SCIENTIFIC CRITERIA DOCUMENT FOR THE DEVELOPMENT OF CANADIAN SOIL QUALITY GUIDELINES FOR THE PROTECTION OF HUMAN HEALTH

Cadmium

NOTE TO READERS

The Canadian Council of Ministers of the Environment (CCME) is the primary minister-led intergovernmental forum for collective action on environmental issues of national and international concern.

This scientific criteria document provides the background information and rationale for the development of Canadian Environmental Soil Quality Guidelines for Human Health for Cadmium. For convenience, Canadian Environmental Soil Quality Guidelines for Ecological Receptors for Cadmium, developed in 1999, are included.

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EXECUTIVE SUMMARY

Canadian environmental quality guidelines, developed under the auspices of the Canadian Council of Ministers of the Environment (CCME), are numerical concentrations or narrative statements recommended to provide a healthy, functioning ecosystem capable of sustaining the existing and likely future uses of the site by ecological receptors and humans. Canadian soil quality guidelines can be used as the basis for consistent assessment and remediation of contaminated sites in Canada.

The soil quality guidelines (SoQGs) were derived according to procedures described in *A Protocol for the Derivation of Environmental and Human Health Soil Quality Guidelines* (CCME 2006).

According to this protocol, both environmental and human health soil quality guidelines are developed for four land uses: agricultural, residential/parkland, commercial and industrial. CCME recommends the lowest value generated by the two approaches for each of the four land uses as the Canadian Soil Quality Guideline (CSoQG) (CCME 2006). This scientific supporting document provides the scientific background and rationale for the derivation of human health SoQG for cadmium. This document contains a review of the chemical and physical properties of cadmium, its sources and emissions in Canada, its distribution and behaviour in the environment and its behaviour and effects in humans and experimental animals. This information can be used to derive soil quality guidelines for cadmium to protect human and ecological receptors for the four types of land use. However, the SoQGs for the protection of environmental health have not been updated in this report. Therefore, the generic SoQGs are based on the present update of the guidelines for the protection of human health and the 1999 guidelines for the protection of environmental health (CCME 1999; EC 1999).

Based on the CCME (2006) protocol, this document evaluates three types of exposure pathways: required pathways (direct contact and soil ingestion), applicable pathways (soil ingestion by secondary and tertiary environmental receptors, indoor air, groundwater, and produce, meat and milk ingestion) and check mechanisms (off-site migration of substances). Table 1 lists the SoQGs for each of the pathways calculated.

137 **Table 1. Soil quality guidelines for cadmium ($mg \cdot kg^{-1}$)**

	Land use			
	Agricultural	**Residential/parkland**	**Commercial**	**Industrial**
Guideline (SoQG)[a]	**3.8**	**10**	**20**	**22**
$SoQG_{HH}$[b]	13	13	20	180
$SoQG_{E}$[c]	3.8	10	22	22

Notes: $SoQG_{HH}$ = soil quality guideline for human health; $SoQG_{E}$ = soil quality guideline for environmental health. Soil guidelines and the data used to calculate them are, by convention, always expressed on a dry weight basis to allow the data to be standardized. In case of doubt and if the scientific criteria document does not specify whether wet or dry weight is used, readers are advised to check the references provided.

[a] The SoQG is the lower of the 2023 $SoQG_{HH}$ and the 1999 $SoQG_{E}$ for the given land use.

[b] Data are sufficient and adequate to calculate an $SoQG_{HH}$.

[c] The $SoQG_{E}$ is the 1999 value (CCME 1999). The $SoQG_{E}$ is not updated in this current revision.

1.0 INTRODUCTION

CSoQGs for contaminated sites are numerical limits for contaminants in soil and water intended to maintain, improve or protect environmental quality and human health.

CSoQGs are developed using formal protocols to ensure scientifically defensible values that are consistent throughout Canada, as described in *A Protocol for the Derivation of Environmental and Human Health Soil Quality Guidelines* (CCME 1996, revised in 2006). Both SoQG$_{ES}$s and SoQG$_{HHS}$s are developed for four land uses: agricultural, residential/parkland, commercial and industrial. CCME recommends the lowest value generated by the two approaches for each of the four land uses as the CSoQG. In addition, check mechanisms considering indirect pathways of exposure (e.g., the off-site migration of substances via wind and water erosion) provide protection for resources and receptors not otherwise considered. Soil guidelines and the data used to calculate them are, by convention, always expressed on a dry weight basis to allow the data to be standardized. In case of doubt and if the scientific criteria document does not specify whether wet or dry weight is used, readers are advised to check the references provided.

