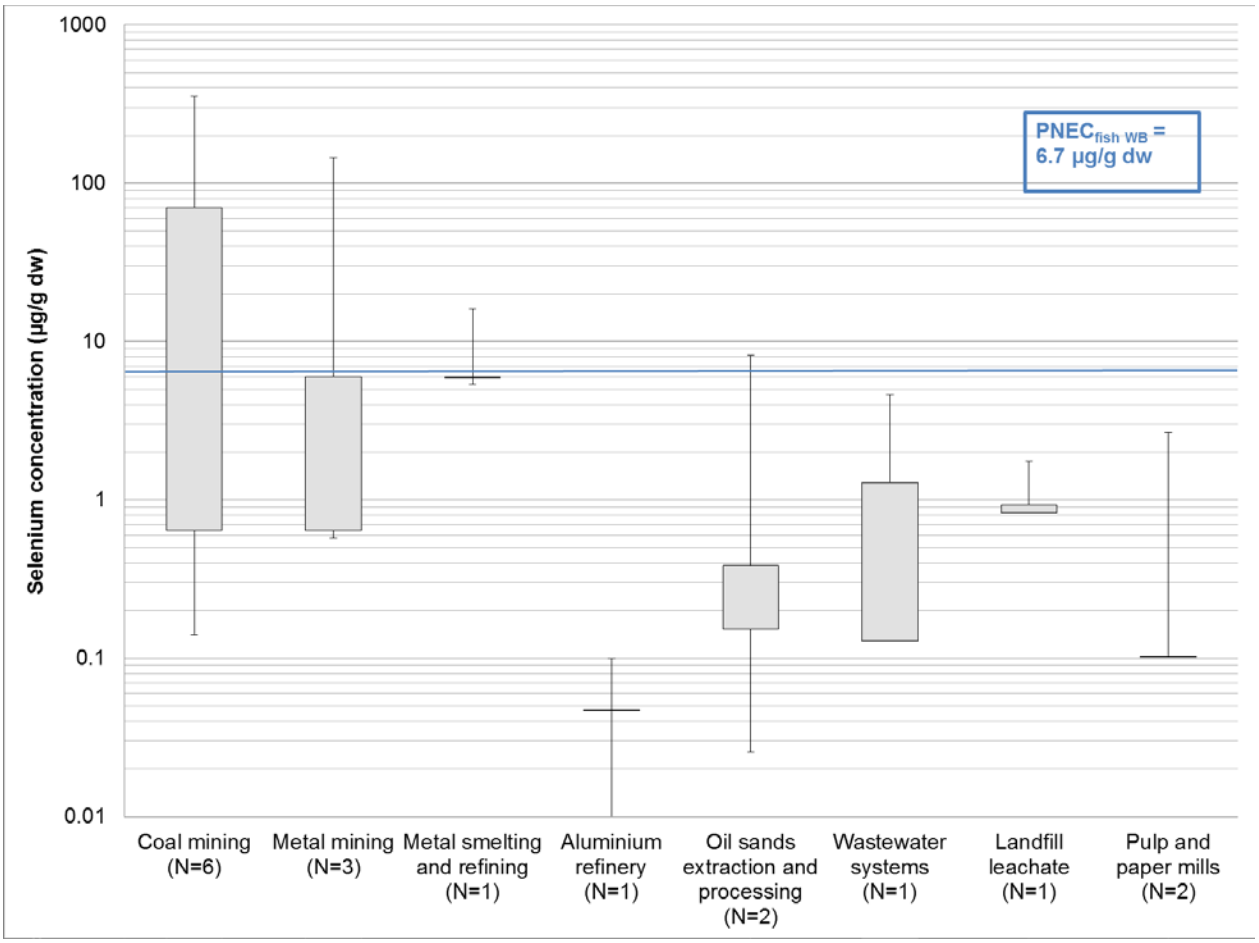

Figure 6-5: Selenium concentration in fish tissues, estimated from surface water concentration and BAFs for lotic areas in the vicinity of sectors of interest, in comparison to the $PNEC_{fish\ WB}$

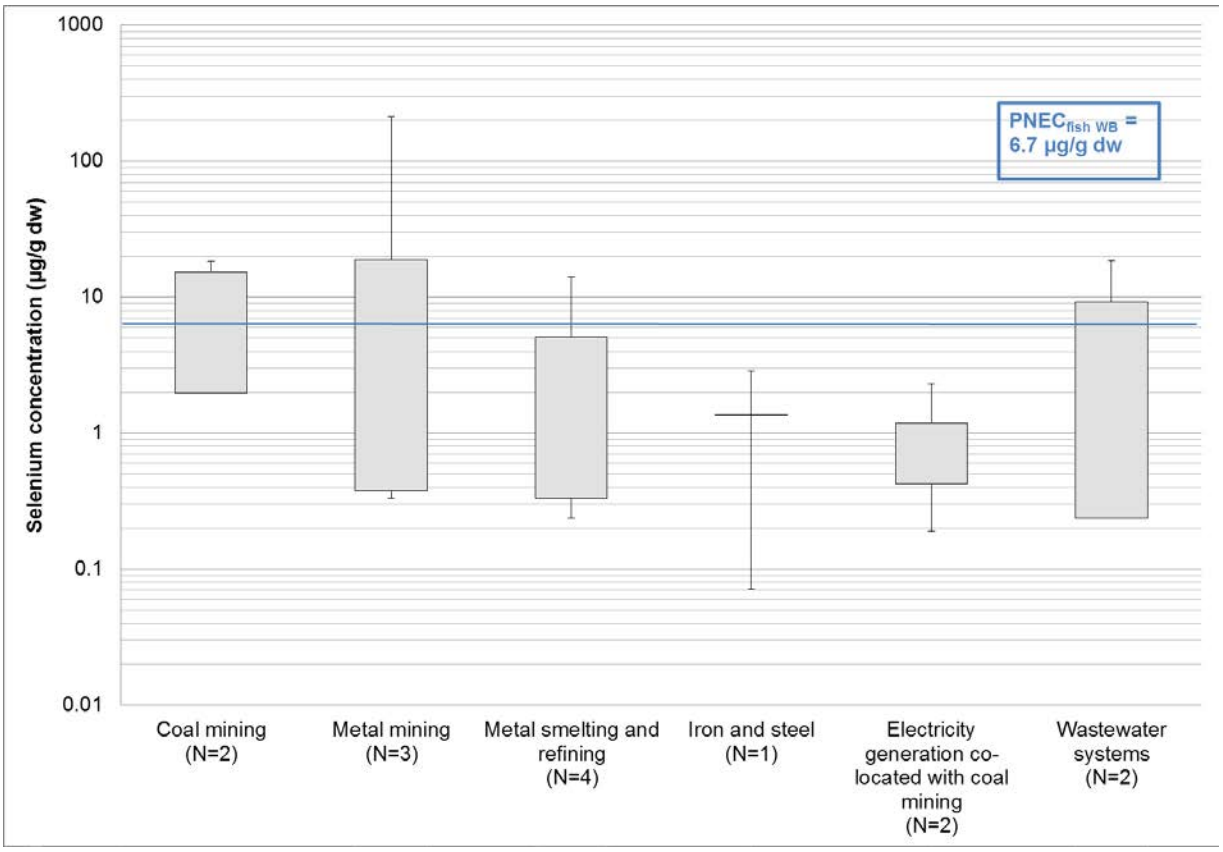

Figure 6-6: Selenium concentration in fish tissues, estimated from surface water concentration and BAFs for lentic areas in the vicinity of sectors of interest, in comparison to the $PNEC_{fish\ WB}$

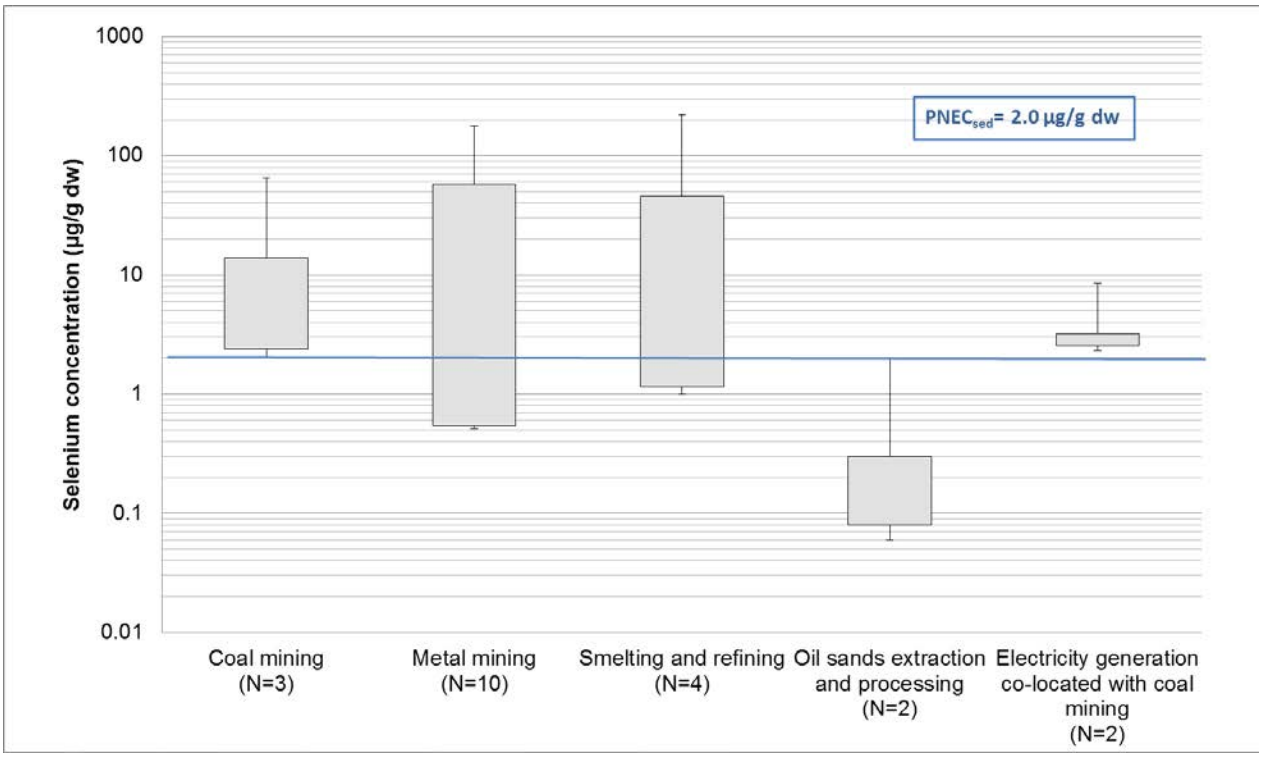

Figure 6-7: Selenium concentration in sediments near the discharge point of the effluents from sectors for lotic and lentic environments combined, in comparison to the PNEC$_{sed}$

Releases of selenium to air are reported to the NPRI for facilities meeting the reporting requirements. Releases to air may lead to elevated selenium concentrations in surrounding soils as a result of deposition. Measured concentrations of selenium in soil near known point sources were found only for the base metal smelting and refining sector. Selenium concentrations in soil surrounding Trail (BC), Flin Flon (MB) and Sudbury (ON) ranged from 0.1 µg/g dw to 447 µg/g dw, with medians reported for each site varying between 0.35 µg/g dw and 3.9 µg/g dw (ECCC 2017d). In agricultural areas, the concentration of selenium in soil was estimated to lie between 0.26 and 1.67 µg/g dw, with a median of 0.65 µg/g dw (ECCC 2017i).

Selenium deposition to soil from a glass manufacturing facility was simulated using the atmospheric dispersion model AERMOD and a soil concentration model (ECCC 2013, ECCC 2017k). The resulting maximum concentration of selenium in soil surrounding the facility, following five years of atmospheric releases, was 0.74 µg/g dw.

Model results for the dispersion and deposition of various substances on soil were obtained from Health Canada (personal communication from the Air Quality Division, Health Canada, to the Ecological Assessment Division, Environment and Climate Change Canada, unreferenced; more details on the modelling are available in ECCC 2017d, 2017j and 2017k). These included results for the deposition of selenium on soil as a result of atmospheric releases from cement manufacturers, aluminium refineries,

base metal smelters and refineries, pulp and paper mills, natural gas power plants, and fertilizer manufacturers. Three representative facilities for each of these sectors were modelled using the atmospheric dispersion model Calpuff. Subsequently, the annual quantities of selenium deposited on soil in the vicinity of the stacks were modelled using equations developed by ECCC (2013), to estimate the concentration of selenium in the top 10 cm of soil, following 10 years of operation. With the exception of base metal smelters and refineries, for which it is estimated that releases would lead to a maximum of 0.11 µg/g dw of selenium in soil, the estimated selenium concentrations obtained by the method described above were between $3x10^{-10}$ µg/g and $1.5x10^{-4}$ µg/g. These modelled concentrations of selenium in soil are well below the background concentration range for selenium, estimated to be between 0.2 µg/g and 0.6 µg/g in Canada (CCME 2009). These results suggest that these sectors have a negligible impact on selenium presence in soils.

6.5 Field evidence of ecological harm

This section describes documented cases of field evidence of selenium impacts on ecological receptors in Canada and the United States. No attempts were made to conduct an exhaustive site-specific ecological risk characterization; rather, this section summarizes the highlights and conclusions of some existing risk or hazard studies conducted in North America. Preference was given to recent cases of ecological harm, but older cases are also presented.

Observed adverse effects in the field are believed to be highly relevant for ecological risk characterization. Although field effects observed may not be exclusively attributable to one contaminant, the case studies were examined and chosen either for their elevated selenium concentrations or for the effects endpoints observed in the field being typical of selenium effects. Such effects include edema, dorso-spinal and craniofacial deformities, as well as egg hatchability for birds and axial malformation in amphibians (see the Effects Section).

6.5.1 Egg hatchability in aquatic birds

The Elk River Valley in southeastern BC is the site of five large coal mines, and appears to comprise the best-documented and most complete case study of selenium risk characterization in Canada. Harding et al. (2005) found a significantly higher concentration of selenium in the eggs of the Spotted Sandpiper (mean egg concentration of 2.2 µg/g ww in selenium-exposed areas, versus 1.2 µg/g ww in reference areas), a bird that feeds on aquatic invertebrates from lotic areas, and they found a reduction of egg hatchability in selenium-exposed areas (78% hatchability in exposure areas versus 92% in reference areas). However, no reduction in overall nesting productivity was observed for the Spotted Sandpiper. Despite the elevated selenium concentration in water in the exposed areas (8.1–34.2 µg/L), no relationship was observed between the concentration of selenium in water and the selenium concentrations in eggs of the American Dipper, nor were any effects observed in the birds (Harding et al. 2005). Another study on Red-winged Blackbirds feeding in lentic

areas of the Elk River Valley did not demonstrate a significant relationship between egg hatchability and selenium concentration in the bird eggs (Harding 2008). The high variability of the results is explained by many factors, including the geochemistry of the exposure and reference areas, the prey selection, and natural variations such as weather and the presence of predators.

Selenium effects on bird egg hatchability were first demonstrated at the Kesterson Reservoir in California, which was located in the heart of a large agricultural area where multiple waterbird species came to nest. Following agricultural activities in the area, selenium concentrations in the reservoir increased from 15 µg/L to 430 µg/L. Over 300 nests of Eared Grebes, American Coots, a few duck species, stilts and avocets were monitored for hatching, embryotoxicity, deformities, and reproductive success (Ohlendorf 2002). Depending on the individual species sensitivity, between 4% and 49% of the eggs monitored would not hatch (Skorupa 1998), compared to less than 1% in the reference area. The eggs contained between 4 and 70 µg/g dw of selenium, and less than 3 µg/g dw in the reference area.

6.5.2 Embryo toxicity and deformities in birds

In the Kesterson Reservoir area, 20% of eggs collected contained deformed embryos (Skorupa 1998; Ohlendorf 2002). With all species pooled, over 39% of the collected and incubated eggs were non-viable, compared to 1% in the reference area (Ohlendorf 2002). The concentration of selenium in the Kesterson Reservoir reached 430 µg/L, compared to 2 µg/L in the reference area.

Another example comes from Tulare Basin, California, documented for avocets and stilts nesting at a selenium-rich agricultural-affected basin (Skorupa 1998). A few lakes and ponds make up the basin, where selenium concentrations varied from less than 1 µg/L to over 1000 µg/L. Embryo teratogenesis occurred in four nesting locations; 10–50% of the embryos had deformities of eyes, beaks or limbs. The lowest concentration of selenium in water within these four sites was 15 µg/L, and 20 µg/g dw in bird eggs, resulting in a 10% embryo mortality/deformity rate. In reference areas, at selenium concentrations of 1–2 µg/L in water and 1.5–3.0 µg/g dw in eggs, less than 0.5% of the embryos were not viable.

Alberta, Saskatchewan and Manitoba contain areas of cretaceous marine sedimentary rock rich in selenium, with elevated aridity and evaporation indices. Combined with agricultural activities that may be undertaken in such areas and in proximity to hydrologically closed wetlands, these geologic and climatic conditions are similar to those associated with field cases of avian deformities and embryotoxicity in the southwestern United States (Outridge et al. 1999). Hu et al. (2009) proposed two principal reasons why, despite these similarities, field evidence of selenium impacts has not currently been reported in the Canadian prairies. Unlike agricultural areas of the San Joaquin Valley, the majority of prairie soils have an overall higher degree of soil drainability and vertical movement of selenium to groundwater (Hu et al. 2009, Presser and Ohlendorf, 1987). Also, there is presently a much smaller scale of irrigation intensity

in the Canadian prairies (Hu et al. 2009). It may be for these reasons that similar field cases of harm to avian wildlife have not been reported to date in Canada. However, if agricultural irrigation practices were to significantly change or intensify, there may be a potential for such harm. In surface water in the Prairies, the median concentration of selenium in water stands between 0.2 µg/L and 6 µg/L (Outridge et al. 1999) and is mostly in the form of selenate (Hu et al. 2009).

A few studies have been conducted in Canada in selenium-exposed areas to detect the presence of teratogenesis and embryotoxicity effects related to selenium in bird eggs (Orr et al. 2006; Weech et al. 2012). Evidence of teratogenesis or embryotoxicity for waterbirds has not been reported in Canada. Despite relatively high selenium concentration in Tree Swallow eggs from the northern Saskatchewan area exposed to the effluents of uranium mines (up to 13.3 µg/g dw), no reproductive-success effects were observed by Weech et al. (2012).

6.5.3 Embryo toxicity and deformities in fish

Typical selenium-induced fish deformities include craniofacial and dorso-spinal deformities and edema, appearing when the yolk sac is resorbed. Like bird terata, these effects, if severe, may be lethal for juvenile fish by preventing them from feeding normally and escaping predators as they grow. However, the deformities may not be discernable when the fish matures, and, consequently, adult deformed fish are not typically found.

Holm et al. (2005) reported a correlation between egg-selenium levels and the incidence of craniofacial deformities in rainbow trout (Oncorynchus mykiss) swim-up fry from the McLeod River drainage in Alberta. In Luscar Creek, a tributary of the McLeod River, the water body of the area with the highest selenium concentration (6–32 µg/L), Holm et al. (2005) found a 33.3% incidence of craniofacial deformities, 25% of skeletal deformities, 15% of finfold defects and 34% of edema in swim-up fry from egg selenium concentrations of 9.9 µg/g ww (25.4 µg/g dw, 61% moisture). The mean concentration of selenium in eggs from the reference site was of 3.5 µg/g ww, corresponding to a concentration of 9 µg/g dw, and the incidence of all defects was < 9.2% (Holm et al. 2005).

Rickwood et al. (2008) studied the frequency of craniofacial, skeletal and edema deformities in fathead minnow (Pimephales promelas) larvae from parents exposed to water from Junction Creek receiving effluent from both the Copper Cliff Mine in Ontario (45% of the creek flow) and a wastewater treatment system. In this mesocosm study, the fish were exposed to selenium through both water and diet; the selenium concentration was 7.2 µg/L in water from the exposed area and 0.97 µg/L in the reference set-up mesocosm. The occurrence of craniofacial, skeletal and edema deformities in larvae, summed in a deformity index, was six times higher in the water from Junction Creek than in the reference area.

Elevated concentrations of selenium were observed in fish eggs and tissues collected downstream of two uranium mining and milling operations in Saskatchewan (Muscatello et al. 2006). Craniofacial, skeletal and edema deformities were reported in selenium-exposed areas for northern pike (Esox lucius) fry. Deformity frequency was significantly different between the reference area and the high- and medium-level exposed areas, where mean selenium concentrations in fish eggs were 48.2 µg/g dw and 31.3 µg/g dw, respectively. Consistent with the maternal transfer hypothesis, deformities were substantially higher among embryos from high- and medium-exposure areas, whether raised in reference or exposed water, compared to embryos from reference areas. The mean concentration of selenium in fish eggs collected form the reference area was 3.2 µg/g dw, and less than 10% total deformities was observed when incubated in reference water.

6.5.4 Reproductive success in amphibians

Hopkins et al. (2000) studied the development of axial malformations on American Bullfrog (Rana catesbeiana) larvae in a swamp receiving coal combustion waste from a coal power plant in South Carolina's Savannah River Basin. Selenium concentrations in larvae from the exposed areas reached 20–28 µg/g dw, and were between 1.7 and 2.8 µg/g dw in the reference areas. The axial malformation frequency in larvae from the exposed areas ranged from 18–37%, and was less than 5% in the reference areas. The authors also observed that axial malformations decreased the frogs' swimming abilities.

Metts et al. (2013) studied the effects of coal combustion waste on Southern Toads (Bufo terrestris) from the Savannah River Basin. The females from the exposed area accumulated an average of 4.2 µg/g dw of selenium in their body, and transferred the accumulated selenium to their eggs. In the reference area, the average selenium concentration in the female bodies was of 2.2 µg/g dw. Although the deformity occurrence in offspring observed between the exposed and reference areas was similar, overall reproductive success was reduced by 27% in the exposed area compared to the reference area. The authors suggest that the adverse effects observed could eventually lead to a decline in the population of Southern Toads in this area.

6.5.5 Fish diversity

Gillespie and Baumann (1986) investigated the effects of selenium on the progeny of bluegills collected from the Hyco Reservoir in North Carolina, an area exposed to wastes from a coal-fired power plant. Male and female fish were collected in the exposed area (4.1–7.2 µg/g dw of selenium in whole-body tissues) and gametes were crossed in the laboratory. The selenium whole-body concentration in fish from the reference area was 0.4 µg/g dw. Fertilization and hatching of the eggs appeared unaffected by the high selenium concentrations accumulated from parents from the exposed area. However, an elevated concentration of selenium in the females resulted in larvae with edema, and the larvae did not survive the swim-up stage. The authors concluded that elevated selenium concentrations in the bluegills may explain the population decline of this species in the Hyco Reservoir.

In 1970, a coal-fired electric power plant was constructed in North Carolina. Water from its fly-ash settling basin entered Belews Lake, resulting in high selenium concentrations in water and biota (Skorupa 1998): the concentration of selenium in the exposed lake-area water averaged 10 µg/L, and there was an elevated occurrence of teratogenic fish (10–70% of the fish, versus a baseline of 1-3%). Regular monitoring ascertained that, out of 16 fish species populating the lake before the operations, only 4 remained in 1978 (Skorupa 1998).

Canton (2010) reviewed the fish population studies conducted in the Arkansas River and its tributaries in Colorado, a river with an elevated concentration of selenium in water. Mean selenium water concentrations from 10 sampling locations ranged from 3 to 418 µg/L, with high relative standard deviations at each location. For most sampling locations, the mean selenium water concentration was on the order of 10 µg/L. In contrast with Belews Lake, no effect on the fish populations and fish diversity was observed. Population metrics were better correlated with habitat availability and characteristics. The author hypothesized that the lack of association between population-level effect and elevated selenium could be attributable to several mechanisms (e.g. protection from a high co-occurrence of sulfate, population maintenance by escapees from upstream reservoirs, and reproductive strategies organized around seasonal patterns in selenium water concentrations).

6.6 Characterization of ecological risk

This ecological screening assessment examined various lines of evidence and developed conclusions based on a weight-of-evidence approach and using precaution as required under CEPA. Lines of evidence included results from risk quotient calculations for key exposure scenarios, information on fate, persistence, bioaccumulation, toxicity, and sources of selenium, and observed effects of selenium on the Canadian environment.

The compilation of measured environmental concentrations in the field (fish eggs, fish tissues, sediments and soils) focused on samples collected in the vicinity of industrial or commercial facilities and settings, to produce the $PEC_{measured}$. The environmental concentrations estimated in fish tissues ($PEC_{estimated}$) were based on calculations using measured selenium concentrations in surface water, subsequently multiplied by the generic BAF for either the lotic environment (1281 L/kg) or lentic environment (2363 L/kg) as appropriate. In addition, the impacts of selenium observed in the field were summarized, and compared to the risk quotients for the sectors where such an analysis is possible. A summary section brings together all lines of evidence, leading to a conclusion on the potential for ecological harm.

6.6.1 Risk quotient analysis

A risk quotient analysis, integrating measured selenium concentrations and realistic worst-case estimates of exposure with toxicity information, was performed for the aquatic and terrestrial environments to determine whether there is potential for

ecological harm in Canada. For the industrial exposure scenarios presented in Section 6.4 and ECCC (2017a to 2017k), risk quotients were derived and are presented in Table 6-4. Where data for both measured and predicted environmental concentrations in fish tissues were available, the presented risk quotient was based on the measured concentrations. A graphical representation of the risk quotient analysis is also provided by presenting the PNEC threshold as a line in the figures of Section 6.4; these figures include data for both $PEC_{measured}$ and $PEC_{estimated}$.

Efforts were made to identify data on the most significant anthropogenic sources of selenium to the environment, and to link assessment endpoints and exposure scenarios to the industrial activities involving them, to the extent possible. Although the $PEC_{estimated}$ were not used in the risk quotient calculation when $PEC_{measured}$ were already available, the $PEC_{estimated}$ are presented in italics in Table 6-4 for comparison and show the similarlity between the predictions with the measured concentrations.

Table 6-4: Summary of risk quotients obtained for different envrironmental compartments and exposure scenarios for selenium

Sector	Environmental Compartment	PNEC[a]	N[b]	Mean[c] $PEC_{measured}$[a]	Max PEC measured[a]	Mean[c] PEC estimated[a]	Max $PEC_{estimated}$[a]	RQ (based on means)[d]	RQ (based on max)[d]
Coal mining	Fish eggs	14.7	7	4.3–72	144.5	-	-	0.3–4.9	9.8
Coal mining	Fish whole-body	6.7	9	1.8–34.5	92.4	0.6–70	351	0.3–5.1	13.8
Coal mining	Sediment	2.0	3	2.4–14	62.3	-	-	1.2–7.0	31.1
Iron and steel[e]	Fish whole-body	6.7	1	3.9	7.55	1.4	1.5	0.6	1.1
Metal mining	Fish eggs	14.7	6	1.3–95	> 95	-	-	0.1–6.5	> 6.5
Metal mining	Fish whole-body	6.7	26	1.1–38	91.6	0.4–17.4	212.8	0.2–5.7	13.7
Metal mining	Sediment	2.0	10	0.5–58.1	177.5	-	-	0.3–29.1	88.8
Base metals smelting and refining	Fish whole-body	6.7	8	0.7–17.9	25.5	0.3–10	13.7	0.1–2.7	3.8
Base metals	Sediment	2.0	4	1.2–45.8	220	-	-	0.6–22.9	110

Sector	Environmental Compartment	PNEC[a]	N[b]	Mean[c] $PEC_{measured}$[a]	Max PEC measured[a]	Mean[c] PEC estimated[a]	Max $PEC_{estimated}$[a]	RQ (based on means)[d]	RQ (based on max)[d]
smelting and refining									
Base metals smelting and refining	Soil	1	3	0.3–4.9	447	NA	0.1	0.3–4.9	447
Oil sands extraction and processing	Fish whole-body	6.7	2	1.2	2.1	0.2–0.4	8.1[f]	0.2	0.3
Oil sands extraction and processing	Sediment	2.0	2	0.1–0.3	1.9	-	-	0.1–0.2	0.95
Electricity generation[e] co-located with coal mining	Fish whole-body	6.7	2	1.2–15.7	27.3	0.4–1.2	1.9	0.2–2.3	4.1
Electricity generation co-located with coal mining	Sediment	2.0	2	2.5–3.2	5.9	-	-	1.3–1.6	3.0
Wastewater treatment systems	Fish whole-body	6.7	3	-	-	0.1–9.2	18.4	0.01–1.4	2.7
Landfill	Fish whole-body	6.7	1	-	-	0.8–0.9	0.9	0.1	0.1
Agriculture	Soil	1	1	-	-	0.7	-	0.7	-
Agriculture	Fish whole-body	6.7	1	2.7–4.8	10.3	-	-	0.4–0.7	1.5
Pulp and paper	Fish whole-body	6.7	2	-	-	0.1	2.6	0.01	0.4
Glass manufacturing	Soil	1	1	-	-	-	1.0[g]	-	1.0

PNEC = Predicted no effect concentration, $PEC_{measured}$ = Measured environmental concentration, $PEC_{estimated}$ = Predicted environmental concentration, RQ = Risk quotient.
[a] All PNEC, PEC units are µg/g dw for fish eggs, fish tissues, sediment, and soil.
[b] N = number of studies considered for the sector and environmental compartment. The number of studies behind $PEC_{measured}$ is presented when both $PEC_{measured}$ and $PEC_{estimated}$ are available. When $PEC_{measured}$ is not available for the fish whole-body compartment, the sum of the number of studies with lentic and lotic water concentrations used to calculate $PEC_{estimated}$ is presented.
[c] Median, mean or geometric means, following the reported endpoints. Medians were preferred over arithmetic mean concentration for data assumed to follow a lognormal distribution.
[d] Risk quotient values are calculated for $PEC_{measured}$ when both $PEC_{meaured}$ and $PEC_{estimated}$ are available. Italicized PECs were not used in the risk quotient calculation.
[e] The data presented cannot be attributed solely to one sector therefore the risk quotient was attributed to the co-location of coal-fired power generation / coal mining industrial activity .
[f] Only 2/981 water samples converted to fish tissues were above the $PNEC_{fish\ WB}$ for this sector.
[g] For this modelled scenario, the background concentration of selenium in Canadian soil of 0.3 µg/g (McKeague 1979), was summed to the concentration of selenium modelled. It is estimated that, for 7 to 16 receptors out of 180 receptors modelled, a risk quotient between 1.00 and 1.05 is calculated.

6.6.2 Consideration of the lines of evidence

Once released into the environment, selenium is expected to be persistent in water, soil and sediment. Selenium can therefore accumulate in the environment from year to year, resulting in long-term exposure (mainly in soil and sediment). Increased exposure to selenium may result in adverse effects to fish, birds, sediment-dwelling organisms, and terrestrial organisms, by affecting survival, growth or reproduction. As a result, biological diversity and population-level effects may occur, potentially affecting the stability and structure of food webs in certain areas in the Canadian environment. Although the biomagnification potential of selenium is variable, its high bioaccumulation potential has been demonstrated in this assessment. The concentrations of selenium found in aquatic organisms living near point sources in Canada may be well in excess of required concentrations of the essential element, and may be causing harm to sensitive species. As selenium is persistent and will bioaccumulate, it can be transferred through the food chain and thus has the potential to cause long-term damage to the environment, particularly near areas where continuous emissions to the environment occur.

The effects of selenium are most apparent in egg-laying vertebrates (fish, birds and amphibians), and these effects occur at lower concentrations than other effects. Risk quotients presented in Table 6-4 demonstrate the potential for ecological harm from selenium in Canada. Evidence of effects in the field help offset data gaps in exposure levels and toxicity endpoints by providing real-world cases of the impacts of selenium observed in the environment. Field effects of selenium on fish have been found in the vicinity of some Canadian coal mines and metal mines; effects of selenium on fish and waterbirds have been documented in the United States for lentic areas affected by coal-fired power plants and agriculture. Although not specific to the Canadian environment, these cases indicate potential impacts resulting from releases of selenium from these activities.

Efforts were made in this assessment to evaluate the relative contributions of selenium to the environment across sectors for which the potential for ecological harm was identified.

The coal and metal (including uranium) mining sectors are higher relative contributors of selenium to all environmental compartments. A high level of confidence can be expected for the risk quotient analysis for these sectors given the richness of the datasets. Moreover, field evidence of effects on fish exposed to the wastewaters of the coal and metal mining sectors was observed; the management of liquid mining wastewaters appears to be the primary concern for selenium releases.

Although no field studies could be found on the effects of the base metal smelting and refining sector, the high risk quotients calculated in the aquatic environment, sediments and soil indicate that levels of selenium released from this sector may also be contributing significantly.

The electricity generation (coal-fired power plants) co-located with coal mining, intensive agriculture, and wastewater-treatment system sectors are lower relative contributors compared to the aforementioned sectors. A potential risk is found in the aquatic environment downstream of some wastewater treatment systems, which gather and manage liquid waste from a variety of sources. A portion of the selenium in the influent originates from industrial sources, and another portion originates from consumer use of selenium-containing products that are discarded down-the-drain (e.g. shampoos, multi-vitamin/mineral supplements).

Oil sands extraction and processing as well as glass manufacturing are lower relative contributors,as a relatively limited number of PEC values are approaching or equal to the PNECs.

6.6.3 Conclusion of the ecological risk characterization

Considering all lines of evidence presented in this screening assessment, there is risk of harm to organisms and biodiversity, but not to the broader integrity of the environment, from selenium and its compounds. It is therefore concluded that selenium and its compounds meet the criteria under paragraph 64(a) of CEPA, as they are entering 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 concluded that selenium 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.

6.6.4 Uncertainties in the evaluation of the ecological risk

Information on manufacture, importation and/or uses

The releases of selenium to the environment result principally from incidental production, as indicated from the analysis of NPRI data. However, there is a lack of data on the quantities of selenium and selenium-containing substances manufactured, imported and used, as well as a lack of information to identify the industries involved. As

a result, it is possible that some sectors with selenium releases that present a potential risk for the environment have not been identified in this assessment.

Source apportionment for selenium concentrations from wastewater treatment systems and from the electricity generation sector

Some relatively high concentrations of selenium were found downstream of wastewater treatment systems. These concentrations were used to estimate fish tissue concentrations, some of which exceed the whole-body PNEC. Given the multiple potential contributors and the scarcity of manufacture and use data for selenium, source apportionment was not possible at the sites from which the monitoring data was obtained.

Similarly, in the case of electricity generation, sampling sites did not allow for measurements to be attributed solely to this specific sector, because coal power plants are generally located in the vicinity of coal mines. As a result, estimates were attributed to the co-location of both coal-fired power generation and coal mining industrial activities. Additional data from stand-alone coal-fired power plants would better define the source attribution for the electricity generation sector.

The high uncertainty as to the specific source in these cases does not negatively affect the confidence in the overall determination of the potential for harm to the environment from selenium, but is more relevant to the relative contributions of selenium to the environment.

Historical and recent contamination

Historical contamination may be reflected as a component of the measured selenium concentrations in soils and sediment, depending on depth. Dating the contamination is challenging, and the available data did not indicate the depth pattern of selenium concentrations in soil and sediment. Therefore, for these scenarios, the aggregate exposure (historical and recent) is presented, potentially overestimating the risks from current activities. In the water compartment, recent measured selenium concentrations can reasonably be expected to originate from recent releases of active or closed sites.

Estimates of fish whole-body concentration from the water-measured concentration

The bioavailability of selenium to aquatic organisms is highly variable, depending on environmental conditions and the selenium oxidation state, and between fish, waterbird and amphibian species. To account for these confounding factors, a tissue residue PNEC was proposed for the aquatic compartment. However, for many sectors, the concentration of selenium in water in the vicinity of point sources was the only information available. The concentration of selenium in water was therefore multiplied by a lotic or lentic BAF depending on the exposure site. This approach has some limitations: the fish species identified to derive the BAFs may not be present at the

exposure site, fish species do not bioaccumulate selenium equally, and many environmental factors modify the selenium cycle. This decreases the level of confidence and the weighting of the risk quotients for estimated fish tissue concentrations, since these could either be overestimated or underestimated. The respective median BAFs were selected to minimize the impact of the uncertainty from unequal bioaccumulation across species. To further account for uncertainty in the BAF approach, when both were available, the $PEC_{estimated}$ calculated using BAFs are compared to the $PEC_{measured}$ for a sector. Although the estimated and measured PECs were very similar, ultimately the $PEC_{measured}$ were used to calculate the risk quotients in Table 6-4, when available. Thus measured fish tissue concentrations, when available, were given higher weight in the risk characterization than those calculated from water concentrations.

Essentiality and background level

Selenium is an essential element, but the difference between essentiality and toxicity is small. The exposure concentrations considered for the risk quotient analysis are above the essential requirements for most organisms and above the background concentration for most Canadian environments. However, given the wide diversity of ecoregions in Canada, the PNECs proposed may be within the background concentration range and essentiality requirements in some cases.

Confidence in exposure data sources

Some of the reported concentrations originate from studies that result from an extensive sampling campaign, while others are derived from only a few samples. A weighted approach could have been used to present the measured concentrations of selenium in the vicinity of point sources, but this presents a number of difficulties, such as discrepancy in the richness of data available for different sites, variability in the completeness of reporting and parameters reported, and sampling site selection. To avoid basing the conclusion for a sector solely on one potentially outlying measurement, the mean, median or geometric mean concentration range of various studies have also been presented.

7. Potential to Cause Harm to Human Health

7.1 Essentiality

Selenium is an essential nutrient in humans, with its nutritional functions achieved by 25 selenoproteins that have selenocysteine at their active centre (Rayman 2012; Fairweather-Tait et al. 2011). Common selenoproteins in the body include selenoprotein P, which transports selenium and has enzymatic activity; various glutathione peroxidases, which have antioxidant activity; and iodothyronine deiodinases, which catalyze conversion of the thyroid hormone thyroxine (T_4) to the active form triiodothyronine (T_3) (Ralston and Raymond 2010). In addition, selenium plays a role in reproductive function, hepatic biotransformation reactions, and neurological and immune functions (Rayman 2012).

In humans, selenium deficiency is associated with Keshan disease (a cardiomyopathy that occurs mainly in children) and Kashin-Beck disease (degenerative osteoarthritis) when it co-occurs with other stressors (Fairweather-Tait et al. 2011; ATSDR 2003; IOM 2000).The current EAR and recommended dietary allowances (RDA) for selenium in adults (excluding pregnancy and lactation), developed by the IOM in 2000 to ensure population-level nutritional adequacy, are set at 45 and 55 µg per day, respectively. These are based on the amount of selenium required to maximize plasma glutathione peroxidase activity, a selenoenzyme commonly measured to assess selenium status (IOM 2000). However, the UL is only 400 µg/day. Several authors have commented on the range between essentiality and toxicity (Stranges et al, 2010; Laclaustra et al. 2010; Vinceti et al. 2013c; Hayes et al. 2014; Thiry et al. 2012; Fairweather-Tait et al. 2011).

7.2 Exposure assessment

Selenium is a naturally occurring element and is ubiquitous in environmental media. All Canadians are exposed to selenium, primarily from the diet. Selenium is present in food, drinking water, air, soil and dust, and is also an ingredient in agricultural products (soil supplements and animal feed), cosmetics, natural health products (such as multi-vitamin/mineral supplements), drugs, pigments, and products available to consumers (including electronics and electrical equipment, and paints and coatings). Concentrations of selenium in Canadians as well as in environmental media and food in Canada, along with intake estimates, are presented in the following sections.

7.2.1 Biomonitoring

Selenium has been measured in a wide variety of biological media, including whole blood, serum, plasma, urine, human tissues, nails and hair (ATSDR 2003). It is measured in different biological media (e.g., blood, urine, proteins) depending on the purpose of the investigation. Functional biomarkers such as selenoprotein P and glutathione peroxidase are commonly measured in studies when assessing nutritional status. Once nutritional requirements have been met, levels will be maximized and there will be no further increase in selenoprotein P and glutathione peroxidase concentrations

with increasing selenium intake (Rayman 2000; Hays et al. 2014; IOM 2000). Total selenium in serum and/or plasma is also commonly measured when assessing nutritional status, because those concentrations respond rapidly to changes in the diet (Hays et al. 2014). Selenium is present in erythrocytes, and, as a result, whole blood concentrations respond more slowly to changes in dietary selenium intake than serum or plasma. Longnecker et al. (1996) examined the relationship between whole blood, serum, toenail and urine as surrogate measures of selenium intake, and found that selenium concentrations in whole blood, serum and toenails were adequate as surrogate measures of long-term intake. A systematic analysis of the relationship between selenium intakes and biological concentrations based on 75 published biomonitoring studies was recently carried out by Noisel et al. (2014), who found strong correlations between selenium intakes and whole blood concentrations, plasma concentrations and urinary excretion rates; blood and plasma concentrations were also strongly related. The whole blood measurements of total selenium are representative of all forms of selenium, from all routes (e.g., oral, dermal and inhalation) and sources (e.g., food, water and products) to which people were exposed.

Total selenium in whole blood is commonly measured when investigating elevated exposure and potential toxicity (Hansen et al. 2004; Lemire et al. 2012). Plasma is not a good biomarker for examining selenium status in Inuit as a plateau in plasma concentrations of selenium have been observed in two studies despite increasing selenium intake and increasing selenium concentrations in whole blood (Hansen et al. 2004, Ayotte et al. 2014). Plasma selenium concentrations plateaued at approximately 140 µg/L in Greenland Inuit and 160 to 180 µg/L (with a maximum of 221 µg/L) in Inuit in Nunavik (Hansen et al. 2004; Ayotte et al. 2014). In Nunavik Inuit, maximum selenium concentrations in whole blood reached 3555 µg/L, while plasma concentrations only reached a maximum concentration of 221 µg/L. In both these populations, the primary source of exposure to selenium is the consumption of marine mammals, likely as selenoneine. In contrast, there was a linear relationship between plasma and whole blood selenium in an indigenous population in the Brazilian Amazon where the main source of selenium was from Brazil nuts, as selenomethionine (Lemire et al. 2012).

Recently, the selenium protein selenoneine has been explored as an important biomarker for fish consumption and selenium antioxidant and detoxification functions (Yamashita et al. 2013). Selenoneine was identified as the major form of selenium in the blood cells (erythrocytes, leukocytes and platelets) of a fish-eating population in Japan as well as the major form of selenium in ocean fish including tuna, mackerel and swordfish (Yamashita and Yamashita 2010, Yamashita et al. 2010, Yamashita et al. 2011). Selenoneine is also being investigated as a major form of selenium in Nunavik Inuit as part of a project under the Northern Contaminants Program. As part of this project, selenoneine was identified as the major form of selenium in beluga mattaaq, a traditional marine food (or country food) consumed by Inuit, and as a key biomarker of importance when examining selenium in Inuit (Ayotte et al. 2014, Lemire et al. 2015a, Ayotte et al. 2015). However, at this time, there is no published data on the concentrations of selenoneine in Inuit.

For the reasons noted above, and due to abundance of whole blood selenium concentration data, concentrations of selenium in whole blood are considered to be an appropriate biomarker for exposure and risk characterization for Canadians and are summarized in the paragraphs below.