This report reviews the sources and emissions of cadmium, its distribution and behaviour in the environment, and its toxicological effects on humans. While the toxicological effects on plants, invertebrates, birds and experimental animals have not been updated in this report, they can be found in the 1999 *Canadian Soil Quality Guidelines for the Protection of Environmental and Human Health: Cadmium* document (CCME 1999). The 1999 cadmium SoQGs for the protection of ecological receptors (SoQG$_{ES}$) are included in this report and considered in the determination of the SoQGs for all land uses.

The SoQGs presented in this document are intended as general guidance. Site-specific conditions should be considered when applying these values (see CCME [1996] for guidance on developing site-specific soil objectives). CCME (2006) provides further generic implementation guidance pertaining to the guidelines. SoQGs are calculated to approximate a “no- to low-effect” level (or threshold level) based only on the toxicological information and other scientific data (fate, behaviour, etc.) available for the substance of concern. The guidelines do not consider socio-economic or technological factors. Site managers should consider these non-scientific factors at the site-specific level as part of the risk management process. Since the guidelines may be applied differently in various jurisdictions, the reader should consult appropriate authorities for the laws and regulations of the jurisdiction in which they are working for applicable implementation procedures.

2.0 BACKGROUND INFORMATION

2.1 Physical and Chemical Properties

Cadmium (CASRN 7440-43-9) belongs to Group IIB of the transition series of the Periodic Table of Elements. Cadmium, atomic symbol Cd, is a silver-white, blue-tinged, lustrous metal with a melting point of 321°C and a boiling point of 765°C (Eisler 1985). Elemental cadmium has an atomic number of 48 and a molecular weight of 112.40 g/mol. It is among the least abundant trace elements and is seldom found as a pure mineral.

Cadmium occurs in nature predominantly as the divalent cation (Cd^{2+}), present in a variety of inorganic compounds and organic complexes. Chemically, cadmium closely resembles zinc and occurs as an impurity in almost all zinc ores as both a sulphide and a carbonate. Its chemical form depends on such factors as the medium in which it is found and ambient environmental conditions.

The key physical and chemical properties of cadmium and its principal inorganic salts are presented in Table 2.

Table 2. Physical and chemical properties of some cadmium compounds

Property	Cadmium	Cadmium chloride	Cadmium oxide	Cadmium sulphide	Cadmium carbonate	Cadmium acetate
Chemical formula	Cd	$CdCl_2$	CdO	CdS	$CdCO_3$	$Cd(C_2H_3O_2)_2$
Molecular weight (g/mol)	112.40	183.32	128.40	144.47	172.42	230.49
Physical state	Soft white metal	Small white crystals	Colourless, amorphous crystals	Yellow powder	White, amorphous powder	Colourless crystals
Boiling point (°C)	765	960	1,559	No data	No data	No data
Melting point (°C)	320.9	568	900	980	<500	255
Density (g/cm^3)	8.642	4.047	8.15	4.5-4.82	4.258	2.01–2.34
Vapour pressure (mm Hg)	1.4	No data	No data	No data	No data	No data
Solubility at 20°C (mg/L)	Insoluble	≥1,000	5	1.3	Insoluble	N/A

Sources: Eisler 1985; United States Environment Protection Agency [US EPA] 1985; Weast *et al*. 1985; Budavari *et al*. 1989; Lide 1992.

2.2 Geological Occurrence

Cadmium is a relatively rare element. It is uniformly distributed in the Earth's crust, where it is generally estimated to be present at an average concentration of between 0.1 and 0.5 mg/kg (Health Canada [HC] 2020). Cadmium occurs in nature in the form of various inorganic compounds and as complexes with naturally occurring chelating agents; organo-cadmium compounds are extremely unstable and have not been detected in the natural environment (HC 1986; World Health Organization [WHO] 1992*a*). The highest cadmium concentrations tend to occur in shales and marine phosphorites, with concentrations up to 90 and 340 mg/kg reported, respectively (WHO 1984). Typical concentrations in igneous, metamorphic and sedimentary rocks are 0.001 to 1.8, 0.04 to 1.0, and 0.3 to 11 mg/kg, respectively (WHO 1984).