Total selenium concentrations in various biological media have been measured in several biomonitoring programs in Canada through inductively coupled plasma mass spectrometry (ICP-MS), including the Canadian Health Measures Survey (CHMS), the First Nations Biomonitoring Initiative, the Inuit Health Survey through the Northern Contaminants Program, the Alberta Biomonitoring Program, and studies conducted in British Columbia, Québec City and among pregnant women across Canada (Health Canada 2013a; AFN 2013; Laird et al. 2013; Alberta Health and Wellness 2008; Government of Alberta 2010; Clark et al. 2007; INSPQ 2004; Foster et al. 2012). Concentrations of selenium in whole blood are presented in Table 7-1 and described below.

In Cycle 1 of the CHMS (2007–2009), median and 95th percentile whole blood concentrations in the Canadian population aged 6–79 were 190 and 250 µg/L, respectively (see Table 7-1 and Health Canada 2013a). Whole blood concentrations measured in Canadians aged 3–79 as part of CHMS Cycle 2 (2009–2011) were slightly lower, but not significantly different than Cycle 1, with median and 95th percentile values of 180 and 240 µg/L, respectively (Health Canada 2013a). Males had slightly higher concentrations than females; however, concentrations were not significantly different. Children aged 3–11 had significantly lower selenium levels than the total population; with median whole blood concentrations of 160 µg/L for children aged 3–5 and 170 µg/L for children aged 6–11 (Health Canada 2013a). The CHMS is a population-level survey designed by Statistics Canada. Population-weighted data is representative of 96.5% of the Canadian population, but excludes people living on reserves or in other Aboriginal settlements in the provinces, as well as residents of institutions, full-time members of the Canadian Forces, people living in certain remote areas, and people living in areas with a low population density. Although the CHMS did not capture children under 3 years of age, total selenium in whole blood was measured in 214 children in Canada under 3 years of age as part of a follow-up study to the Maternal-Infant Research on Environmental Chemicals (MIREC) cohort (MIREC-Child Development Plus): preliminary median and 95th percentile concentrations were 150 and 190 µg/L, respectively (Liang 2016). Selenium whole blood concentrations in the U.S. population, measured in the National Health and Nutrition Examination Survey 2011–2012, are similar to concentrations in Canadians. Geometric mean and 95th percentile concentrations for the total U.S. population were 190 and 236 µg/L, respectively (CDC 2015).

Selenium whole blood concentrations were measured in adults from 15 rural and isolated First Nations communities south of the 60th parallel, as part of the First Nations Biomonitoring Initiative conducted in 2011 (Table 7-1 and AFN 2013). Median and 95th percentile concentrations were 182 and 235 µg/L, respectively (AFN 2013). Selenium was also measured in adult Cree in Eeyou Istchee, the Cree Territory of James Bay in

Québec. Median and 95th percentile whole blood selenium concentrations were 173 and 234 µg/L, respectively (Ayotte 2014; Nieboer et al. 2013). Selenium whole blood concentrations were measured in Inuit living in Nunavut, the Inuvialuit Settlement Region (Northwest Territories) and Nunatsiavut (northern Labrador), as part of the Inuit Health Survey in 2007–2008. Median and 95th percentile concentrations of 280 and 945 µg/L, respectively, were measured in 2170 adult Inuit, with concentrations ranging from 85 to 2800 µg/L (modified from Laird et al. 2013; Chan et al. 2013; Chan 2014). Selenium whole blood concentrations have also been measured in different Inuit populations living in Nunavik, Québec, including children aged 5 and 11, pregnant women, and adults (Saint-Amour et al. 2006; Valera et al. 2009; Muckle et al. 2001; Lemire et al., 2015b). Median concentrations ranged from 177 to 297 µg/L and 95th percentile concentrations ranged from 325 to1101 µg/L (see Table 7-1). The highest median and 95th percentile concentrations were in the 5-year-olds, although higher maximum values (> 3500 µg/L) have been found in adults in these communities (Ayotte 2014, Lemire et al. 2015b, Valera et al. 2009). The whole blood selenium concentrations measured in the adults from the Nunavik Inuit Health Survey were very highly correlated with whole blood mercury concentrations ($p < 0.0001$) (Lemire et al. 2015b).

In addition to dietary intake, selenium whole blood concentrations in Canadians are influenced by many other factors, including age and geographical location. Although selenium crosses the placental barrier and is passed to the developing fetus, concentrations of selenium are higher in maternal blood than cord blood, and are higher in cord blood than newborns (Aylward et al. 2014; Lombeck et al. 1977). Newborns are exposed to selenium from breast milk and formula, and whole blood concentrations of selenium increase steadily in children until the teen years, when concentrations plateau through adulthood. On the basis of data from Canada and the U.S., children in general have significantly lower selenium blood concentrations than adults (Health Canada 2013a; Laing 2016; CDC 2008; CDC 2015). However, this pattern appears to be different in Inuit in northern Canada where concentrations in children aged 5 were higher than 11 year old children and similar to adults (see Table 7-1).

Although no statistical differences were observed between males and females at the population level in Canada and the U.S., several studies in the two countries have found that males tend to have higher blood concentrations than females (Health Canada 2013a; CDC 2014; AFN 2013; INSPQ 2004; Kafai and Ganji 2003; Laclaustra et al. 2010). Higher concentrations in males have been attributed to a higher dietary intake and a higher muscle mass (see Table 7-2 and Clark et al. 2007).

In a study of 125 pregnant women in five Canadian cites (Vancouver, Calgary, Hamilton, Ottawa and Halifax), there were no significant differences in whole blood selenium concentrations between Canadian-born and foreign-born women (Foster et al. 2012). Concentrations measured in these pregnant women are similar to women of reproductive age measured in the CHMS; pregnancy does not appear to have a significant impact on whole blood selenium concentrations.

Concentrations of selenium are consistently higher in Inuit populations in northern Canada than the general Canadian population (Laird et al. 2013). Between 2% and 27.5% of study participants in various studies conducted in Nunavik, Nunavut, Inuvialuit Settlement Region and Nunatsiavut had blood concentrations above 480 µg/L, and up to 7% had concentrations above 1000 µg/L (data modified from Laird et al. 2013; Chan 2014; Ayotte 2014). However, symptoms of selenosis (e.g., hair loss, nail deformities and sloughing) were not directly measured during the health examination as part of the study (Laird et al. 2013). Concentrations of selenium in Inuit from the northern Canadian are similar to concentrations in Greenland Inuit who consume traditional foods (Hansen et al. 2004).

Table 7-1: Concentration of total selenium in whole blood (µg/L) in U.S. and Canada

Study/ Population	Sampling year(s)	Age years	Sex	n	Median (95% CI)	95th percentile (95% CI)
CHMS[a]	2007–09	6–79	M+F	5319	190 (190–200)	250 (240–260)
CHMS[a]	2009–11	3–79	M+F	6070	180 (180–190)	240 (230–250)
NHANES[b] (U.S.)	2011–12	1 and older	M+F	7920	190 (187–193)	236 (231–241)
MIREC–CD Plus[c]	2013-2014	< 3	M+F	214	150	190
CHMS[a]	2009–11	3–5	M+F	495	160 (160–170)	200 (200–210)
CHMS[a]	2009–11	6–11	M+F	961	170 (160–170)	210 (200–220)
CHMS[a]	2009–11	12–19	M+F	997	180 (180–180)	230 (220–240)
CHMS[a]	2009–11	20–39	M+F	1313	190 (180–190)	240 (220–270)
CHMS[a]	2009–11	40–59	M+F	1222	190 (180–190)	240 (240–250)
CHMS[a]	2009–11	60–79	M+F	1082	180 (180–190)	240 (230–240)
Quebec Region[d]	2001	18–65	M+F	472	227	261[i]
CHMS[a]	2009–11	3–79	M	2940	190 (180–190)	240 (230–260)
Quebec Region[d]	2001	18–65	M	155	232	266[i]
CHMS[a]	2009–11	3–79	F	3130	180 (180–180)	240 (230–250)
Quebec Region[d]	2001	18–65	F	317	223	260[i]
Canadian pregnant women[e]	2005–07	16–40	F	93	GM 192 (187– 197)	NA
First Nations[f]	2011	20+	M+F	473	182 (175–189)	235 (217–253)
First Nations[f]	2011	20+	M	188	182 (176–188)	237 (214–261)
First Nations[f]	2011	20+	F	285	183 (174–192)	231 (214–248)
Inuit – Nunavut, Inuvialuit Settlement	2007–08	> 18	M+F	2170	280 (210–450)	945

Study/ Population	Sampling year(s)	Age years	Sex	n	Median (95% CI)	95th percentile (95% CI)
Region, Nunatsiavut [g]						
Inuit – children Nunavik[h]	NA	5	M+F	112	260 (226–295)	1101 (462–1740)
Inuit – children Nunavik[h]	NA	11	M+F	294	177 (172–182)	325 (276–374)
Inuit – pregnant women Nunavik[h]	NA	NA	F	212	297 (277–317)	583 (488–677)
Inuit – adults Nunavik[h]	2004	> 18	M+F	914	256 (248–265)	793 (705–881)
Cree – adults Nunavik[h]	NA	NA	M+F	1101	173 (171–175)	234 (228–240)

NA = not available, GM = Geometric mean
[a] Health Canada 2013a
[b] CDC 2015
[c] Liang 2016,; preliminary data, not peer-reviewed.
[d] INSPQ 2004, converted to µg/L using the molecular weight of selenium.
[e] Foster et al. 2012
[f] AFN 2013
[g] Modified from Laird et al. 2013, Chan et al. 2013, Chan 2014.
[h] Ayotte 2014
[i] 90th percentile

7.2.2 Environmental media and food data

7.2.2.1 Air

Although airborne selenium originates from both natural and anthropogenic sources, the latter, specifically the combustion of coal and other fossil fuels, is the primary source (ATSDR 2003). Selenium dioxide (CAS RN 7446-08-4), methyl selenide, and dimethyl selenide are the most prevalent forms of selenium found in the atmosphere (ATSDR 2003). Hydrogen selenide is also a volatile selenium compound; however, it is highly reactive and will rapidly oxidize to elemental selenium and water (ATSDR 2003). Biomethylated selenium will volatilize from plants and water and return to the Earth's surface through wet and dry deposition. In 2009, total selenium was measured in particulate matter (PM) as part of the National Air Pollution Surveillance (NAPS) Program in 1500 samples from 22 sites across Canada, with median concentrations in coarse PM (PM_{10}) ranging from 4–11 ng/m^3 (NAPS 2012). The highest concentrations of total selenium measured (116 ng/m^3) were in proximity to base metal refining and smelting activities, which likely contributed to higher airborne concentrations.

Matched indoor, outdoor and personal air data (fine PM [$PM_{2.5}$] and PM_{10} samples) were collected from Windsor Ontario (Rasmussen et al. 2013), with the highest selenium concentrations measured in outdoor air (median PM_{10} 1.2 ng/m^3), whereas indoor and personal air concentrations were similar (median PM_{10} 0.23 and 0.28 ng/m^3) (Rasmussen et al. 2013). Low indoor-air concentrations (less than 1 ng/m^3) were also measured in different PM fractions in Edmonton and the U.S. (Health Canada 2013b; Kinney et al. 2002; Hidy et al. 2000). Inhalation of airborne selenium is a minor source of total intake.

7.2.2.2 Dust

Nationally representative total and bioaccessible selenium concentrations from Canadian homes were available from the Canadian House Dust Study (CHDS). Total selenium concentrations ranged from < 0.1 to 11 µg/g, with a median concentration of 0.9 µg/g (n = 1025). Bioaccessible selenium concentrations (i.e., in simulated stomach fluids) ranged from < 0.1 to 9 µg/g, with a median concentration of 0.2 µg/g (n = 1025) (Rasmussen et al. 2014). Median bioaccessibility was 13%, and bioaccessibility decreased with weathering in prolonged humid conditions (Rasmussen et al. 2014). Selenium has also been measured in dust around point sources in Canada, e.g., mean indoor dust concentrations of 5.8 µg/g (n = 38) were measured around Flin Flon, Manitoba, which would fall in the upper tail of the CHDS data (Intrinsik 2010). On the basis of a comparison of selenium concentrations in outdoor soil and indoor dust in the CHDS, selenium does not appear to become enriched in indoor environments; a similar trend was also observed in the Flin Flon study (Rasmussen et al. 2001; Intrinsik 2010). However, in the Sudbury Area Soils Study, indoor dust concentrations were higher than corresponding soil concentrations (SARA 2008). Overall, dust is a negligible source of selenium intake.

7.2.2.3 Soil

Selenium is present in the soil in numerous forms including selenides (Se^{2-}), elemental selenium (Se^0), selenites (Se^{4+}), selenates (Se^{6+}), and organic selenium compounds which are generally present in humus. The form of selenium in the soil and its bioavailability depend on pH, texture, mineralogy, the presence of competing ions and the organic matter content of the soil (CCME 2009, NRC 1983).

Selenium soil concentrations in Canada are well-described in the Canadian Soil Quality Guideline for Selenium (CCME 2009): concentrations range from 0.02 to 5.7 µg/g, and the average background selenium concentration in soil was assumed to be 0.7 µg/g, which is slightly higher than the global average (CCME 2009). Seleniferous soils (≥ 0.5 µg/g selenium) are present in southeastern Alberta, southern Saskatchewan and southern Manitoba, and result from the underlying Cretaceous shales (NRC 1983). Selenium-rich soils also exist in the copper ores in Noranda, Quebec; Sudbury, Ontario; and Flin Flon, Manitoba (CCME 2009). Average soil concentrations ranging from 2 to 32 µg/g have been found near Flin Flon and surrounding communities, with maximum concentrations up to 286 µg/g due to the nearby copper deposit and mining facility

(Intrinsik 2010). Average selenium levels in Canadian soils are well below the selenium soil quality guideline for human health on residential and park land of 80 µg/g, which is based on the IOM UL of 400 µg/d (CCME 2009). Direct exposure to soil is not a significant source of selenium intake.

Broad areas of Canada have plants containing low levels of selenium, which is an indicator of low soil-selenium quantity (NRC 1983), with low-selenium soils in eastern Canada containing less than 0.2 µg/g selenium (Levesque 1974). Selenium deficiency disorders in livestock (e.g., white muscle disease) have been most prevalent in almost all areas east and north of the Great Lakes, northern areas of the prairie provinces, and parts of the Rocky Mountains (NRC 1983). In these areas of Canada, soil supplementation and feed supplements are common practices to prevent nutritional deficiencies in grazing livestock.

7.2.2.4 Drinking water

Selenium is present in water primarily in inorganic forms as selenate and selenite (Health Canada 2014a). In Canada, selenium is commonly measured at water treatment facilities and distribution systems. Concentrations of selenium in drinking water are generally low across the country (less than 2 µg/L, which is well below the proposed drinking water guideline of 50 µg/L based on the IOM UL of 400 µg/d) (Health Canada 2014a), but higher concentrations (> 10 µg/L) have been measured in drinking water sources around point sources (e.g., septic systems and fertilizers) and areas where the underlying geology has higher selenium concentrations (e.g., southern Saskatchewan) (BC MOE 2014; CCME 2009; Health Canada 2014a). Overall, provincial and territorial data were available from Newfoundland and Labrador, Nova Scotia, New Brunswick, Ontario, Saskatchewan and the Northwest Territories (n > 30 000), and were documented in the Guideline for Canadian Drinking Water Quality – Guideline Technical Document for Selenium (Health Canada 2014a). Data were also available from First Nations communities in British Columbia and Manitoba (Chan et al. 2011, 2012a). Selenium is used as a replacement for lead in brass alloys in fittings and lead in brass components that are used in distribution system and plumbing components, which is an additional potential source of selenium in drinking water (BC MOE 2014; Health Canada 2014a). Overall, drinking water is a minor source of selenium intake.

7.2.2.5 Food

Food is the most important source of exposure to selenium. Selenium enters the food web through plants, which uptake selenium from the soil based on the selenium content in soil and on bioavailability, which are influenced by the form of selenium, soil pH, organic content of the soil, and other factors (Rayman et al. 2008).

The selenium status of animals depends on the forage or feed they consumed; and therefore, the selenium levels in plants and animals vary greatly depending on the soil selenium content (Ralston and Raymond 2010). The forms of selenium present in food are the organic selenocysteine (predominantly in animal proteins), selenomethionine

(predominantly in plant products, animal tissue and selenium yeast) and, to a lesser extent, inorganic selenite and selenate. Selenoneine (2-selenyl- Nα,Nα,Nα -trimethyl-L-histidine) is a recently recognized form of dietary selenium, which is the major selenium compound present in a variety of ocean fish such as tuna and mackerel (Yamashita and Yamashita 2010).

Anthropogenic inputs of selenium into the food web include the use of selenium soil supplements, livestock feed, food packaging (in glass and plastics), fortification of processed foods including infant formulas and vitamin/mineral-enhanced beverages, and addition of selenium-enriched yeast to processed foods (see section 4.2.2 for further details). Industrial point sources, such as leaching and agricultural run-off, can be a significant source of selenium in aquatic food sources such as fish and shellfish.

Selenium concentrations vary in different food commodities based on the geographical region in which a plant was grown, or on where the animal was raised or where fishes were harvested. Globally, higher concentrations of selenium are found in organ meats, retail market marine fish and seafood (0.4–1.5 µg/g ww), followed by muscle meats (0.1–0.4 µg/g ww) and grains, nuts and cereals (0.1–0.8 µg/g) (Rayman 2008). Dairy, fruits and vegetables have relatively low levels of selenium. There are notable exceptions to these general trends; for example, Brazil nuts can have very high levels of selenium but are also variable (ranging from 0.03 to greater than 500 µg/g ww) (Rayman 2008). Concentrations of selenium within the same food commodity can be highly variable depending upon the underlying geology of the region and point sources of exposure (Rayman 2008). Selenium accumulates in the aquatic food web, meaning that fish, seafood and marine mammals can have elevated selenium concentrations (ATSDR 2003). Selenium is also present in breast milk, a source of food for nursing infants. An average concentration of 21 µg/L was found in the breast milk of 818 Canadian mothers between 2008 and 2011 as part of the Maternal Infant Research on Environmental Chemicals study (Cockell 2014).

Selenium concentrations are measured as part of several food monitoring surveys and programs by Health Canada and the Canadian Food Inspection Agency, including the Total Diet Study, the National Chemical Residues Monitoring Program, the Children's Food Projects and the Food Safety Action Plan (Health Canada 2007; CFIA 2014). Probabilistic dietary intake estimates for the general population 6 months of age and older were derived by Health Canada's Food Directorate using concentrations of selenium in food commodities collected between 2009 and 2013 (n > 30 000), provincial drinking water data, and food and water consumption rates from the Canadian Community Health Survey (Statistics Canada 2004). Dietary intakes for 0 to 5 month old infants were estimated deterministically using selenium residue data from the Canadian Total Diet Study (2005 to 2010), mean and 95th percentile 'eaters only' infant formula consumption figures from the United States Department of Agriculture's (USDA) Continuing Survey of Food Intakes by Individuals (CSFII; 1994-96, 98), and mean body weights for infants between 0 and 5 months from the USDA's CSFII survey.

Table 7-2 presents dietary intake estimates for various age groups. When normalized by body weight, dietary intake estimates are highest in children. Breads, baked goods, cereal grains, and flours were the primary sources of dietary intake, accounting for approximately 30% of intake, followed by poultry, pork, dairy and eggs. Intake levels in Canadians are considered to be adequate to meet nutritional requirements for selenium, as they exceed the adequate intake levels for infants (15 - 20 µg/d) and the EAR for all other age groups (17 - 45 µg/d) set by the IOM (2014 email from the Bureau of Nutritional Sciences, Food Directorate, to the Existing Substances Risk Assessment Bureau, Health Canada, unreferenced).

Table 7-2: Percentiles of dietary intakes for selenium for the general Canadian population based on food and water[a]

Age / sex	Median µg/d (95% CI)	Median µg/kg/d (95% CI)	95th percentile µg/d (95% CI)	95th percentile µg/kg/d (95% CI)
0-5 months (M&F)[b]	25.69 mean	4.40 mean	45.31	7.77
6 months–1 yr. (M&F)	39.68 (36.63, 43.29)	4.17 (3.89, 4.53)	86.73 (73.13, 103.10)	8.56 (7.45, 10.15)
1–3 yrs. (M&F)	75.28 (73.65, 77.83)	5.49 (5.36, 5.63)	123.38 (116.61, 130.46)	9.20 (8.73, 9.77)
4–8 yrs. (M&F)	95.30 (93.02, 97.44)	4.07 (3.98, 4.17)	143.50 (135.59, 150.53)	6.55 (6.22, 6.85)
9–13 yrs. (M)	124.68 (121.16, 128.65)	2.87 (2.79, 2.96)	183.23 (172.77, 193.67)	4.82 (4.60, 5.05)
9–13 yrs. (F)	101.64 (98.53, 105.40)	2.40 (2.32, 2.48)	145.01 (135.20, 154.81)	4.24 (4.01, 4.48)
14–18 yrs. (M)	151.13 (147.52, 155.26)	2.22 (2.16, 2.28)	244.69 (232.17, 258.54)	3.88 (3.69, 4.08)
14–18 yrs. (F)	104.11 (100.81, 107.33)	1.77 (1.72, 1.82)	169.36 (160.14, 179.96)	3.11 (2.95, 3.31)
19–30 yrs. (M)	150.56 (145.96, 156.55)	1.93 (1.86, 2.00)	236.44 (220.04, 255.28)	3.34 (3.13, 3.61)
19–30 yrs. (F)	101.04 (97.60, 104.33)	1.56 (1.51, 1.61)	151.90 (141.47, 161.42)	2.65 (2.49, 2.81)
31–50 yrs. (M)	143.32 (139.06, 148.86)	1.73 (1.67, 1.79)	219.42 (202.27, 236.09)	2.81 (2.62, 3.02)
31–50 yrs. (F)	105.68 (102.31, 109.27)	1.57 (1.52, 1.62)	168.22 (159.00, 181.06)	2.76 (2.62, 2.93)
51–70 yrs. (M)	123.90 (121.12, 127.31)	1.49 (1.46, 1.53)	192.11 (182.51, 203.17)	2.47 (2.34, 2.59)
51–70 yrs. (F)	98.31 (95.37, 101.47)	1.43 (1.39, 1.47)	141.87 (132.50, 152.84)	2.32 (2.19, 2.48)
71+ yrs. (M)	108.35 (103.82, 114.50)	1.40 (1.34, 1.47)	176.34 (157.67, 209.44)	2.38 (2.14, 2.81)
71+ yrs. (F)	83.01	1.28 (1.24, 1.32)	131.03	2.23

Age / sex	Median µg/d (95% CI)	Median µg/kg/d (95% CI)	95th percentile µg/d (95% CI)	95th percentile µg/kg/d (95% CI)
	(80.56, 85.18)		(124.04, 139.25)	(2.11, 2.39)

CI = Confidence interval

[a] All estimates of intake from food (including infant formula) and drinking water, except those for the 0-5 month old age group (see text above Table 7-2 for information on how these figures were derived), were generated in Statistical Analysis Software (SAS) using 24-hour recall consumption data from the Canadian Community Health Survey (CCHS), Cycle 2.2 on Nutrition (Statistics Canada 2004); concentration data from Canadian Food Inspection Agency data sources, including the National Chemical Residues Monitoring Program, the Children's Food Projects and the Food Safety Action Plan; and data from Health Canada's Nutrition Survey System. Log-normal distributions were fitted to drinking water data provided by provincial drinking water programs (NL, NS, NB, ON, SK). For each iteration (n = 500), selenium levels were randomly selected from a matched list of assayed values. Age- and sex-based probabilistic exposure estimates were generated. The 0 to 6–month age group estimates were considered too unreliable to publish, in accordance with Statistics Canada requirements for publication of statistical analysis using CCHS consumption data. Body weights were measured or self-reported. Estimates were generated by the Food Directorate, Health Canada.

[b] Dietary intakes (excluding breast milk) for 0 to 5 month infants were obtained from the Canadian Total Diet Study results from 2005 to 2010; the exposure estimates generated using the United States Department of Agriculture's (USDA) Continuing Survey of Food Intakes by Individuals (CSFII; 1994-96, 98) data. The USDA's survey included measured body weights for infants under 6 months of age and also included a large sample size of infants, which Canadian food consumption survey (CCHS cycle 2.2, Statistics Canada, 2004) did not. Therefore, infant formula consumption rates and body weights from the USDA's study were employed as they were determined to be a reasonable surrogate for Canadian data. Selenium exposure in infants 0 to 5 months was deterministically estimated; therefore the 95% confidence interval could not be generated for this age group as was done for the other age and sex groups for which exposure was estimated probabilistically.

First Nations People

Concentrations of selenium in traditional foods were measured as part of the First Nations Food, Nutrition and Environment Study (FNFNES) conducted in British Columbia (Chan et al. 2011). Selenium concentrations in the most common traditional foods consumed were up to 0.87 µg/g ww in salmon, up to 0.49 µg/g ww in moose meat and up to 0.38 µg/g ww deer meat. Selenium concentrations were higher in organ meats (e.g., liver, heart) over muscle meats of animals and were particularly high in fish eggs (up to 4.14 µg/g ww). Concentrations of selenium measured in traditional food sources in the BC FNFNES were similar to those measured in retail market foods presented above. This study did not sample traditional target foods around point sources; rather, traditional foods were collected from each participating community to represent foods consumed that season/year in that region of BC (AFN 2013).

Northern Populations - Inuit

As part of the selenium cycle, selenium bioaccumulates in the aquatic food web (Section 5.3.1; ATDSR 2003). High selenium concentrations are found in marine mammals in Canada—such as seals and Beluga Whales, which are key traditional foods in Inuit diets. It is likely that selenium found in marine mammals is primarily from naturally occurring sources; however, there will be anthropogenic contribution. The

extent of the anthropogenic contribution has not been fully investigated. High concentrations in seal liver (up to 38 µg/g ww), Beluga and Narwhal mattaaq (skin and blubber) (up to 6 µg/g ww), and jumper (i.e., porpoise) skin (34 µg/g ww) have been measured in the North (Ayotte et al. 2014; Laird et al. 2013). Probabilistic dietary intake estimates have been derived for Inuit in Nunatsiavut, Nunavut and the Inuvialuit Settlement Region of northern Canada based on the consumption of traditional foods, as ascertained in the Inuit Health Survey (Laird et al. 2013). Intakes ranged from 10 to 600 µg/d (10^{th}–90^{th} percentiles), and median intake was 91 µg/d. These intake estimates did not account for selenium intake from the consumption of non-traditional food sources (e.g. cereals); the primary sources of selenium intake were Ringed Seal liver, and Beluga and Narwhal mattaaq. Inuit also have a high intake of mercury (Hg) from their diet, and Hg and selenium intakes were highly correlated in this study (Laird et al. 2013); the primary sources of Hg intake, such as Ringed Seal liver, are also major sources of selenium intake. In Nunavut, caribou meat and Arctic Char are important sources of dietary selenium intake as well (Chan et al. 2013). In Nunavik, Beluga mattaaq, Caribou meat and Arctic Char were the primary contributors to daily selenium intakes (Lemire et al. 2015b). Selenium species in arctic Beluga Whale have been investigated by Lemes et al. (2011): selenomethionine, methylselenocysteine and selenite were present in tissues, while selenate and selenocysteine did not appear to be present. The highest concentrations, found in the liver, were predominantly selenite, which was also the predominant species found in the brain and kidneys. Selenomethionine dominated in the muscle tissue (Lemes et al. 2011). Two unknown selenium species were also present, likely organo-selenium species. A selenium-mercury complex was also found in these Beluga. In other ongoing work conducted under the Northern Contaminants program, selenoneine has been identified as a major selenium source in Beluga mattaaq (Ayotte et al. 2014, Ayotte et al. 2015).

Subsistence Fishers

Elevated selenium concentrations in fish have been found around mining operations in Canada, including coal mines in British Columbia and Alberta and uranium mines in Saskatchewan, compared with fish from non-mining areas (BC MOE 2014). Concentrations of selenium in fish tissues around different point sources (e.g. coal mining, metal mining, smelting and refining) are presented in Figure 6.4. Concentrations of up to 18.4 µg/g ww (92 µg/g dw based on 80% water content) have been found in fish in the Elk River watershed in BC downstream from coal mines, and mean concentrations of 23 µg/g ww (115 µg/g dw based on 80% water content) have been found in fish in Beaverlodge Lake, near decommissioned uranium operations in the Eastern Athabasca Region of Saskatchewan (Minnow 2009; SENES 2003). These values are much higher than typical selenium concentrations in retail marine fish and seafood which range from 0.4 to 1.5 µg/g ww (Rayman 2008). Subsistence fishers, and to a lesser extent recreational fishers, who consume fish with high concentrations of selenium could have elevated selenium intakes. To mitigate any potential health effects from the consumption of fish containing elevated selenium levels, fish consumption advisories have been issued in Canada by entities other than Health Canada since 2003 for some lakes in the Eastern Athabasca Region of Saskatchewan, due to high

concentrations of selenium in fish resulting from historical uranium mining operations (CNSC 2013a, 2013b; Saskatchewan Ministry of Environment 2009) and in 2015 and 2017 for certain fish species in some lakes and creeks in and around Sudbury, Thunder Bay, and Kenora districts in Ontario (Ontario Environment and Climate Change 2017). The BC MOE and United States Environmental Protection Agency (U.S. EPA) have established screening values for human consumption of fish for selenium (BC MOE 2014; U.S. EPA 2000 (Table 8-4)).

Globally, dietary intakes of selenium vary widely. Canada has one of the highest dietary intakes, primarily due to the consumption of wheat which is grown in high-selenium prairies, and the consumption by some sub-populations of marine mammals which bioaccumulate selenium . Subsistence fishers consuming fish downstream from mining operations also have the potential for elevated dietary intake. Globally, dietary intakes of selenium range from extremely high in parts of China where intakes are approaching or exceed hazardous levels, to moderately high in Venezuela and some parts of North America, to adequate levels in other parts North America (e.g. east) and Japan, to low or deficient in parts of eastern Europe and parts of China (Rayman 2008). Dietary intakes in Canada are similar to the U.S. and higher than Europe (IOM 2000; EFSA 2006).

7.2.3 Products

Selenium is present in licensed natural health products in Canada, including multi-vitamin/mineral supplements, anti-dandruff shampoos, and lotions for the treatment of skin conditions (LNHPD 2014). Products that conform to the requirements of either the NNHPD Selenium monograph or the NNHPD Multi-Vitamin/Mineral Supplements monograph, may include doses of up to 400 µg/d for adults[9], which is equivalent to the UL established by the IOM for adolescents and adults (age ≥ 14) (Health Canada 2016a, 2016b; IOM 2000). In 2014, there were approximately 2000 licensed oral natural health products containing both organic and inorganic forms of selenium in Canada; less than 2% provide 400 µg/d of selenium and 94% provide 300 µg/d or less (LNHPD 2014). The top-five-selling multi-vitamin/mineral supplements contain 55 µg of selenium (2014 email from the Bureau of Nutritional Sciences to the Existing Substances Risk Assessment Bureau, Health Canada, unreferenced). Selenium is not permitted in children's multi-vitamin/mineral supplements without additional evidence demonstrating a favourable risk-benefit profile. Selenium as selenium sulfide is permitted in anti-dandruff shampoos and skin lotions at concentrations of up to 2.5% (Health Canada 2006; LNHPD 2014). Selenium is also a component of some licensed homeopathic products (LNHPD 2014).

[9] A maximum dose of 200 µg/day for selenium is under consultation by Health Canada (Health Canada 2016b).

Selenium and its compounds are described as prohibited for use in cosmetic products, with the exception of selenium sulfide (CAS RN 7488-56-4), on the List of Prohibited and Restricted Cosmetic Ingredients (more commonly referred to as the Cosmetic Ingredient Hotlist or simply the Hotlist), an administrative tool that Health Canada uses to communicate to manufacturers and others that products containing certain substances are unlikely to be classified as a cosmetic under the Food and Drugs Act (FDA), and in addition, that certain substances, when present in a cosmetic at certain concentrations, may contravene the general prohibition found in section 16 of the Food and Drugs Act or a provision of the Cosmetic Regulations (Health Canada 2014b). On the basis of notifications submitted under the Cosmetic Regulations to Health Canada, selenium sulfide is currently used in a small number of hair shampoos in Canada (2014 email from the Consumer Product Safety Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, unreferenced). Selenium has been detected in cosmetics in Canada, included as part of compliance testing conducted by Health Canada, as well as testing conducted by a non-governmental organization (Health Canada 2008; Environmental Defence 2011). Total selenium was detected in approximately 14% of body and eye makeup and lipstick products, at very low concentrations of up to 0.004% (Health Canada 2008; Environmental Defence 2011). In these cases, it is likely that selenium was present as an impurity in the starting materials.

Selenium compounds (cadmium selenide sulfide CAS RN 12214-12-9, cadmium selenide sulfide CAS RN 12626-36-7, C.I. Pigment Orange 20 CAS RN 12656-57-4 and C.I. Pigment Red 108 CAS RN 58339-34-7) are a component of a few inorganic pigments that can be used in glass, plastics, printing inks, paints and coatings, textiles and tattoos. However, the use of these pigments is declining, in part due to the health effects associated with cadmium (Cheminfo 2013a, 2013b; ToxEcology 2014; CPIMA 2010), although there is still extensive use in artist paints as well as automotive coatings and heat-resistant coatings (Household Products Database 1993–; PPG 2006; Sherwin-Williams Company 2013). Selenium was detected in tattoo inks at low concentrations (less than 0.00004%, and in only 2 of 28 samples) as part of compliance testing conducted by Health Canada, and was not detected in a study of 12 tattoo inks by the Swedish Chemicals Agency (Health Canada 2011; KEMI 2010, 2014). It is unclear if selenium was present as an impurity or as part of cadmium sulphoselenide pigments in the tattoo ink.

Selenium has been measured in many products available to consumers. In studies carried out by the Danish Environmental Protection Agency, selenium was detected in Slimy Sludge toys (Svendsen et al. 2005), school bags, toy bags, pencil cases and erasers (Svendsen et al. 2007), toys for animals (Neilsen et al. 2005), toothbrushes (Svendsen et al. 2004), leather products (Borling et al. 2002), wooden toys (Hansen and Pedersen 2005), and kohl and henna cosmetics (Bernth et al. 2005). The presence of selenium in the surface coatings of a wide variety of toy specimens with different colours of paint has been examined as part of compliance testing conducted over several years by Health Canada. In 182 toys tested, there were only 3 detections of leachable selenium, all of which fell below the surface coating limits as specified in the

Toys Regulations under the Canada Consumer Product Safety Act (Health Canada 2009a, 2009b; Health Canada 2012; Canada 2010). In a study conducted by the École Polytechnique de Montréal, selenium was measured at very low concentrations (less than 0.005%) in 3 of 24 metallic toys and children's jewellery tested, and in 1 of 18 plastic toys tested. Selenium was not detected in toys with a paint or coating or in brittle or pliable toys (Guney et al. 2013). Selenium, as 5% selenious acid (CAS RN 7783-00-8), is present in gun bluing (metal polishing) products used to polish and tint guns (Birchwood Casey LLC 2012).

7.2.4 Intake estimates and exposure summary

Selenium, an essential nutrient for human health, is present in all Canadians. Total selenium measured in whole blood provides a measure of integrated exposure from all routes (oral, dermal and inhalation) and sources, including environmental media, diet, and products to which people are exposed. Median and 95th percentile selenium whole blood concentrations in the general Canadian population aged 6–79 are 190 and 250 µg/L, respectively (Health Canada 2013a). Selenium whole blood concentrations are higher in Inuit living in northern Canada: median concentrations of 177–297 µg/L and 95th percentile concentrations of 325–1101 µg/L were measured in individuals participating in various studies (data modified from Laird et al. 2013; Chan et al. 2013; Chan 2014; Ayotte 2014). Up to 7% of Inuit had blood concentrations greater than 1000 µg/L (Laird et al. 2013; Chan 2014; Ayotte 2014).

Although the whole blood biomonitoring data provide a measure of integrated exposure from all routes and sources for the general population to selenium, this does not mean that all products available to Canadians or all potential exposure sources are captured in these studies. In addition, the biomonitoring data do not provide information on source attribution. Accordingly, average intake estimates were derived for the general Canadian population in order to identify the main sources of intake. These estimates were derived based on concentrations of selenium measured in food, drinking water, air, soil and dust, and are presented in Appendix B, Table B-1. Daily intake of selenium for the general public ranges from 2.08–5.49 µg/kg bw/d (16–137 µg/d). Food is the primary source of total daily intake for the general public, accounting for >99% of intake. Breads, baked goods, cereal grains, and flours are the key sources of dietary and total intake. Drinking water accounts for less than 1% of daily intake for all age groups, and air, soil and dust are negligible sources of selenium. Intake estimates, when normalized by body weight, are highest in children despite lower whole blood concentrations. Dietary intake is also the primary source of exposure for intake among Inuit in northern Canada, predominantly from the consumption of traditional foods such as Ringed Seal liver, Beluga Whale mattaaq, Narwhal muktuk, caribou and Arctic Char (Chan et al. 2012b, Lemire et al. 2015b). Subsistence fishers (including First Nations), and to a lesser extent recreational fishers, who consume fish with high concentrations of selenium (e.g., near mining operations) could have elevated dietary intake as well, although there is little data on this sub-population in Canada. Targeted studies can provide information on these sub-populations; there are no known datasets that capture

subsistence fishers living near point sources of selenium such as coal and metal mining operations.

Multi-vitamin/mineral supplements may account for a significant proportion of daily discretionary intake among individuals ingesting these products: a typical daily dose for adults would account for 29% of daily intake (based on a 55-µg dose), the amount present in the top-five-selling multi-vitamin/mineral supplement brands. Daily intake estimates for adults consuming multi-vitamin/mineral supplements with typical selenium levels range from 156 to 192 µg/d (see Appendix B, Table B-2). For adults consuming multi-vitamin/mineral supplements providing the maximum permissible level of 400 µg/d[10], the supplement would be an even greater source of daily intake and result in an exceedance of the UL with daily intakes ranging from 501 – 537 µg/d (see Appendix B, Table B-2). The extent to which multi-vitamin/mineral supplements containing higher levels of selenium are captured in the CHMS dataset remains unknown. However, it is unlikely as these are not common products relative to the overall number of approved products and based on the top 5 selling brands. Targeted studies can provide information on these sub-populations; there are no known biomonitoring datasets available which capture intake of multi-vitamin/mineral supplements containing 400 µg of selenium.

Products available to consumers, cosmetics and natural health products other than multi-vitamin/mineral supplements (e.g. anti-dandruff shampoos) are not considered to contribute significantly to total selenium intake. The dermal route is the most common route of exposure for most of these products, and because most selenium substances have low dermal absorption (ATSDR 2003), uptake via the dermal route, regardless of source, is expected to be minimal relative to oral intake. There may be potential for limited dermal exposure to selenium in products if they are used on abraded skin (Ransome et al. 1961).

7.3 Health effects assessment

The following human health effects section describes the toxicokinetics of selenium and the critical health effects related to excess exposure to selenium. However, the current human health effects assessment does not discuss the beneficial health effects of selenium or the adverse health effects associated with selenium deficiency. A summary of health effects of excess selenium exposure in humans and experimental animals is contained in Appendix B, Tables B-4 and B-5.

7.3.1 Toxicokinetics

[10] A maximum dose of 200 µg/day for selenium is under consultation by Health Canada (Health Canada 2016b).

While the majority of ingested selenium substances are absorbed from the small intestine, the rate of absorption is determined by several factors: the form of selenium; the concentration; the presence of certain amino acids; ingestion of vitamin C; the presence of sulphur compounds; and the presence of heavy metals such as mercury ((Davis and Hall 2011; Thiry et al. 2012, Whanger et al. 1976; Wolffram et al. 1985). Although selenite is absorbed via passive diffusion, organic selenium such as selenocysteine and selenomethionine are absorbed through active transport mechanisms and are considered to be more bioavailable than inorganic selenium compounds (Burk et al. 2006; Davis and Hall 2011; Combs and Combs 1986; Fairweather-Tait et al. 2011). Studies with common selenium supplements (L-selenomethionine, sodium selenate, sodium selenite, and high selenium yeast) indicated that the selenium from these sources is readily absorbed, often to greater than 80% of an ingested dose (ATSDR 2003; Combs and Combs 1986; DiSilvestro 2005).

Occupational studies indicate that selenium can be absorbed via inhalation exposure; however, estimates of uptake following inhalation exposure in humans have not been quantified (ATSDR 2003). Studies in rats (Medinsky et al. 1981) and dogs (Weissman et al. 1983) provided evidence for selenium absorption following inhalation of selenious acid aerosol and elemental selenium aerosol.

Absorption of selenium through intact skin depends on the chemical form, although most selenium substances have low dermal absorption (ATSDR 2003). Dermal absorption of selenium was not detected when L-selenomethionine was applied to human skin as a lotion (Burke et al. 1992). However, a recent study indicated that L-selenomethionine was readily absorbed by the skin under both in vitro and in vivo experimental conditions (Lin et al. 2011). In contrast, selenium sulfide did not show any dermal absorption through healthy intact skin when volunteers were repeatedly treated with a selenium sulfide–containing shampoo (Noisel et al. 2010). Similarly, Lin et al. (2011) studied the dermal absorption of selenium sulfide using in vitro experiments with porcine skin, and concluded that dermal absorption of selenium sulfide was negligible. Previous investigators found evidence of dermal absorption in some cases following application of lotions and shampoos containing selenium sulfide, although these studies were less reliable due to experimental limitations and poor statistical analysis (Ransome et al. 1961; Farley et al. 1986). Dermal absorption was also reported for sodium selenite and seleninyl chloride. Dermal penetration of seleninyl chloride could be associated with its corrosive nature, because seleninyl chloride readily destroys skin on contact (Mackison et al. 1981; O'Neil 2001).

Similar to absorption, the distribution of selenium after ingestion depends on its chemical form, the amount ingested, nutritional status, and other components of food such as presence of heavy metals and vitamins (Reilly 2006). Selenium absorbed from selenate, selenite, selenomethionine and selenocysteine is transported to organs with a high rate of selenoprotein synthesis: liver, kidney, spleen, skeletal muscle, heart, lung, brain; testis and erythrocytes (Deagen et al. 1987; Willhite et al. 1992; Schrauzer 2000; Thiry et al. 2012). Usually, more than half of the selenium contained in blood plasma is in the form of selenoprotein P, which is mainly synthesized in the liver and plays an

important role in the transport of selenium (Ducros et al. 2000; Hill et al. 2012; Suzuki et al. 2013). Selenium compounds are transported in the blood to various organs by albumin and other proteins containing sulphydryl groups, such as low-density lipoproteins, selenoprotein P and glutathione peroxidase (IARC 1975; Schrauzer 2000; Thiry et al. 2012). In general, for humans with adequate selenium nutrition, about 30% of tissue selenium is contained in the liver, 15% is in the kidneys, 30% is in muscles, and 10% is in plasma (mostly as selenoprotein P) (WHO/FAO 2002). Figure 7-1 below shows the proposed metabolic pathways for various forms of selenium. Hydrogen selenide (H_2Se) plays a central role in selenium metabolism.