No significant deposits of cadmium-containing ores are known.

2.3 Production and Uses in Canada

Cadmium is produced mainly as a by-product from mining, smelting and refining sulfidic ores of zinc and, to a lesser degree, lead and copper (Nordic Council of Ministers 2003). Small amounts of cadmium are produced from secondary sources. Approximately 10 to 25% of the production of cadmium in the western world now comes from recycled batteries and from residues or intermediate products (Natural Resources Canada [NRCan] 2009; United States Geological Service [USGS] 2013). Global production of refined cadmium metal was estimated at 22,000 metric tonnes in 2013, with a relatively constant production level since 1995 (NRCan 2009; USGS 2015). Canada is among the top five global producers of refined cadmium, with an estimated output of approximately 55 metric tonnes in 2016 (NRCan 2016). Approximately 90% of Canadian cadmium production, produced at four facilities (New Brunswick, Québec, Ontario and British Columbia), is exported (NRCan 2016).

Cadmium has a low melting point, excellent electrical conductivity and no definite odour or taste. Compounds containing cadmium exhibit excellent chemical and temperature resistance (International Cadmium Association [ICdA] 2004). Cadmium pigments produce intense colourings such as yellow, orange and red. There are five main industrial uses of cadmium: nickel/cadmium (NiCd) batteries, coatings, pigments, stabilizers in plastics and synthetic products, and alloys (USGS 2013). About 86% of total consumption in 2013 was for batteries, 9% for pigments, 4% for coatings and plating, and 1% for other uses including alloys, stabilizers and solar cells (USGS 2015). Canadian industrial consumption increased steadily between 1990 and 2001,

from 35.2 tonnes (Hoskin 1991; Koren 1992) to 213 tonnes (NRCan 2003) and remained relatively constant thereafter (207.9 and 204.5 in 2006 and 2007, respectively) (NRCan 2009).

2.4 Sources and Concentrations in the Canadian Environment

Cadmium has been detected in most environmental media in Canada, including air, freshwater, seawater, soils, sediments and biota. Cadmium is commonly found combined with other elements, for example CdO, $CdCl_2$ and CdS. Relatively high concentrations of metals can occur naturally in Canadian soils, stream sediments and water, blurring the distinction between anthropogenic pollution versus naturally occurring ore bodies. In general, there is a lack of data on the speciation of cadmium in the environment. Much of the cadmium found in mammals, birds, fish and components of the diet derived from these animals is probably bound to protein molecules such as metallothionein (MT).

Cadmium is found in the atmosphere (0.1 to 5 ng/m^3), crust (0.1 to 0.5 µg/g) and seawater (<5 to 110 ng/L) (Agency for Toxic Substances and Disease Registry [ATSDR] 2012; HC 2020; Nriagu 1989; Richardson *et al*. 2001). Rock erosion (wind-blown dust), forest fires, sea salt spray and volcanic eruptions result in cadmium emissions into the air. Richardson *et al*. (2001) estimated an annual release of 5.3×10^4 kg from natural sources in Canada (7.1×10^5 kg in North America and 4.1×10^7 kg globally). This global estimate is substantially greater than the previous estimate of 144 × 10 kg annually (Nriagu 1989). Globally, the production of non-ferrous metals and the combustion of fossil fuels contribute greatly to atmospheric cadmium emissions, accounting for 73 and 23% of anthropogenic cadmium emissions, respectively (Pacyna and Pacyna 2001).

Environment Canada (EC 2014) reported a decrease of about 90% (82 metric tonnes) in cadmium emissions into the air from 1990 to 2012, mainly due to a reduction from industrial sources (particularly non-ferrous smelting and refining). A reduction of 45% (~2 metric tonnes), mainly attributed to wastewater treatment plants, was also observed in cadmium releases into water from 2003 to 2012 (EC 2014). The National Pollutant Release Inventory reports indicate a continued decreasing trend in cadmium emissions in Canada. In 2013, releases of 7.2 metric tonnes into the air, 2.8 into water and 0.4 onto land (10.4 total; difference due to rounding) were reported (EC 2013) and, for 2015 and 2016, 6.35 metric tonnes into the air, 0.12 into water and 0.41 onto land (7.0 total; difference due to rounding) (Environment and Climate Change Canada [ECCC] 2017).