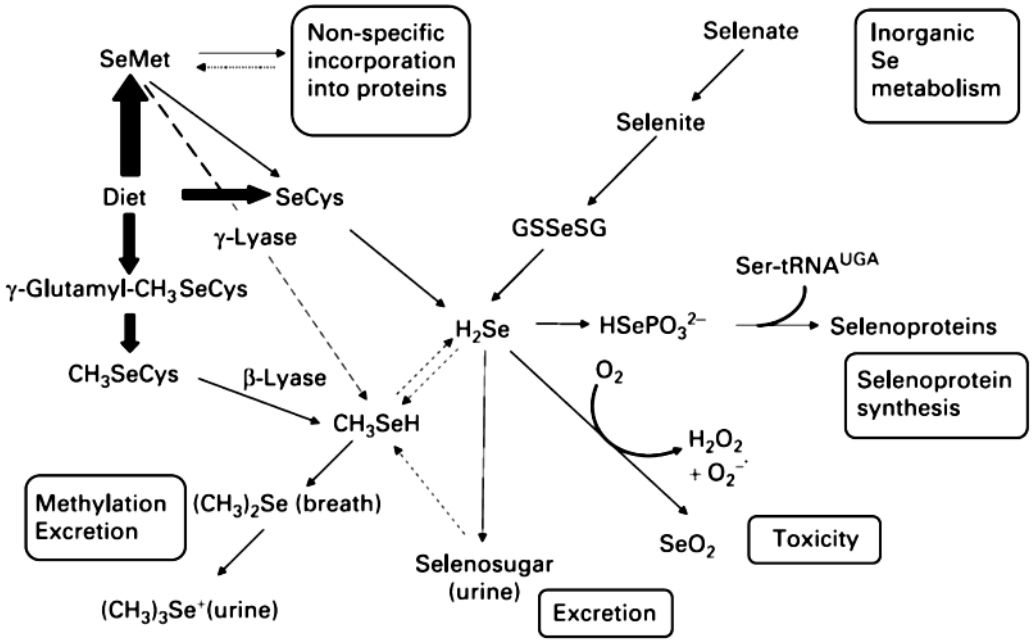

Figure 7-1: Metabolic pathway of dietary selenium in humans.
Se, selenium; SeMet, selenomethionine; SeCys, selenocysteine; GSSeSG, selenodiglutathione; c-glutamyl-CH_3SeCys, c-glutamyl-Se-methylselenocysteine; H_2Se, hydrogen selenide; $HSePO_3$ 2-, selenophosphate; CH_3SeCys, Se-methylselenocysteine; CH_3SeH, methylselenol; (CH_3)2Se, dimethyl selenide; SeO_2, selenium dioxide; (CH_3)3Se+, trimethyl selenonium ion. (Reproduced with permission from Rayman et al. 2008, Rayman 2004, Combs et al. 2001, Suzuki et al. 2006a, b).

Organic (e.g. selenomethionine, selenocysteine) and inorganic (e.g. selenite, selenate) dietary selenium are incorporated into selenide pool and from there selenium is used either to synthesis selenoproteins or excreted through urine as selenosugar (Fairweather-Tait et al. 2010, 2011). Selenocysteine can come from two sources; one is directly from diet and the other one is selenomethionine catabolised from proteins which can be trans-selenated to selenocysteine. The selenocysteine from either of these

sources can be converted to selenide and thereby undergo selenoprotein synthesis process as explained in Figure 7-1. Selenomethionine can also be directly incorporated non-specifically into methionine-containing proteins through the replacement of methionine (Fairweather-Tait et al. 2011). Since selenomethionine is non-specifically incorporated into protein, it could engage in many cycles of protein synthesis as a methionine equivalent before it is eventually degraded. Due to its non-specific incorporation into proteins, selenomethionine effectively serves as a reservoir for selenium with a longer biological half-life (Davis and Hall 2011). Glutathione peroxidase present in liver acts as another reservoir of selenium (IOM 2000). In contrast to selenomethionine and other amino acids, selenocysteine is not recycled for reincorporation into new protein; instead, it is degraded to release inorganic selenium (Ralston and Raymond 2010). Excess selenium that does not undergo selenoprotein synthesis is transformed to methylated metabolites and is excreted through urine or breath. During excretion, selenides methylate to selenosugar (1b-methylseleno-Nacetyl-D-galactosamine) and are excreted in urine. Selenosugar is the most significant urinary metabolite in most people for commonly found organic and inorganic selenium. At excess selenium exposure, selenide can also methylate to dimethyl selenide ($(CH_3)_2Se$) and be exhaled in breath, and trimethyl selenonium ion ($(CH_3)_3Se^+$) which is excreted in urine (Fairweather-Tait et al. 2010, 2011, Ralston and Raymond 2010, Rayman et al. 2008). Dimethyl selenium gives the breath an unpleasant garlic odour, which is a sign of selenium toxicity.

While the above described metabolic pathway is the widely accepted metabolic pathway for commonly found dietary selenium forms, a different pathway is followed by the organic compound γ-glutamyl methylselenocysteine, found in brassica (cruciferous) and allium (e.g. onion and garlic) vegetables. γ-glutamyl methylselenocysteine is first converted to Se-methylselenocysteine and then transformed by beta-lyase into methylselenol, which is primarily excreted in breath and urine but may also enter the selenide pool (Fairweather-Tait et al. 2010).

Currently, there is a limited knowledge regarding the metabolic pathway of selenoneine, the predominant form of selenium found in some marine fish and marine mammals as well as in red blood cells in Inuit in Nunavik (Ayotte et al. 2014, Lemire et al. 2015a, Ayotte et al. 2015).

In humans and experimental animals, selenium is predominantly excreted in urine irrespective of route of exposure (Yang et al. 1989a; Thomson and Robinson 1986). In rats, about 10% of absorbed selenium was excreted in feces, and less than 10 % was excreted in the breath, except at the highest dose, for which respiratory losses during the first day were 35% of the dose administered (Burk et al. 1972). The urinary excretion ranged from 6% in the group fed basal diet and 67% in the highest dose group (Burk et al. 1972). The proportion excreted through each route depends on several factors, including intake level, the time since exposure, the physiological state of the body (e.g. pregnancy and lactation) and the level of exercise. Lactating women and individuals with deficient levels of selenium show decreased levels of selenium excretion in urine and feces (Martin et al. 1989a, 1989b). The importance of selenium excretion via breath increases with exposure levels (Burk et al. 1972). Selenium from

selenite has a shorter half-life in the body compared to selenomethionine (Patterson and Levander 1997), because selenomethionine is an amino acid, which is recycled by the body (Swanson et al. 1991; Wastney et al. 2011). The half-life in the body is 252 days for selenium from selenomethionine and 102 days for selenium from selenite (Schrauzer 2000).

7.3.2 Acute and short-term health effects

Acute toxicity of selenium substances is dependent on the animal species and age, and the form and dose of selenium (Davis and Hall 2011). The oral lethal doses (LD_{50}) reported for selenium substances range from approximately 1 mg of selenium per kilogram of body weight (Se/kg-bw) (for sodium selenite in rabbits) to 6700 mg Se/kg-bw (elemental selenium in rats) (Pletnikova 1970; Cummins and Kimura 1971).

A human case study has reported lethality from ingestion of 90 mg selenious acid/kg-bw from a gun bluing agent, which contains a selenious acid concentration of approximately 4% (Matoba et al. 1986). Post-mortem examination of the patient revealed pulmonary edema with pleural effusion and congestion of the kidneys, and necrosis of proximal tubules in the kidneys.

The symptoms of short-term high selenium intake from supplements or selenium-rich foods are similar to those of long-term exposure to selenium, e.g., nausea, nail changes, alopecia, vomiting, diarrhea, fatigue, peripheral paresthesias, weakness and decreased cognitive function (Nuttal 2006; Senthilkumaran et al. 2012; Kerdel-Vegas 1966). MacFarequhar et al. (2010) reported 201 cases of selenosis (selenium poisoning) due to improperly formulated dietary supplements at a daily intake of 20–30 mg of selenium per day (320–460 µg Se/kg-bw/d) for a median period of 29 days (range 1–109 days). The symptoms include diarrhea, fatigue, hair loss, joint pain, nail discoloration or brittleness, nausea, headache, tingling sensations, foul breath, vomiting, and cutaneous eruptions. Persistent symptoms present 90 days or more after patients stopped taking the supplement included memory loss in 22% of the cases. The whole blood selenium concentration ranged from 150–732 µg/L, after an average of 27 days of cessation of supplement intake (Aldosary et al. 2012). A follow-up at 2.5 years post-exposure confirmed the persistence of adverse effects, including muscle and joint pain (75% of subjects), fatigue (71% of subjects), and neurological symptoms (50% of subjects) (Morris and Crane 2013).

7.3.3 Chronic health effects

7.3.3.1 Chronic selenosis

Long-term exposure to elevated levels of selenium can cause selenosis, characterized by symptoms similar to those that follow short-term exposure to high doses, e.g., gastrointestinal upset, hair loss, nail loss, changes in nail morphology, excessive decay and discolouration of teeth, garlic odour in breath, nervous system abnormalities, and fatigue (Hadjimarkos 1973; Smith et al. 1936, 1937; Yang et al. 1983; IOM 2000). Some

epidemiology studies indicated that the hair loss may occur more frequently and at lower dose levels than the nail effects (CDC 1984; Lippman et al. 2009; MacFarequhar et al. 2010; Yang and Zhou 1994).

Yang et al. (1989a, 1989b) studied the relationship between selenium in the diet (mostly selenium rich vegetables and maize) or whole blood and symptoms of selenosis in people living in a seleniferous region in China. Selenosis was diagnosed mainly on the basis of fingernail morphology, because hair loss was too difficult to judge by clinical examination. Symptoms of selenosis were found at or above a whole blood selenium concentration of 1050 µg/L, which corresponded to an intake of about 910 µg Se/d (16.5 µg Se/kg-bw/d, assuming an average body weight of 55 kg). On the basis of the results, the authors concluded that a marginal level of safe selenium intake may be 750–850 µg Se/d (13.6–15.4 µg Se/kg-bw/d). While the study was mainly on adults and only few children participated, the authors noted that over 90% of study participants with selenosis symptoms were older than 18 years. The symptoms of selenosis were not observed in children below 12 years of age (Yang et al 1989b; Yang and Zhou 1994). The sample size in children in the Yang et al. studies may not be sufficient to rule out the possibility of selenosis in children. In addition, several factors may have contributed to the increased susceptibility to selenium toxicity in adults including, the longer-term exposure to excess selenium and the stress associated with physical work affecting finger nail morphology. However, severe signs of selenosis have been reported in people of all age groups living in seleniferous regions of Punjab state of India (Dhillon and Dhillon 1997) as well as signs of selenosis were also noted in school children in seleniferous areas of Venezuela (Jaffe et al. 1972).

Yang and colleagues (1989a) have derived the correlation between selenium whole blood concentrations and dietary intake levels as follows:

$\log B_{Se} = 0.767 \times \log DD_{Se} - 2.248$ ($r = 0.962$)

where B_{Se} is total selenium in whole blood in mg/L and DD_{Se} is daily intake of selenium in µg/d.

In a follow-up study, Yang and Zhou (1994) monitored the recovery from clinical signs of selenosis in five individuals from the seleniferous region in China. On the basis of the decline in selenium levels in blood and the disappearance of symptoms, the authors concluded that “the safe intake per day” was approximately 800 µg Se/d (15 µg Se/kg-bw/d), which is proposed as the mean NOAEL by the authors. The authors also proposed that 400 µg as “the maximum safe daily dietary selenium intake” to ensure safety. Similarly, an absence of toxicity was reported in other studies in China and the United States at exposure levels of 724–750 µg Se/d (Yang 1987; Yang et al. 1983; Longnecker et al. 1991). The IOM used a NOAEL of 800 µg Se/day, based on the NOAEL in Yang and Zhou (1994) and the evidence from Longnecker et al. (1991), to derive the Tolerable Upper Intake Level of 400 µg Se/d for U.S. and Canadian adolescents and adults (age ≥14 years) (IOM 2000). The resulting whole blood equivalent for the UL is 480 µg/L (Hays et al. 2014), described in Appendix B, Table B-

3. The ATSDR (2003) also used the NOAEL from Yang and Zhou (1994) to derive the minimal risk level of 5 µg Se/kg bw/d.

The UL of 400 µg Se/d for adults and adolescents (age ≥ 14) derived by IOM (2000) based on the NOAEL for selenosis was identified as the suitable reference value for risk characterization of selenium. However, recent epidemiological studies indicated that chronic selenium exposure through diet, supplements and drinking water could be associated with adverse health effects (such as neurotoxicity, selenosis, type -2 diabetes) at much lower concentrations (as low as 290 µg Se/d) than previously believed (Vinceti et al. 2013b; Lippman et al. 2009; Stranges et al. 2007). Similarly, clinical investigations into the manifestations of selenosis were not comprehensive. In these cohorts where selenosis has been reported, other potential health impacts, such as neurotoxicity, have not been fully investigated. Both acute and short-term overdose studies have reported neurological impacts, such as muscle and joint pain, motor weakness, memory loss and paresthesia (Matoba et al. 1986; MacFarequhar et al. 2010; Morris and Crane 2013). In addition, other epidemiological studies have reported that higher levels of selenium exposure were associated with an excess risk of amyotrophic lateral sclerosis (ALS), a motor neuron disease occurring primarily in adult males (Vinceti et al. 2000, 2013a, 2013b). It is noteworthy that selenium is the only chemical known to be selectively toxic to motor neurons, indicating biological plausibility for its potential role in ALS (Yang et al. 2013; Vinceti et al. 2013b). Similarly, in a developmental neurotoxicity study, Saint-Amour et al. (2006) examined the effects of traditional diet containing fish and sea mammals on visual brain processing in Inuit children from Nunavik. This study reported that the averaged blood selenium concentration of 4 to 8 years old children was on average twice the blood equivalent of UL (i.e. 2.76 µmol/L) recommended by the IOM. Approximately to 20% of the children had blood selenium concentrations exceed the maximum safe levels recommended for adults, which was in the range of 8 to 10 µmol/L. In children with very high selenium concentrations, the authors observed a tendency for longer latency for visual evoked potentials (VEPs) under some conditions. The authors also examined the association between visual impact and exposure to methyl mercury and polychlorinated biphenyls (PCBs) through traditional diet. Results indicated that both of these pollutants were associated with alterations of VEP response; however, VEP components for these pollutants were different from selenium (Saint-Amour et al. 2006). On the basis of the results, the authors commented that “the associations observed between selenium and VEP latencies suggest that high intake of selenium during childhood could have a negative impact on the visual system instead of being beneficial or protective against mercury neurotoxicity.”

In another study, Yang et al. (2013) reported a negative association between cord-blood selenium levels and behavioural assessment scores of 3-day-old Chinese neonates. Their study indicated that there is an inverted U-shape relationship between cord serum selenium and neonatal neurobehavioral score suggesting higher susceptibility to selenium neurotoxicity in the early developmental stage (Yang et al. 2013). The authors suggested that a cord blood concentration greater than 100 µg Se/L was associated with decreased neurobehavioural test scores. However, since this is the only study

identified in the current literature which evaluated these endpoints, there is insufficient information to establish a relationship between high selenium status and neonatal neurotoxicity. On the basis of the overall evidence, the selenosis reported in Chinese populations is considered an appropriate point of departure for the risk characterization, although some uncertainty remains regarding the full pathological impact of long-term high selenium exposure.

Symptoms of selenosis have also been reported in seleniferous regions in the Punjab state of India (Dillon and Dhillon 1997, Hira et al. 2003, Chawla et al. 2015). Chawla et al. (2015) studied the selenium toxicity in 600 individuals from seleniferous regions and 50 individuals from non-seleniferous regions (control group) of Punjabi state. The people are exposed to selenium primarily through locally grown cereals, vegetables and drinking water. Out of total study population, 43% displayed symptoms of selenium toxicity, including dystrophic changes in the finger nails (42.2%), hair loss (40%) and garlic odour in breath (4.22%). In addition to selenosis, the study population also showed impaired organ functions (liver, kidney, pancreatic and thyroid) compared to the control group. The mean selenium concentrations in hair and finger nail samples from the study group were 50.9±58.0 µg/g (range 8.7-583.9 µg/g) and 154.0±91.5 µg/g (range, 21.5-819.6 µg/g), respectively. The control group showed a significantly lower ($P<0.01$) hair and finger nail selenium concentrations, which were 22.5±10.7 µg/g (range, 8.4-58.5 µg/g) and 117.4±49.8 µg/g (range, 51.8-267.5 µg/g), respectively. According to Yang et al. (1989b), the hair and nail selenium concentrations associated with “the maximum safe daily dietary intake of selenium” (i.e., 400µg/d) in Chinese cohorts were 3.60 and 4.25 µg/g, respectively. Hence, results of the current study suggest that the selenium concentrations in the people living in the seleniferous regions in Punjab state of India are much higher than that of “the maximum safe daily dietary intake of selenium” levels reported by Chinese study.

In a recent study (Selenium and Vitamin E Cancer Prevention Trial [SELECT]), 8752 men 50 years of age or older, living in the United States, Canada or Puerto Rico, were supplemented with 200 µg Se/d as L-selenomethionine for an average of 5.5 years (range 4.17–7.33 years). The study authors reported a statistically significant increase in alopecia (2.4–3%) and mild-to-moderate dermatitis (6–7%) in these individuals (Lippman et al. 2009). The dietary selenium intake of SELECT subjects was not measured.

Available epidemiology studies of Brazilian Amazon, Greenland Inuit and Canadian Inuit populations indicate that the blood selenium concentrations in a small proportion of these individuals could exceed the levels where selenosis would be anticipated (Hansen 2000; Hansen et al. 2004; Hansen and Pedersen 1986; Lemire et al. 2009, 2012; Valera et al. 2009). In six communities in the Brazilian Amazon, whole blood selenium concentrations of 142–2247 µg/L were measured in 137 subjects who were 15 years of age or older (Lemire et al. 2009). A later study of 448 volunteers in the Brazilian Amazon reported the whole blood selenium concentrations ranging up to 1500 µg Se/L due to a selenium-rich diet that includes Brazil nuts and fish. Although the blood selenium concentrations exceeded levels where selenosis would be expected, the

frequency of signs and symptoms of selenosis in these individuals was not significantly different from individuals with lower whole blood selenium levels (≤ 560 µg Se/L), and the authors concluded that there was no evidence of selenosis in this population (Lemire et al. 2012). Blood selenium levels in the range of 80–1890 µg Se/L were reported in Greenland Inuit who consume a traditional diet (Hansen et al. 2004), while levels in Canadian Inuit were reported in the range of 210-945 µg/L (Chan et al. 2013, 2014). Other authors have reported an even higher range of blood selenium concentrations in Inuit, e.g., Valera et al. (2009) reported whole- blood selenium concentrations in Inuit adults from Nunavik in the range of 118–3533 µg/L (mean 291 µg/L), while the plasma concentrations in Inuit adults from Salluit ranged from 227–2069 µg/L (mean = 674 µg/L) (Ravoori et al. 2010). However, selenosis was not specifically monitored in Canadian and Greenland Inuit populations (Laird et al. 2013; Hansen et al. 2004). In a short report, published by the Selenium-Tellerium Development Association, Hansen (2000) noted that the overt signs of clinical selenosis have not been recorded in Inuit from North Greenland where blood selenium levels were in the range of 330-4400 µg/L. Based on lack of clinical signs of selenosis, the author indicated that selenium exposure through marine diet may be tolerated at levels higher than the generally accepted levels. However, the author provided no information to support this hypothesis and the author did not describe how indications of selenosis were investigated. In this report, the author also noted that subtle signs of selenosis were observed in the finger nails of well-preserved mummies from the region, which could be an indication of selenium toxicity at high exposure; however, selenium levels in the mummies were not reported.

7.3.3.2 Selenium and heavy metals Interaction

Inuit populations in northern Canada and Greenland are co-exposed to high levels of selenium and other toxic compounds (such as mercury [Hg], arsenic [As], cadmium [Cd] and persistent organic pollutants [POPs]) through their traditional diet, which includes marine mammals and fish. The form of selenium present in these marine organisms has been determined to be mainly selenoneine (Yamashita and Yamashita 2010), which is likely to be different from the selenium forms found in plants and other meats.

Traditional diets rich in selenium in Northern communities may play a role in mitigating some deleterious effects of methyl mercury exposure in humans, including negative impacts on motor and visual functions, the appearance of age-related cataracts of the eyes, and the observation of cardiometabolic risk factors such as increased blood pressure, inhibition of paraoxonase 1 (PON1) activity, and an increase in oxidative stress biomarkers (Alkazemi et al. 2013, Valera et al. 2009, Lemire et al. 2010, 2011, Ayotte et al. 2011, Ravoori et al. 2010, Valera et al. 2013a). Inorganic mercury and methyl mercury directly bind to selenium following in situ demethylation, and as a result reduce its bioavailability for target proteins and organs (Khan and Wang, 2009, Ralston and Raymond 2010). Hence, selenium and mercury co-exposure in Inuit populations may moderate the toxicity of both metals (Alkazemi et al. 2013; Ayotte et al. 2011; Hansen et al. 2004; Lemire et al. 2010; Khan and Wang 2009; Ravoori et al. 2010; Valera et al. 2009; Valera et al. 2013a). However, to date there has been inadequate

investigation into possible selenosis in northern Canadian Inuit. Similarly, more studies are needed in order to better understand whether high selenium intake from a marine diet is beneficial in mitigating the adverse effects of methylmercury exposure at different life stages in northern communities.

Recent studies have shown that selenium rich lentils grown in Canadian prairies, where soils are rich in selenium, were capable of reducing arsenic toxicity in experimental mammals (Sah et al. 2013, Krohn et al. 2015). The form of selenium found in the selenium rich lentils was Se-methylselenocysteine (selenomethionine) (Sah et al. 2013, Thavarajah et al. 2007).

7.3.3.3 Carcinogenicity and genotoxicity

The International Agency for Research on Cancer (IARC) has classified selenium as Group 3: not classifiable as to its carcinogenicity to humans (IARC 1987). The U.S. National Toxicology Program (NTP) has identified selenium sulfide as “reasonably anticipated to be a human carcinogen” based on sufficient evidence of carcinogenicity in experimental animals (NTP 2011).

In the United States, the National Cancer Institute (NCI) and NTP evaluated the effects of selenium sulfide using rats and mice. When male and female rats and mice were administered selenium sulfide through oral gavage for 103 weeks, a significant increase in hepatocellular carcinoma was reported in male and female rats and female mice at the highest dose tested (15 and 100 mg SeS/kg/d, respectively). Selenium sulfide was not carcinogenic to male mice at the dose levels tested (NCI and NTP 1980b). Dermal application of selenium sulfide at 0.5 or 0.1 mg/d or anti-dandruff shampoo (Selsun) with 2.5% selenium sulfide to ICR Swiss mice did not cause a carcinogenic effect in mice. According to the study authors’ conclusion, “the study was limitedby the relatively short lifespan of this mouse strain” (NCI and NTP 1980a, 1980c). Also, the application sites were not covered, so some of the material may have been ingested (ATSDR 2003).

Some authors suggest that selenium may play an important anti-carcinogenic role (Rayman 2012; Hurst et al. 2012). For some selenium compounds, prospective cohort studies have provided some evidence for beneficial effects on the risk of lung, bladder, colorectal, liver, oesophageal, gastric, thyroid and prostate cancers (Rayman 2012). Most of the evidence for the protective effects of selenium was reported for breast and prostate cancers (Navarro-Alarcon and Cabrera-Vique 2008). However, other well-conducted prospective cohort studies did not show beneficial effects of selenium on cancer. In the Nutritional Prevention of Cancer trial (NPC), volunteers with a history of non-melanoma skin cancer were supplemented with 200 µg Se/d as high selenium yeast for an average of 4.5 years. The study concluded that selenium supplementation at 200 µg Se/d apparently did not reduce the risk of cancer for people with baseline plasma selenium levels above approximately 122–123 µg Se/L, and may have increased their risk (Clark et al. 1996). The SELECT trial similarly demonstrated that daily supplements of 200 µg Se/d as selenomethionine did not reduce the risk of prostate cancer, cancer mortality or all-cause mortality during the median follow-up

period of 5.5 years. The baseline plasma selenium levels of these individuals were approximately 136 µg Se/L (Lippman et al. 2009).

Tests of genotoxicity of the forms of selenium relevant to dietary and supplement intakes have yielded mixed results (Ferguson et al. 2012; ATSDR 2003; Letavayova et al. 2006). In vitro testing has provided evidence that selenate, selenite, selenomethionine and selenide are genotoxic (Whiting et al. 1980; Khalil 1989; Biswas et al. 2000). However, available information indicates that selenium compounds (other than selenium sulfide) are not human carcinogens or direct genotoxic agents.

There is also evidence suggesting that selenium compounds can protect DNA from damage (Davis et al. 1999, 2000; Letavayova et al. 2006; Zeng et al. 2011). Selenium has been shown to reduce toxic effects of some substances that are carcinogens, such as arsenic cadmium and PCBs (Davis et al. 1999; Sun et al. 2014; Zhou et al. 2009; Zwolak and Zaporowska 2012, Ravoori et al. 2010).

7.3.3.4 Selenium and Type 2 diabetes

The current evidence related to the risk of type 2 diabetes from elevated selenium ingestion is conflicting. Some authors have reported lower toenail and serum selenium concentrations in individuals with type 2 diabetes (Rajpathak et al. 2005; Kornhauser et al. 2008). In a prospective analysis of cohorts from the United States, Park et al. (2012) found a linear inverse relationship between toenail selenium concentrations and type 2 diabetes, and concluded that men and women with higher toenail selenium concentrations are at a lower risk of developing type 2 diabetes. In France, a prospective study with a nine-year follow-up period found a decrease in the risk of type 2 diabetes or impaired fasting glucose in men in the highest tertile for plasma selenium relative to the lowest tertile. For women, no such significant relationship was found (Akbaraly et al. 2010).

Several epidemiological cross-sectional studies have found a statistically significant association between high selenium concentrations and the prevalence of type 2 diabetes or fasting plasma glucose (Bleys et al. 2007; Laclaustra et al. 2009; Stranges et al. 2011; Gao et al. 2007; Czernichow et al. 2006; Stranges et al. 2007). However, the causal effects cannot be established in cross-sectional studies due to confounding factors, such as body weight. A secondary analysis of data from the NPC randomized controlled trial also found a statistically significant increase in the incidence of type 2 diabetes among volunteers with a history of non-melanoma skin cancer taking high-selenium yeast supplements at 200 µg Se/d for 4.5 years, and with a mean follow-up period of 7.7 years (Stranges et al. 2007). This was the critical study for revision of the Japanese UL to 260–300 µg Se/d for adolescents and adults 15 years of age and older, with a proportionally lower UL for children based on weight (Yoshida et al. 2013).

However, in the SELECT trial, the supplementation of Canada, U.S. and Puerto Rico men with 200 µg Se/d as selenomethionine had no effect on the risk of type 2 diabetes after a median follow-up of 5.5 years (Lippman et al. 2009). In an analysis of the

association between blood selenium levels from CHMS data (Health Canada 2013a) and Type 2 diabetes among Canadian adults, Oulhote and Bouchard (2014) concluded that “the higher selenium levels were not associated with the prevalence of Type 2 diabetes among adult Canadians.”

In a review article, Rayman and Stranges (2013) concluded that “the relationship between selenium and Type 2 diabetes is undoubtedly complex. It is possible that the relationship is U-shaped, with possible harm occurring both below and above the physiological range for optimal activity of some or all selenoproteins.” Overall, the available information is insufficient to establish a relationship between high selenium status and diabetes risk.

7.3.3.5 Reproductive and developmental effects

There is limited evidence available in humans for reproductive or developmental toxicity of selenium. On the basis of the data from occupational studies and people living in high-selenium regions in the world, selenium does not show any reproductive or developmental effects in humans (IOM 2000; Vinceti et al. 2000; OEHHA 2010; Yang et al. 1989b). Hawkes et al. (2009) did not report any adverse effects on sperm parameters of 42 healthy U.S. men aged 18–45 who were supplemented with high selenium yeast. The estimated selenium intake level of these men was approximately 437 µg Se/d.

While most of the available developmental toxicity studies on experimental animals did not show any developmental effects, developmental toxicity demonstrated in some studies was determined to be secondary to maternal toxicity (Ferm et al. 1990; Hawkes et al. 1994; Schroeder and Mitchener 1971b; Tarantal et al. 1991). Nobunaga et al. (1979) reported decreased fetal body weight and delayed vertebral ossification at the highest dose when female mice were exposed to either 170 or 340 µg Se/kg-bw/d during 30 days pre-gestation, and gestation days 0–18. Although this was the lowest dose level associated with developmental effects, it was unclear that maternal toxicity was observed in the treated dams. This dose level is more than 22 times higher than the dose levels reported for selenosis in humans. In rats, selenium supplementation (approximately 100–130 µg Se/kg bw/d) was associated with elevated incidence of sperm midpiece abnormalities or reduced sperm counts or motility (Kaur and Parshad 1994; Shalini and Bansal 2008). Altered menstrual and estrous cycles were reported in female monkeys and rats at approximately 80 and 100 µg Se/kg bw/d, respectively (Cukierski et al. 1989; NTP 1994). The lowest dose level reported for reproductive effects in animals is approximately five times higher than the dose level reported for selenosis in humans.

7.4 Characterization of risk to human health

Although selenium is essential for human health (having an EAR of 45 µg/day), the UL is only 400 µg/d. Selenosis is considered to be the critical health effect for excess selenium exposure. A UL of 400 µg/d for adolescents and adults (age ≥ 14) was

established by the IOM based on a NOAEL of 800 µg/d for selenosis observed in a Chinese cohort by Yang and Zhou (1994), adjusted by an uncertainty factor (UF) of 2 (IOM 2000) (the UF of 2 was selected by the IOM to protect sensitive individuals). The toxic effect is not severe, but may not be readily reversible, so a UF of greater than 1 was needed (IOM 2000). Health Canada has used the IOM UL previously for setting maximum permissible levels of selenium in multi-vitamin/mineral supplements, soil quality guidelines for human health, and proposed drinking water guidelines (Health Canada 2016a, 2016b; CCME 2009; Health Canada 2014a). This UF is also considered appropriate for this screening assessment, and the resulting whole blood equivalent for the reference dose is 480 µg/L (Hays et al. 2014). The IOM has established lower ULs for younger age groups, adjusted for body weight: 45 µg/d for 0–6 months, 60 µg/d for 7–12 months, 90 µg/d for 1–3 years, 150 µg/d for 4–8 years, and 280 µg/d for 9–13 years. Intake estimates, when normalized by body weight, are highest in children. However, children also have higher urinary excretion of selenium than adults and significantly lower circulating selenium in whole blood than in adults. For the purposes of this assessment, whole blood is considered to be a better indicator of bioavailable selenium.

Recent studies, including the studies with Canadian Inuit children, have indicated that children may be more susceptible to selenium-induced neurotoxicity during early developmental stages (Saint-Amour et al. 2006; Yang et al. 2013). Researchers are currently re-evaluating data related to Inuit children visual system development and high levels of selenium. However, there is currently inadequate information available to fully characterize the neurotoxic potential of high levels of selenium exposure.

With the availability of selenium biomonitoring data, the risk to human health posed by selenium will be characterized based on a comparison of whole blood concentrations, where available, to the critical health effect. Whole blood is considered to be the best available measure of bioavailable selenium for examining elevated selenium exposure. The populations considered for risk characterization using a biomonitoring approach are the general Canadian population, and Inuit in northern Canada (a sub-population with higher exposures to selenium). Whole-blood concentrations provide a measure of integrated exposure and are representative of long-term steady-state exposure. Subsistence fishers consuming fish with elevated selenium concentrations (e.g. around mining operations) and individuals consuming a subset of multi-vitamin/mineral supplements providing higher levels of selenium are two additional sub-populations in Canada with the potential for elevated selenium intake.

Exposures for the general population, including children, based on the median and 95th percentile total selenium whole blood concentrations of 190 and 250 µg/L from the CHMS, are below the whole blood equivalent of the UL (480 µg/L). However, 2–27.5% of Inuit living in various communities in northern Canada have selenium exposures exceeding the whole blood equivalent of the UL (> 480 µg/L) and up to 7% have total selenium blood concentrations exceeding 1000 µg/L(data modified from Laird et al. 2013; Ayotte 2014), a level where selenosis has been observed in other human populations (Yang et al. 1989b)). As there are no biomonitoring data to characterize

exposure to subsistence fishers living near point sources of selenium (e.g. mining operations) or for individuals using certain multi-vitamin/mineral supplements providing higher levels of selenium, alternative approaches were taken to characterize risk to these sub-populations.

The BC MOE health-based screening value for high fish consumption (BC MOE 2014), which is considered appropriate for subsistence fishing, was used to characterize potential risk for subsistence fishers including First Nation populations. The health-based screening value of 7.3 µg/g dw, which is derived from the IOM UL, was compared to selenium concentrations found in fish near high-emitting sectors. Median selenium fish tissue concentrations exceeded the screening value across multiple sectors, but most notably in the coal mining, metal mining, smelting and refining and electricity generation co-located with coal mining sectors. Further details on risk management tools such as the BC MOE health-based screening value for high fish consumption and fish consumption advisories can be found in the Risk Management Approach document for selenium.

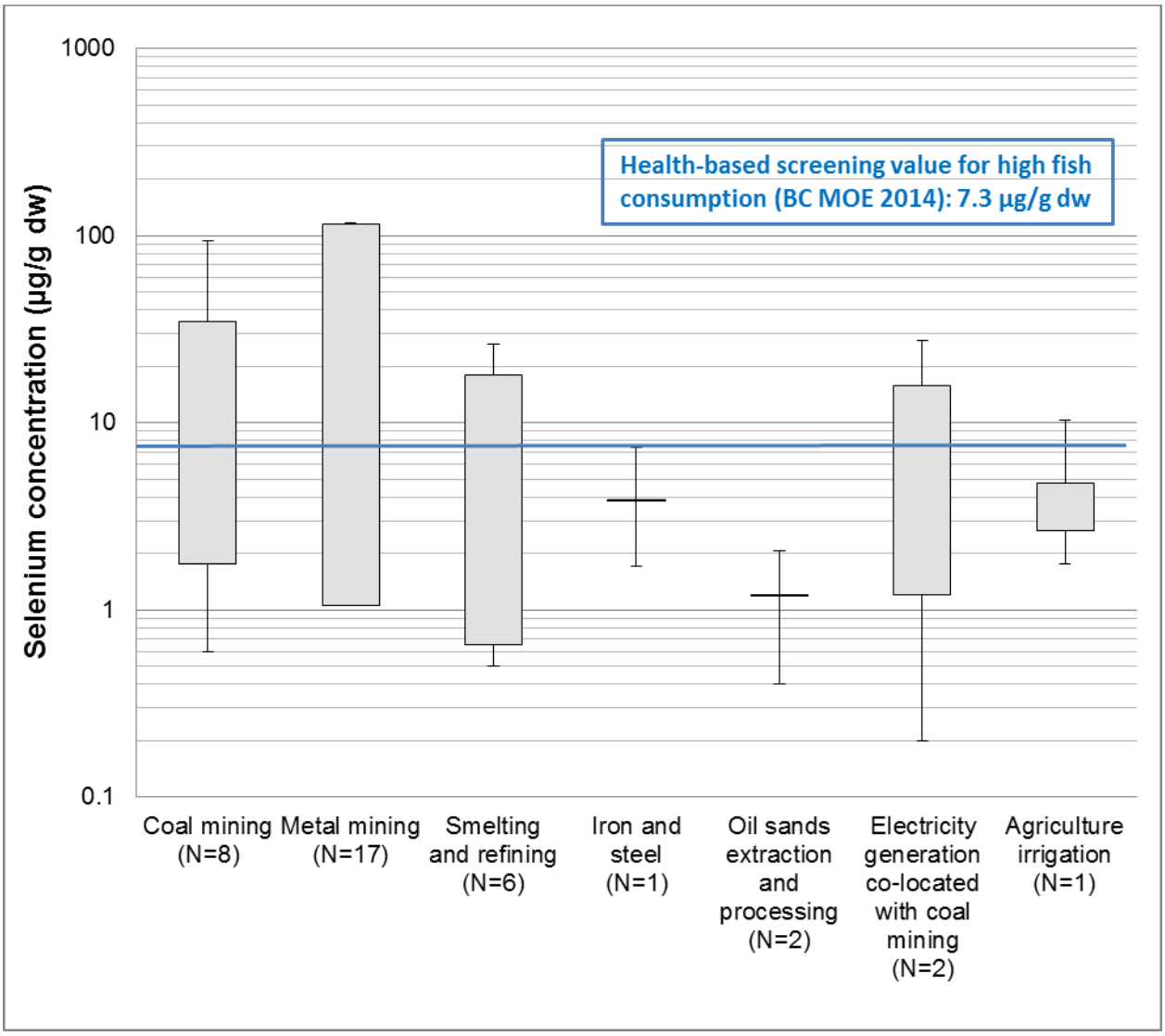

Figure 7-2: Selenium fish tissue concentrations reported by sector against a health-based screening value for high fish consumption. The solid bars represent the range of average or median concentrations reported in the studies, refer to Figure 6.4. The error bars are used to indicate the lowest and highest values reported in all reports at sites downstream of releases from sectors.

Potential risk to individuals consuming multi-vitamin/mineral supplements was characterized by taking into account daily intake of selenium from environmental media, food, drinking water and comparing these intakes to the IOM UL. For multi-vitamin/mineral supplements with typical doses of selenium (55 µg/d), intake estimates of 156 to 192 µg/d were below the IOM UL. For multi-vitamin/mineral supplements with

the maximum permissible daily dose of selenium (i.e., 400 µg/d)[11], intake estimates of 501 to 537 µg/d exceeded the IOM UL of 400 µg/d.

It is determined that there is potential for harm to human health in Canada at current levels of exposure. This determination is based on exposures in Canadians (measured or predicted) which exceed the IOM UL for selenosis. Three groups of Canadians were identified as having elevated exposures which exceed the IOM UL. These include up to 27.5% of Inuit in some communities in northern Canada, subsistence fishers consuming fish caught near point sources of selenium (e.g., coal mines, metal mines, smelting and refining facilities, electricity generation co-located with coal mining sectors) and individuals taking multi-vitamin/mineral supplements providing the maximum permissible levels of selenium.

Selenium sulfide is the only carcinogenic selenium compound identified in the grouping. While it was noted to have carcinogenic potential following oral exposure in laboratory animals, there are no identified oral exposures to this compound by Canadians. There are a limited number of dermal uses, but dermal absorption through intact skin is low.

7.5 Uncertainties in evaluation of risk to human health

Confidence is high that selenosis is an indicator of excess selenium exposure. Epidemiology studies (predominantly in China), human case studies with accidental selenium overdose, and animal studies conducted in multiple species have consistently shown symptoms of selenosis attributed to high selenium exposure. There is less confidence in the other health effects associated with selenium exposure, such as carcinogenicity, type-2 diabetes and neurological effects. There is a large body of data that examines the association between Type 2 diabetes and chronic excess exposure to selenium. However, most indications of selenium toxicity reported from human investigations are limited to clinical observations, and detailed examinations of other indicators of toxicity (e.g. blood chemistry, histopathology, mode of action studies) have not been conducted. Given that the data are inconclusive for carcinogenicity, type-2 diabetes and neurotoxicity, there is uncertainty as to the relevance of these health outcomes to the current assessment. There is also some uncertainty in the findings of the Inuit child development study because the study authors are currently conducting a re-evaluation of the data due to the various discrepancies in the previous analysis.

The IOM UL of 400 µg/d is only valid for adults and adolescents (age ≥14 yrs), and the IOM has established lower ULs for younger age groups, adjusted for body weight: 45 µg/d for 0–6 months, 60 µg/d for 7–12 months, 90 µg/d for 1–3 years, 150 µg/d for 4–8 years, and 280 µg/d for 9–13 years.These ULs were developed based on the absence

[11] A maximum dose of 200 µg/day for selenium is under consultation by Health Canada (Health Canada 2016b).

of adverse effects in nursing infants and subsequently adjusted for older infants and children on the basis of relative body weight. As such, exceeding these ULs is of uncertain toxicological significance and does not necessarily constitute a health risk. In addition, dietary intake estimates, particularly the high-end (95^{th} percentile) values, likely overestimate exposure to selenium due to limited availability of quantitative information that enables the expression of exposure estimates on a long-term basis.

Some important target populations were not covered in the CHMS and other available biomonitoring studies. In the CHMS, a population-level survey designed by Statistics Canada, population-weighted data are representative of 96.5% of the Canadian population, but the survey excludes people living on reserves or in other Aboriginal communities in the provinces/territories, and people living in certain remote areas or areas with a low population density. Therefore, the CHMS does not cover Inuit living in northern Canada. However, selenium concentrations in Inuit living in northern Canada were available from other studies beyond the CHMS. Due to the sampling locations of the CHMS and the First Nations Biomonitoring Initiative, it is unlikely that these studies cover subsistence fishers consuming fish with elevated tissue selenium concentrations near mining operations or other point sources of selenium. The Northern Saskatchewan Prenatal Biomonitoring Project measured serum selenium concentrations in pregnant women, however, this data is not representative of mining areas; rather it is a reflection of average serum selenium concentrations in northern Saskatchewan. Serum selenium concentrations in this population were similar, or lower, than serum selenium concentrations in pregnant women in the Alberta Biomonitoring Program (Irvine 2015; Alberta Health and Wellness 2008). There are limited data to characterize intake for subsistence fishers consuming fish with elevated selenium, due to proximity to point sources (e.g. mining operations). It remains unknown whether the CHMS is representative and inclusive of individuals using multi-vitamin/mineral supplements providing higher levels of selenium. Further information on the the exposure levels of selenium from other sources in these individuals, and the bioavailability of selenium from the multi-vitamin/mineral supplements would aid in reducing uncertainty associated with exposure characterization for this population.

Confidence is high in the use of total selenium concentrations in whole blood for assessing selenosis for the general population of Canada. There was a strong correlation between total selenium in whole blood and dietary intake in the Chinese cohort studies that formed the basis of the IOM UL for selenosis (Yang et al. 1989a, 1989b; Yang and Zhou 1994), and models relating selenium in whole blood to dietary intakes using a different cohort in the U.S. provided similar results (Longnecker et al. 1996). In the Chinese cohort studies, the U.S. studies (Longnecker et al. 1991), and the general Canadian population, selenomethionine from the diet was the primary form and source of intake. As stated by the authors, there was likely additional minor exposure to inorganic selenium in the Chinese cohort from the use of coal as a fuel source for cooking and heating and from drinking water.

There is lower confidence in the use of total selenium concentrations in whole blood and selenosis as the critical effect level for Inuit in northern Canada. Inuit consuming

traditional foods may be exposed to a different form of dietary selenium, selenoneine and to a lesser extent mercury selenide, in addition to selenomethionine, because their primary dietary source is marine mammals. Total selenium represents all bioavailable forms of selenium but does not differentiate between the different forms. Very recent science conducted under the Northern Contaminants Program has identified selenoneine as a major form of selenium found in beluga mattaaq and in red-blood cells in Inuit. Regardless, there is no data on how selenoneine would behave in the body; there are no ADME studies or toxicity studies on selenoneine. At this time, total selenium is still considered the best indicator of exposure due to the availability of data. Total selenium concentrations in whole blood in some Inuit far exceed the UL, but none of the available studies that monitored blood selenium levels in Inuit populations have investigated the symptoms of selenosis. In addition to selenium, these populations have co-exposure to high levels of Hg from their traditional diet. Some investigators believe that a Se-Hg (or Se-MeHg) complex could reduce the bioavailability of Hg and selenium and thereby protect these populations from toxicity (Alkazemi et al. 2013; Ayotte et al. 2011; Hansen et al. 2004; Lemire et al. 2010; Khan and Wang 2009; Valera et al. 2013b; Nakamura et al. 2014). These theories have not been adequately examined in highly exposed Canadian populations to date.

Therefore, further research to look for evidence of selenosis or neurotoxicity in highly exposed Canadian populations (Inuit and subsistence fishers) would reduce uncertainty in the human health assessment. The forms of selenium present in the selenium-rich traditional diet (e.g. selenoneine) and the associated health effects of those selenium forms are also important areas of ongoing research focus and will be important in the future for assessing potential risk to Inuit with elevated total selenium concentrations in whole blood.

8. Conclusion

Considering all available lines of evidence presented in this screening assessment, there is risk of harm to organisms and biodiversity from selenium and its compounds. It is concluded that selenium 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 concluded that selenium 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.

The selenium concentration in whole blood of Canadians represents total selenium exposure to the selenium moiety from all sources. The whole blood concentrations found in some sub-populations of Canadians exceed internationally accepted regulatory reference values, including the Tolerable Upper Intake Levels established by the IOM for North American populations and blood concentrations at which health effects have been observed in humans. On the basis of the information presented in this screening

assessment, it is concluded that selenium 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.

Therefore, it is concluded that selenium and its compounds meet one or more of the criteria set out in section 64 of CEPA.

The selenium moiety has been determined to meet the persistence and bioaccumulation criteria as set out in the Persistence and Bioaccumulation Regulations of CEPA.

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Appendices

Appendix A: Substances identities

Table A-1: 29 Selenium-containing substances on the Domestic Substances List

CAS RN[12]	Substance name
7446-08-4	Selenium oxide (SeO_2)
7446-34-6	Selenium sulphide
7783-00-8	Selenious acid
7791-23-3	Seleninyl chloride
10102-18-8	Selenious acid, disodium salt
56093-45-9	Selenium sulfide
5819-01-2	Dodecane, 1,1'-selenobis-
7488-56-4	Selenium sulfide (SeS_2)
13410-01-0	Selenic acid, disodium salt
21559-14-8	Selenium, bis(diethylcarbamodithioato-S)bis(diethylcarbamodithioato-S,S')-
12002-86-7	Silver selenide (AgSe)
12069-00-0	Lead selenide (PbSe)
12214-12-9	Cadmium selenide sulfide (Cd_2SeS)
12626-36-7	Cadmium selenide sulfide (Cd(Se,S))
12656-57-4	C.I. Pigment Orange 20
58339-34-7	C.I. Pigment Red 108
67711-98-2	Slags, dore furnace
129618-35-5	Electrolytes, copper-manuf.
152923-45-0	Slimes and sludges, mercury conc. roasting off gas condensate
69029-73-8	Leach residues, tellurium
121053-28-9	Electrolytes, cobalt-manuf.
10214-40-1	Selenious acid, copper(2++) salt (1:1)
12137-76-7	Palladium selenide (PdSe)
20405-64-5	Copper selenide (Cu_2Se)
1306-24-7	Cadmium selenide (CdSe)
3425-46-5	Selenocyanic acid, potassium salt
7782-49-2	Selenium
7783-07-5	Hydrogen selenide (H_2Se)
144507-49-3	Slimes and sludges, sulfuric acid manuf., sulfur dioxide cooling tower, selenium-contg.

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Appendix B: Human intake estimates and health effects data

Table B-1: Average estimates of daily intake (µg/kg-bw/d) of selenium by the general population in Canada via environmental media, food and drinking water

Route of Intake	0–6 months breast fed[a,b]	0-6 months, excluding breast milk[a]	0.5–4 years[c]	5–11 years[d]	12–19 years[e]	20–59 years[f]	60+ years[g]
Air[h]	7.84E-05	7.84E-05	1.68E-04	1.31E-04	7.45E-05	6.40E-05	5.56E-05
Dietary (food and drinking water)	2.08	4.40	5.49	4.07	2.22	1.93	1.40
Soil[i]	NA	NA	1.64E-04	1.23E-04	4.29E-06	4.11E-06	3.79E-06
Household dust[j]	1.01E-03	1.01E-03	5.29E-04	2.00E-04	7.14E-06	7.05E-06	6.94E-06
Total intake from environmental media and diet (µg/kg-bw/d)	2.08	4.40	5.49	4.07	2.22	1.93	1.40
Total intake from environmental media and diet (µg/d)	16	33	85	126	132	137	101

NA: not applicable

[a] Assumed to weigh 7.5 kg, to breathe 2.1 m^3 of air per day (Health Canada 1998) and to ingest 38 mg of household dust per day (Wilson et al. 2013). Breastfed infants are assumed to consume solely breast milk for 6 months. Mean dietary intake estimates (formula only) for 0-5 months, as presented in Table 7-2, were used to represent dietary intakes for this age group. Dietary intakes (excluding breast milk) for 0 to 6 month infants were obtained from the Canadian Total Diet Study results from 2005 to 2010; The exposure estimates generated using the U.S. Department of Agriculture's (USDA) Continuing Survey of Food Intakes by Individuals (CSFII; 1994-96, 98) data..

[b] Assumed to consume 0.742 L of breast milk per day (Health Canada 1998). The average concentration of 21 µg Se/L measured in breast milk from 818 Canadian mothers between 2008 and 2011 from the Material Infant Research on Environmental Chemicals study (Cockell 2014).

[c] Assumed to weigh 15.5 kg, to breathe 9.3 m^3 of air per day (Health Canada 1998) and to ingest 14 mg of soil and 41 mg of household dust per day (Wilson et al. 2013). Median dietary intake estimates (food and drinking water) for 1–3 years, as presented in Table 7-2, were used to represent dietary intake for this age group.

[d] Assumed to weigh 31.0 kg, to breathe 14.5 m^3 of air per day (Health Canada 1998) and to ingest 21 mg of soil and 31 mg of household dust per day (Wilson et al. 2013). Median dietary intake estimates (food and drinking water) for 4–8 years, as presented in Table 7-2, were used to represent dietary intakes for this age group.

[e] Assumed to weigh 59.4 kg, to breathe 15.8 m^3 of air per day (Health Canada 1998) and to ingest 1.4 mg of soil and 2.2 mg of household dust per day (Wilson et al. 2013). Median dietary intake estimates (food and drinking water) for males 14–18 years, as presented in Table 7-2, were used to represent dietary intakes for this age group.

[f] Assumed to weigh 70.9 kg, to breathe 16.2 m^3 of air per day (Health Canada 1998) and to ingest 1.6 mg of soil and 2.5 mg of household dust per day (Wilson et al. 2013). Median dietary intake estimates (food and drinking water) for males 19–30 years, as presented in Table 7-2, were used to represent dietary intakes for this age group.

[g] Assumed to weigh 72.0 kg, to breathe 14.3 m^3 of air per day (Health Canada 1998) and to ingest 1.5 mg of soil and 2.5 mg of household dust per day (Wilson et al. 2013). Median dietary intake estimates (food and drinking water) for males 71+ years, as presented in Table 7-2, were used to represent dietary intakes for this age group.

[h] Intake estimated using median 24-hr personal air sample PM_{10} concentration of 0.280 ng/m^3 (n = 148), measured in Windsor, Ontario (Rasmussen et al. 2013). Personal air data are considered to be most representative of air concentrations in the breathing zone.

[i] Intake based on a typical background concentration of 0.7 ppm of total selenium in Canadian soils (CCME 2009). A bioaccessible factor of 0.26 was incorporated based on selenium soil bioaccessibility data generated in the Sudbury Area Soils Study (SARA 2008).

[j] Intake based on the median national baseline concentration of bioaccessible selenium of 0.20 ppm measured in 1025 homes in the Canadian House Dust Study (Rasmussen et al. 2014).

Table B-2: Average estimates of daily intake (µg/d) of selenium by the general population in Canada via environmental media, diet and multi-vitamin/mineral supplements

Route of Intake	20–59 years	60+ years
Average intake from environmental media and diet[a]	137	101
Average intake from environmental media and diet + typical selenium concentrations in multi-vitamin/mineral supplements (55 µg/d)[b]	192	156
Average intake from environmental media and diet + maximum permissible concentrations in multi-vitamin/mineral supplements (400 µg/d)[c]	**537[d]**	**501[d]**

na = not applicable

[a] See Table B-1

[b] 55 µg/d dose - based on the RDA for Se which is a common daily dose in multi-vitamin/mineral supplements and the amount of selenium in the top five selling brands of multi-vitamin/mineral supplements (2014 email from the Bureau of Nutritional Sciences to the Existing Substances Risk Assessment Bureau, Health Canada, unreferenced).

[c] 400 µg/d dose – based on the maximum permissible daily dose in multi-vitamin/mineral supplements outlines in the NNHPD's Selenium and Multi-Vitamin/Mineral Supplements monograph (Health Canada 2016a). A maximum dose of 200 µg/day for selenium is under consultation by Health Canada (Health Canada 2016b).

[d] Exceed the IOM UL of 400 µg/d

Table B-3: Whole blood equivalent derivation based on the IOM UL for adults and adolescents (≥ 14 years)

NOAEL (µg/d) – adults	800

Whole blood equivalent$_{NOAEL}$ (µg/L)[a]	950
Uncertainty factor	2
Whole blood equivalent (µg/L)	480

[a] Derived using log B_{Se} = 0.767×log DD_{Se} – 2.248 (r = 0.962), where B_{Se} is total selenium in whole blood in mg/L and DD_{Se} is daily intake of selenium in µg/d (Yang et al. 1989a; Hays et al. 2014), multiplied by 1000 to convert from mg/L to µg/L, rounded to 2 significant figures.

Table B-4: Summary of the human health effects information for selenium substances (human data)

Study type	Selenium substance	Protocol	Results
Acute, oral	Seleneous acid (in gun bluing agent)		Death at **55 000 µg Se/kg** (Matoba et al. 1986) Additional studies: Carter 1966; Civil and McDonald 1978; Lech 2002; Pentel et al. 1985
Acute, dermal	Seleninyl chloride ($SeOCl_2$)	1 man Less than 0.005 mL seleninyl chloride applied to forearm; area of application was 0.8 cm in diameter	**LOAEL: < 83 µg Se/kg-bw**: chemical burn; at 5 minutes after application there was pain and tissue destruction; swollen painful forearm at 8 hours after application, and then swelling subsided; at 5–10 days, healing progressed, and a scab formed (Dudley 1938).
Short-term repeated dose (2–89 days), oral (selenosis)	Sodium selenite in supplements	A case study of 227 U.S. citizens aged 4–92 (median 54 years), who consumed improperly formulated dietary supplement in 2008 for a median of 29 days (range 1–109 days). Adult dose recommended on label, would have provided 40800 µg Se/d (583 µg Se/kg bw/d for 70 kg person). Out of 227 consumers, 201 met authors' criteria for selenosis. The other 26 either had no symptoms or mild symptoms.	**LOAEL: 41 749 µg Se/d** (596 µg Se/kg-bw/d): based on selenosis. Symptoms of the 201 patients included: diarrhea (78%), fatigue (72%), hair loss (70%), joint pain (67%), nail discolouration or brittleness (61%), nausea (57%), headache (45%), tingling (39%), foul breath (37%), vomiting (26%), cutaneous eruptions (26%). No deaths reported. Persistent symptoms present 90 days or more after stopped taking supplement included memory loss in 22% of the 83 cases. Median estimated dose was 41 749 µg Se/d for the 156 patients for which this information was available. For eight patients, serum selenium measured a median of one day (range 0–33 days) after cessation of product consumption; the median serum concentration was 664 µg Se/L; the mean was 751–761 µg Se/L. (MacFarequhar et al. 2010) **LOAEL: 24 000 µg Se/d** (400 µg Se/kg-bw/d) – selenosis in woman, age 55 years.

Study type	Selenium substance	Protocol	Results
			Symptoms: diarrhea, hair loss, muscle cramps, joint pain, fatigue (Sutter et al. 2008). Additional studies: CDC 1984; Yang 1987
90 days–1 year, oral (selenosis)	Sodium selenite or L-Selenomethionine or High-selenium yeast	81 healthy individuals in the United States (18 years of age and older, mean age 36 yrs., mean weight 83 kg) were randomized into 10 groups (placebo and 3 dose levels of each form of selenium) and given selenium supplements daily for 16 weeks as follows: 1. Sodium selenite: 202, 380, 601 µg Se/day 2. L-Selenomethionine 158, 338, 507 µg Se/day 3. High-selenium yeast 226, 439, 703 µg Se/day Initial plasma Se: 122 µg/L (SD 13)	No signs of selenium toxicity (hair loss, nail changes) observed for any of the selenium supplements at the highest dose tested. 1. Sodium selenite **NOAEL: 601 µg Se/d** (7 µg Se/kg-bw/d) + dietary Se 2. L-Selenomethionine **NOAEL: 507µg Se/d** (6 µg Se/kg-bw/d) + dietary Se 3. High-selenium yeast **NOAEL: 703 µg Se/d** (8.5 µg Se/kg-bw/d) + dietary Se (Burk et al. 2006)
90 days–1 year, oral	High-selenium yeast supplement, and dietary selenium	In a randomized placebo-controlled trial, 42 healthy U.S. men (18–45 years old, average age 31 years, average weight 76 kg) were exposed daily to 300 µg Se/day from a high-selenium yeast supplement, and dietary selenium for 48 weeks. Baseline selenium intake of high-selenium group: 137 µg/day ±42 (±SD)	**NOAEL: approx. 437 µg Se/d** (6 µg Se/kg-bw/d) (300 µg Se/d + approx. 137 µg Se/d dietary selenium) (Hawkes and Laslett 2009) Additional studies: Duffield et al. 1999; Hawkes and Turek 2001; Hawkes and Keim 2003; Hawkes et al. 2008; Burk et al. 2006
90 days–1 year, oral (T-2 diabetes)	High-selenium yeast	PRECISE (Prevention of Cancer by Intervention with Selenium) pilot trial in U.K. 501 elderly volunteers (60–74 years old) were supplemented for six months with 100, 200 or 300 µg Se/day as high-selenium yeast, or placebo yeast. Plasma adiponectin measured (plasma adiponectin is a recognized independent predictor of reduced type 2 diabetes risk).	**NOAEL: 300 µg Se/d** (4 µg Se/kg-bw/d) No effect of selenium supplementation on plasma adiponectin ($P_{overall}$ = 0.86) (Rayman et al. 2012, as cited in Rayman and Stranges 2013).

Study type	Selenium substance	Protocol	Results
90 days–1 year, oral (T-2 diabetes)	Selenium yeast	84 premenopausal Iranian women with central obesity were supplemented with 200 µg Se/day as selenium yeast. All on hypocaloric diet enriched with legumes. Selenium status was not measured.	**NOAEL: 200 µg Se/d** (3 µg Se/kg-bw/d) Rayman and Stranges (2013): After six weeks of selenium supplementation, these women had significantly lowered fasting concentrations of serum insulin (P=.05) and the homeostasis model assessment of insulin resistance index (P=0.04), suggesting that selenium supplementation would reduce type 2 diabetes risk. Only 81% of subjects who finished the trial were included in the data analysis. (Alizadeh et al. 2012, as cited in Rayman and Stranges 2013)
Greater than 1 year, oral (selenosis)	Selenium in diet	349 adult humans living in Enshi County of China where selenium levels are high in soil and food (body weight ~55 kg; Yang et al. 1989a). Main criterion for selenosis was morphological changes in nails. 20 men from high-selenium region, 70% of whom had suffered heavy hair and nail loss, had livers examined with supersonic technology, and underwent electrocardiographic examinations.	**LOAEL: 910 µg Se/d** (16.5 µg Se/kg-bw/d) (blood Se concentration: 1050 µg/L): selenosis and hematological changes **NOAEL: 750–850 µg Se/d** (13.6–15.5 µg Se/kg-bw/d) (blood Se concentration: 906–997 µg Se/L) Authors note that inhabitants of high-Se region may be adapted to high Se intake. No selenosis found in children 12 years of age and younger. No teratogenic effects in babies observed. (Yang et al. 1989b)
Greater than 1 year, oral (selenosis)	Selenium in diet	In a follow-up study to Yang et al. 1989a and 1989b, the oral exposures of selenium in five adults with persistent obvious fingernail signs of selenosis at the time of initial study (1986) were subsequently reduced, and these subjects were re-examined in 1992. They had no signs of selenosis. Their average whole blood selenium concentration had decreased to 0.968 mg/L, which, based on the mathematical relationship in Yang et al. 1989a, is associated with a Se intake	**LOAEL: 910 µg Se/d** (16.5 µg Se/kg-bw/d) (blood Se concentration: 1054 µg/L) based on selenosis: sloughing of nails and brittle hair reported in 1986 observations. **NOAEL: 819 µg Se/d** (15 µg Se/kg-bw/d) (blood Se concentration: 968 µg/L) (Yang and Zhou 1994)

Study type	Selenium substance	Protocol	Results
		of approx. 819 Se/day.	
Greater than 1 year, oral (selenosis)	Selenium in diet	Subjects: 14 humans from a region in China with high selenium levels in soil, but no selenosis.	**NOAEL: 750 µg Se/d** (13.6 µg Se/kg-bw/d) (whole blood Se concentration: mean = 444 µg/L; range = 346–584 µg/L) Average dietary selenium intake: 750±554 µg Se/day (Yang and Zhou 1994; Yang 1987; Yang et al. 1983)
Greater than 1 year, oral (selenosis)	Sodium selenite + dietary selenium	One man in China (62 years old, weighing 60 kg) took sodium selenite tablets daily for over 2 years. Each tablet contained 2 mg sodium selenite (913 µg Se/day). Estimated total Se intake from diet and supplements: 1080 µg Se/day.	**LOAEL: 1080 µg Se/d** (18 µg/kg bw/d) (whole blood Se concentration = 179 µg Se/L): fingernail morphology, garlic odour in dermal excretions After man stopped taking oral sodium selenite tablet, nails gradually recovered. (Yang and Zhou 1994; Yang 1987; Yang et al. 1983)
Greater than 1 year, oral (selenosis)	Selenium in diet	In an epidemiological study, 142 adults were randomly recruited from western South Dakota and eastern Wyoming, in areas with high selenium in soil. Exposure was believed to be many years. Subjects completed questionnaires, underwent physical examinations, and provided blood, urine and toenail samples. For some subjects, there were duplicate-plate food collections for selenium analysis.	**NOAEL: 724 µg Se/d** (10 µg Se/kg-bw/d) (whole blood selenium concentration = 675 µg/L; serum selenium concentration = 363 µg/L) According to authors: no clinically significant changes in laboratory tests or physical findings characteristic of selenium toxicity (selenosis). About half of the 142 adults had selenium intakes greater than 200 µg Se/d (range: 68–724 µg Se/d). (Longnecker et al. 1991) Additional studies: Smith et al. 1936; Smith and Westfall 1937
Greater than 1 year, oral (cancer/T-2 diabetes)	High-selenium yeast + dietary selenium	Subjects from the Nutritional Prevention of Cancer (NPC) trial: Caucasian, a history of non-melanoma skin cancer, residing in eastern United States, mean age 63 years. Double-blind randomized placebo-controlled trial Se group: 600 adults Placebo group: 602 adults Supplement: 200 µg Se/day Objective: To determine whether a nutritional supplement of selenium will	**Cancer:** Supplementation with 200 µg Se/d did not affect the incidence of basal cell or squamous cell skin cancer. **T-2 diabetes:** **LOAEL = 290 µg Se/d** – A secondary analysis of data found a statistically significant increased risk of type 2 diabetes, hazard ratio = 1.55 (95% CI: 1.03–2.33). Tertile analysis found: Statistically significant increased risk of type 2 diabetes in the highest tertile of baseline plasma selenium level (hazard

Study type	Selenium substance	Protocol	Results
		decrease the incidence of cancer (Clark et al. 1996). Secondary data analysis for T-2 diabetes (Stranges et al. 2007) Average follow-up: 7.7 years (SD, 2.7) Average treatment: 4.5 years (Rayman and Stranges 2013)	ratio = 2.70 [95% CI of 1.30–5.61]). Top tertile was plasma selenium level greater than 121.6 µg/L (plasma 122 µg Se//L corresponds to intake of 94 µg Se/L, according to the mathematical relationship in Combs et al. 2001). In the lowest tertile (less than or equal to 105.2 ng Se/mL of plasma) there was a relative risk of 1.03 (95% CI of 0.50–2.09). Mean plasma selenium concentration: 180–190 µg/L while taking selenium supplements 110–120 µg/L for the placebo group Article notes that the NPC trial was conducted in region where average dietary selenium intake is 90 µg Se/day. The mean baseline plasma Se concentration of the Se group was 114.4, which corresponds to an intake of 84 µg Se/d, according to the mathematical relationship in Combs et al. 2001. (Stranges et al. 2007)
Greater than 1 year, oral (cancer/T-2 diabetes/selenosis)	L-selenomethionine + dietary selenium	Men from SELECT (Selenium and Vitamin E Cancer Prevention Trial); healthy men in Canada, United States, Puerto Rico (50 years of age or older) Double-blind randomized placebo-controlled trial **Objective:** To determine whether selenium or vitamin E or both could prevent prostate cancer with little or no toxicity in healthy men. Secondary: T-2 diabetes Se-only group: 8752 men Placebo group: 8696 men Supplement: 200 µg Se/day Exposure: median 5.5 years (range 4.17–7.33)	**NOAEL: 310–460 µg Se/d**: No statistically significant increase in type-2 diabetes or cancers. Statistically significant increase in self-declared alopecia (hair loss) and dermatitis was reported at this dose. Alopecia: RR = 1.28, 99% CI = 1.01–1.62 Dermatitis (Grades 1 and 2): RR = 1.17, 99% CI = 1.00–1.35 Not statistically significant: Halitosis (breath odour): RR = 1.17, 99% CI = 0.99-1.38 Nail changes: RR = 1.04, 99% CI = 0.94–1.16 Type 2 diabetes: 1.07, 99% CI = 0.94–1.22, p = 0.16 There were no significant differences (P > 0.15) in any of the cancer endpoints. At a planned 7-year interim analysis, supplements discontinued because evidence convincingly demonstrated no benefit (Lippman et al. 2009).

Study type	Selenium substance	Protocol	Results
			For follow-up analysis of SELECT data see Klein et al. 2011. Additional studies: Algotar et al. 2010 (no association for Se and blood glucose); Park et al. 2012 (toenail Se and Type 2 diabetes—decreased risk); Stranges et al. 2011 (no association for Se and type 2 diabetes); Akbaraly et al. 2010 (decreased risk of diabetes)
Greater than 1 year, oral (T-2 diabetes)	Selenium in diet and possibly some supplements	The Epidemiology of Vascular Aging study, a 9-yr. longitudinal epidemiological study conducted in France (n=1389, 59–71 yrs.). Plasma fasting glucose was measured at baseline 2, 4 and 9 yrs. Analysis done on 1162 subjects with complete data.	**NOAEL: 140 ug Se/d**[a] (156 µg Se /L plasma selenium concentration) Tertile analysis found that, for men, high plasma selenium (94–156 µg Se /L) was associated with marginally reduced risk of hyperglycemia (impaired fasting glucose or diabetes). No significant relationship was observed in women. (Akbaraly et al. 2010 as cited in Rayman and Stranges 2013)
Greater than 1 year, oral (T-2 diabetes)	Selenium in diet	Observational study, prospective analysis Subjects in United States (mean age at baseline ±SD) 3630 women (53±6.4 yrs.) 3535 men (60±8.8 yrs.) At baseline, subjects were free of type 2 diabetes and heart disease. Selenium in toenail clippings measured.	**NOAEL:** 65 µg Se/d[a] – no increased risk of type 2 diabetes Higher levels of selenium in toenails associated with lower risk of incident type 2 diabetes for concentrations up to approx. 0.95 µg Se/g in toenails. 750 incident cases of type 2 diabetes during 142 550 person years. Relative risk of diabetes decreased across increasing quintiles of selenium in toenails. Mean concentration of selenium in toenails was 0.84 µg/g in men and 0.77 µg/g in women. Data plotted in Figure 1 suggest that, for men, the risk of type 2 diabetes may increase above 0.95 µg Se/g toenail. (Park et al. 2012)
Greater than 1 year, oral (excess Se exposure)	Selenium in diet	**Brazilian Amazon** A cross-sectional study of 407 volunteers (204 women, 203 men), 15–87 years old, living in the Brazilian Amazon. Excluded: pregnant and breastfeeding women; some medical conditions	**NOAEL: 1450 µg Se/d**[a] (whole blood 1500 µg Se/L) No hair, nails, skin or breath signs or symptoms of Se toxicity associated with levels of selenium in blood (compared to subjects with blood level < 560 µg Se/L, corresponding to intake of 400 µg Se/d according to equation from Yang et al. 1989a).

Study type	Selenium substance	Protocol	Results
		Selenium concentration was measured in whole blood and plasma. Nurses (blinded to selenium status of subjects) examined subjects for signs of selenium toxicity (in hair, body hair, nails and skin). Interview-administered questionnaire included possible signs and symptoms of selenosis.	Whole blood Se concentration: • Median: 228 µg Se/L • Range: 103–1500 µg Se/L (Lemire et al. 2012) Additional study: Lemire et al 2010a
Greater than 1 year, oral (excess Se exposure)	Selenium in diet	**Greenland Inuit groups** Selenium, mercury, cadmium and lead were measured in whole blood. Questionnaires were used to collect information on diet. Did not check for selenosis signs or symptoms, but authors state that there were no reports of selenosis.	**NOAEL: 1600 µg Se/day** (22 µg Se/kg-bw/d) (whole blood Se concentration = 1818 µg Se/L) Whole blood concentration group means ranged from 178 µg Se/L for Tasiilaq men to 488 µg Se/L for Uummannaq men. Highest whole blood Se was 1890 µg/L. Two subjects had a blood level above 1818 µg Se/L. (Hansen et al. 2004)
Greater than 1 year, oral (excess Se exposure)	Selenium in diet	**Canadian Inuit** 732 Inuit men and women (ages 18–71) Selenium, mercury and lead concentrations measured in whole blood. No information collected on signs of selenosis.	**Intake up to 4470 µg Se/d**[a] (whole blood 3560 µg Se/L) Whole blood mean: 290 µg Se/L Whole blood range: 119–3560 µg Se/L (Valera et al. 2009) Additional studies: Alkazemi et al. 2013; Ayotte et al. 2011; Ravoori et al. 2010

[a] Health Canada calculated human selenium intake from blood or nail selenium concentrations using the mathematical relationship in Yang et al. 1989a and Combs et al. 2001.

Table B-5: Summary of the human health effects information for selenium substances (animal data)

Study type and reference	Selenium substance	Protocol	Results
Acute, oral	Elemental selenium	Rat – male (Sprague-Dawley)	**Lowest LD_{50}: 6 700 000 µg Se/kg-bw** (Cummins and Kimura 1971)

Study type and reference	Selenium substance	Protocol	Results
Acute, oral	Sodium selenite	Rabbit – female	**Lowest LD_{50}: 1000 µg Se/kg-bw** (Pletnikova 1970) Additional studies: LD_{50} ranged from 2300 (Guinea Pig) to 6000 (pony) µg Se/kg-bw. (Cummins and Kimura 1971; Singh and Junnarkar 1991; NTP 1996; Pletnikova 1970; Stowe 1980)
Acute, oral	Sodium selanate	Rat	**Lowest LD_{50}: 670 µg Se/kg-bw** (HYSAAV 1984, as cited in ChemIDplus) Additional studies: LD_{50} (rabbits) = 940 µg Se/kg-bw (HYSAAV 1984, as cited in ChemIDplus)
Acute, oral	Selenium dioxide	Mouse – male (Swiss)	**Lowest LD_{50}: 16 600 µg Se/kg-bw** (Singh and Junnarkar 1991)
Acute, oral	D,L-selenocystine	Mouse – male (ICR)	**Lowest LD_{50}: 35 800 µg Se/kg-bw** (Sayato et al. 1993)
Acute, inhalation	Hydrogen selenide	Guinea pig Groups of 16 guinea pigs exposed to 1, 4, 4, 6, 6, 7 and 42 µg hydrogen selenide/L	**8-hour LC_{50}: 1000 µg Se/m^3** (1 µg Se/L) (Dudley and Miller 1941) Additional study: Dudley and Miller 1937
Acute, inhalation	Elemental selenium – dust	Rat – female (albino) 20 rats	**LOAEC: 33 000 ± 10 000 µg Se/m^3** for 8 hours – 10% died; hemorrhagic lungs (Hall et al. 1951)
Acute, dermal	Seleninyl chloride ($SeOCl_2$)	Rabbit 10 rabbits Applied 0.01–0.2 ml; 0.01 ml spread over a circular area approx. 1 cm in diameter Doses: 7.2–248 mg seleninyl chloride/kg-bw	**Lowest LOAEL: 3400 µg Se/kg-bw** – death All rabbits died 2–20 hours after application; faster death associated with higher doses. Before death, animals showed gradual increase of swelling over the entire back; area of burn was depressed and surrounded by dark ring. Absorption of Se demonstrated in companion experiment in which Se concentration in whole blood and liver measured. (Dudley 1938)
Sensitization, dermal	Elemental selenium	Guinea pigs – 5 male, 5 female	No evidence of irritation or sensitization (Hall et al. 1951)
Short-term (2–89 days), oral	Sodium selenite	Sodium selenite Rats – male (Sprague-Dawley) Exposure: 40 days Diets: 38 (Se-deficient	**LOEL: 30 µg Se/kg-bw/d**[a] – decrease of approx. 50% in serum T3 concentration **NOEL: 15 µg Se/kg-bw/d**[a] – Serum T3 (Eder et al. 1995 Abstract)

Study type and reference	Selenium substance	Protocol	Results
		diet), 50, 100, 300, 600, 3000 µg Se/kg-bw in diet	**LOAEL: 150 µg Se/kg-bw/d** – castrated pigs: hoof disorder, hoof separation present at the juncture of the coronary band of the hoof (male pig – castrated, initial weight approx. 25 kg) (Kim and Mahan 2001a, 2001b). Additional studies: Skowerski et al. 1997a, 1997b; Johnson et al. 2000; Tsunoda et al. 2000; Wilson et al. 1983, 1989; Halverson et al. 1966; Palmer and Olson 1974; Chen et al. 1993; Mahan and Magee 1991; Koller et al. 1986; Raisbeck et al. 1998; Nobunaga et al. 1979 as cited in ATSDR 2003; El-Zarkouny et al. 1999; Shalini and Bansal 2008; Turan et al. 1999
Short-term (2–89 days), oral	Sodium selenate	Rats – male (Sprague-Dawley), exposed 6 weeks to dietary Se Se doses (6 or 7 rats/dose): • Low Se: 2.5 µg Se/kg-bw/d[a] • Normal Se (n=6): 11.5 µg Se/kg-bw/d[a] • High Se (n=7): 52.5 µg Se/kg-bw/d[a]	Male – **LOEL: 52.5 µg Se/kg-bw/d**, based on significant increases in serum TSH (approx. 30%), GSH-Px in kidneys (approx. 30%) and erythrocytes (approx. 70%). **NOAEL for body weight: 52.5 µg Se/kg-bw/d** (Hotz et al. 1997) Additional studies: Panter et al. 1996; Palmer and Olson 1974; Salbe and Levander 1990; Baker et al. 1989, as cited in ATSDR 2003; NTP 1996
Short-term (2–89 days), oral	L-Selenomethionine	Pregnant Long-tailed Macaque (monkey) 10/group Monkeys were dosed via nasogastric intubation at 0, 10.1, 60.4, 120 µg Se/kg-bw/d during gestation days (GD) 20–50. 2–3 dams were followed until term (GD 165).	**Lowest LOAEL: 60 µg Se/kg-bw/d** – anorexia (2/10). At 120 µg Se/kg-bw/day, vomiting and anorexia (5/10); maternal weight loss significantly greater (Tarantal et al. 1991). Additional studies: Johnson et al. 2000; Salbe and Levander 1990; Panter et al. 1996; Raisbeck et al. 1998, as cited in ATSDR 2003; Cukierski et al. 1989
Short-term (2–89 days), oral (water)	Selenocystine	Mouse (BALB/c) Exposure: 47 days	**LOEL: 173 µg Se/kg-bw/d** – immuno/Lymphoret: reduced B-cell function and OVA-specific antibody concentration (Raisbeck et al. 1998, as cited in ATSDR 2003). Additional studies: Sayato et al. 1993, as cited in ATSDR 2003

Study type and reference	Selenium substance	Protocol	Results
Short-term (2–89 days), oral	Selenium – enriched yeast	Pig (crossbred barrows) Exposure: 12 weeks 10 pigs/dose Doses[a]: 2, 150, 300, 450, 600 µg Se/kg-bw/d[a]	**LOAEL: 300 µg Se/kg-bw/d[a]** – hoof disorder (hoof separation present at the juncture of the coronary band of the hoof) (Kim and Mahan 2001).
Short-term (2–89 days), inhalation	Elemental selenium – dust Median particle diameter was 1.2 microns	Guinea Pig (male) 10 Guinea Pigs 31 mg Se/m^3 ± 16 mg Se/m^3 Exposure: during an 8-day period, there were 4 periods of exposure, each of which was 4 hours, with 48 hours between exposure periods.	**LOAEL: 31 mg Se/m^3** – Mild to moderate interstitial pneumonitis; mild congestion of lungs, liver and spleen. None of the animals lost weight or displayed signs of toxic effects. No deaths.
Sub-chronic (90 days–1 year), oral	Nano-selenium	Rats (Sprague-Dawley) Exposure: 13 weeks 12 males and 12 females per dose Intake (µg Se/kg-bw/d) Male: 140, 220, 310, 420 Female: 190, 330, 440, 500	**NOAEL: 220 µg Se/kg-bw/d** **LOAEL: 310 µg Se/kg-bw/d** – relative to control group, body weights were significantly lower; mottled surface on liver; degeneration of liver cells (Jia et al. 2005).
Sub-chronic (90 days–1 year), oral	Sodium selenite	Rats – males (Wistar) 11/group Doses: 0, 2 or 4.6 µg Se/kg-bw/d via feed on empty stomach for 3 months. Animals had unrestricted access to feed and water.	**LOEL: 2 µg Se/kg-bw/d** – mild hepatic effects (sporadic infiltrations of mononuclear cells in portal canal and weal activation of Kupffer cells). **LOAEL: 4.6 µg Se/kg-bw/d** – hepatic adverse effects (distinct swelling of Kupffer cells in dilated sinusoidal vessels and necrotic areas comprising single groups of hepatocytes) (Kolodziejczyk et al. 2000). Additional studies: Schroeder and Mitchener 1971a; Turan et al. 1999b, as cited in ATSDR 2003; Behne et al. 1992; Pletnikova 1970; Jia et al. 2005; NTP 1994
Sub-chronic (90 days–1 year), oral	Sodium selenate	Rats (Fischer-344) 10 males and 10 females per group Estimated doses: 0, 100, 200, 400, 600 or 1100 (males) and 800 (females) µg Se/kg-bw/d Exposure: 13 weeks	**Lowest LOAEL: 100 µg Se/kg-bw/d** – statistically significant decrease in spermatid count/g testis re controls (15% decrease); statistically significant alteration in duration of stages of estrous cycle (there was more time in diestrus and less time in estrus) (NTP 1994). Additional studies: Rosenfeld and Beath 1954, as cited in ATSDR 2003; NTP 1994 (mice)
Sub-chronic	L-	Rats – males (Wistar)	**LOAEL: 100 µg Se/kg-bw/d[a]** – significant

Study type and reference	Selenium substance	Protocol	Results
(90 days–1 year), oral	Selenomethionine	6 rats/dose Doses (Se/kg-bw/d[a]): • Selenium-deficient: 0.01 • Selenium-adequate: 15 from sodium selenite • Selenium excess: 100 from selenomethionine Exposure: 110 days	reduction in type 1 deiodinase activity; significant decrease in body weight (15%) (Behne et al. 1992).
Sub-chronic (90 days–1 year), oral	D,L-selenocystine	Mice – males (ICR) 10/group Doses: 2350, 4700 or 7050 µg Se/kg-bw/d via oral gavage Exposure: 90 days	**LOAEL: 4700 µg Se/kg-bw/d** – increased serum aspartate aminotransferase and alanine aminotransferase (hepatic effects) and reduced bw (16% lower). **NOAEL: 2400 µg Se/kg-bw/d** (Hasegawa et al. 1994, as cited in ATSDR 2003)
Chronic (> 1 year), oral	Sodium selenate and sodium selenite (rats fed one form, but results reported mainly on basis on Se intake without reference to form of Se)	Rats (Wistar) 1437 rats Exposure: 2 years Doses: 0, 0.5, 2, 4, 6, 8 or 16 ppm (0, 25, 100, 200, 300, 400 or 800 µg Se/kg-bw/d	**LOAEL: 100 µg Se/kg-bw/d** – hyperplastic lesions in liver, and nephritis. At 200 µg Se/kg-bw/d, skeletal effects (soft bones) (Harr et al. 1967; Tinsley et al. 1967). Additional studies: Schroeder and Mitchener 1971b, 1972, as cited in ATSDR 2003; Schroeder 1967, as cited in Harr and Muth 1972
Chronic (> 1 year), oral	Organic (feed)	Rats (Osborne Mendel) 18 rats/group Exposure: 24 months Doses: 0, 250, 350 or 500 µg Se/kg-bw/d	Female: **LOAEL: 250 µg Se/kg-bw/d** – based on slight to moderate cirrhosis (Nelson et al. 1943, as cited in ATSDR 2003).
Chronic, (> 1 year), oral	Selenium sulfide	Rats (F344) and mice (B6C3F1), male and female, 50/sex/group Oral gavage for 7 days/week for 103 weeks Rats: 0, 3 or 15 mg SeS /kg/day (0, 2133 or	Rats (male/female): **LOAEL:** 15 mg SeS (**10 668 µg Se/kg-bw/d)** – based on a statistically significant increase in hepatocellular carcinoma. Mice (female): **LOAEL:** 100 mg SeS/kg/day (**71 118 µg**

Study type and reference	Selenium substance	Protocol	Results
		10668 µg Se/kg-bw/d) Mice: 0, 20 or 100 mg SeS/kg/day (0, 14224 or 71118 µg Se/kg-bw/d) Although the test substance was a mixture of SeS and SeS_2, these conversions are based on SeS, because SeS was the major component.	**Se/kg-bw/d)** – based on significant (p,0.001) hepatocellular carcinoma and increased incidence of alveolar/bronchiolar carcinomas or adenomas. **Selenium sulfide was not carcinogenic to male mice.** (NCI and NTP 1980b)
Reproductive effects	Sodium selenite	Rats (wild) 6/group Doses: 0, 100 or 200 µg Se/kg bw/d[a] for 35 days Exposure: 5 weeks	**LOAEL: 100 µg Se/kg-bw/d[a]** – statistically significant ($p < 0.05$) ↑ in sperm with abnormal midpieces (3.06%). At 200 µg Se/kg-bw/d[a], statistically significant ↑ in sperm with abnormal midpieces (22.5%). (Kaur and Parshad 1994)
Reproductive effects	Sodium selenite	Mice (BALB/c) 6 mice/group Exposure duration: • Groups Ia, IIa, IIIa: 4 weeks • Groups Ib, IIb, IIIb: 8 weeks Doses: • Group I: Se-deficient = 0.02 ppm Se from yeast-based diet (approx. 2.7 µg/kg-bw/d[a]) • Group II: Se-adequate = added 0.2 ppm Se from sodium selenite to yeast-based diet (approx. 27 µg/kg-bw/d[a]) • Group III: Se excess = added 1 ppm Se (approx. 130 µg/kg bw/d[a]) At end of treatment period, male mice were allowed to mate with normal females in ratio of 1:3 or 1:2 for 7 days,	**LOAEL: 130 µg Se/kg-bw/d[a]** Based on statistically significant reduction in sperm concentration, sperm motility, percentage fertility and litter size, and significant increase in lipid peroxidation in testis and liver; abnormal sperm tail midpiece structure (Shalini and Bansal 2008). Additional studies: El-Zarkouny et al. 1999; Kaur and Parshad 1994

Study type and reference	Selenium substance	Protocol	Results
		and females were observed for 21 days for signs of pregnancy or birth of pups. Percentage fertility = number of females giving birth / number of females exposed to mating x100	
Reproductive effects	Sodium selenate	Rats (Fischer-344) Exposure: 13 weeks 10 males and 10 females per group Exposed to 0, 3.75, 7.5, 15, 30 or 60 ppm (0, 100, 200, 400, 600 or 1100 [males] and 800 [females] µg Se/kg-bw/d) via drinking water	Male – reproduction: **LOAEL: 100 µg Se/kg-bw/d** – based on significant ↓spermatid heads/g of testis and significant ↓ spermatid count (these observations are not dose-dependent). At 600 µg Se/kg-bw/d: Significant ↓ sperm motility, but not spermatid count. Female – reproduction: **LOAEL: 100 µg Se/kg-bw/d** – based on more time in diestrus and less time in proestrus, estrus and metestrus than controls (not significant) (NTP 1994). Additional studies: Rosenfeld and Beath 1954; Schroeder and Mitchener 1971b, as cited in ATSDR 2003
Reproductive effects	L-selenomethionine	Female monkeys (Macaca fascicularis) 10/group Exposure: 0, 10, 25–47, 60, 75–81, 120, 240 µg Se/kg-bw/day via nasogastric intubation for 30 days	**LOAEL: 76–79 µg Se/kg-bw/d** (150 µg Se selenite/kg-bw/d) – altered menstrual cycle duration. **NOAEL: 60 µg Se/kg-bw/d** (Cukierski et al. 1989) Additional studies: Tarantal et al. 1991
Reproductive effects	Seleniferous wheat 3 ppm Se	Rats	**LOAEL: 150 µg Se/kg-bw/d**[a] – impaired production and rearing of young (Munsell et al. 1936).
Developmental effects	Selenite	Mice (IVCS) Exposure: 30 days pre-gestation, and gestation days 0–18, at dose levels of 170 and 340 µg Se/kg-bw/day (study was designed to understand Se, Hg interaction)	**LOAEL: 340 µg Se/kg-bw/d** – decreased fetal body weight, delayed vertebral ossification. Female: increased proportion (11.8%) with longer estrous cycles. **NOAEL: 170 µg Se/kg-bw/d** (Nobunaga et al. 1979, as cited in ATSDR 2003) Additional studies: Thorlacius-Ussing 1990, as cited in ATSDR 2003

[a] Health Canada calculated dose in µg Se/kg-bw/d from information in article using conversion factors in the document Human Health Risk Assessment for Priority Substances (Health Canada 1994).