2.5 Ambient Air

The National Air Pollution Surveillance (NAPS) Network monitors ambient air in Canada. The data set most relevant to cadmium exposure via inhalation is the respirable size fraction (i.e., $PM_{2.5}$).

NAPS data (2012 to 2016) provide a range of 0.02 to 14.89 ng/m^3 in ambient air (median = 0.04 ng/m^3) (ECCC 2017; HC 2017), while Bari *et al*. (2015) and HC (2017) provide a range of 0.005 to 1.30 ng/m^3 (median = 0.03 ng/m^3) from a study of indoor air in Edmonton. NAPS data from 2003 to 2009 (5.73×10^{-7} - 1.85×10^{-2} µg/m^3; arithmetic mean = 0.15 ± 0.42 ng/m^3) (EC 2010) were used to develop the ambient air inhalation component of the estimated daily intakes (EDIs) for cadmium for the Canadian population (HC 2011). This data set represented the best and most comprehensive data available for Canada at that time. Given the small contribution of ambient air to EDIs, it was not deemed necessary to review the EDIs based on the newer NAPS data.

Appendix 1 provides concentrations in ambient air away from potential point sources.

2.5.1 Indoor Air

No database exists of cadmium indoor air concentrations for Canada (HC 2011) and limited data were identified in the literature.

HC (2011) estimated the indoor air concentration of cadmium based on data identified in the literature for the purpose of calculating EDIs for the Canadian population. Due to the small Canadian data set, data from two Canadian (Alberta Health 1998; Bell *et al*. 1994), four US (Adgate *et al*. 2007; Graney *et al*. 2004; National Human Exposure Assessment Survey [NHEXAS] 2003; Van Winkle and Scheff 2001), one Austrian (Komarnicki 2005) and one Singaporean study (Balasubramanian and Lee 2007) were used to derive probability distributions. From these, an arithmetic mean indoor air concentration of 0.3 ± 0.63 ng/m^3 (n = 818) was calculated (HC 2011). This indoor air concentration is within the range of the Canadian data summarized in Appendix 1.

2.5.2 Indoor Dust

Ingestion of dust and soil through repeated hand-to-mouth interactions is an important pathway for childhood exposure to cadmium. Environmental tobacco smoke, oil and gas heating, paints,

building materials, carpet dyes (red, orange and yellow), rubber underlay and the presence of a fireplace have been identified as potential indoor sources of cadmium within indoor dust (Bell *et al*. 1994; Fergusson and Kim 1991).

As with indoor air, no Canadian database exists for indoor settled dust. However, some available studies (government reports and peer-reviewed journals) provide measured values for Canadian cities. Due to the small Canadian data set, data from two Canadian (Rasmussen 2004*a* ; Rasmussen *et al*. 2001), two US (NHEXAS 2003; O'Rourke *et al*. 1999), two Australian (Chattopadhyay *et al*. 2003; Davis and Gulson 2005), one New Zealand (Kim and Fergusson 1993), one Bahrani (Madany *et al*. 1994), one Egyptian (Rashed 2008), one German (Seifert *et al*. 2000), one Turkish (Turkoglu *et al*. 2004) and one British study (Turner and Simmonds 2006) were used to develop probabilistic distributions for the derivation of EDIs. Based on this compilation of indoor settled dust data, an arithmetic mean of 6.98 ± 141.1 mg/kg was estimated (n = 5,061) (HC 2011). See Appendix 1.

2.5.3 Soil

Although no single soil concentration can adequately represent the variance in background soil concentrations across Canada (Reimann and Garrett 2005), it is essential to define a reasonable value for the purpose of developing generic national guidelines. Soil cadmium concentrations vary according to local geology; therefore, actual background concentrations at a given site may not resemble the national background soil concentration used to derive the SoQGs.

The Geological Survey of Canada (GSC) is an important source for geochemical data in Canada. Data downloaded from the GSC database for the <63 μm size fraction in till were used to estimate the background soil concentration used to derive the SoQGs (arithmetic mean = 0 .24 ± 0.41 mg/kg, range = 0.005 to 33.7 mg/kg, n = 14,812) (these data are summarized in HC 2011). These data were also used to develop the cadmium EDI values used in the SoQG calculation (HC 2011). The EDI methodology is further discussed in Section 5.2.

It should be noted that till is a mixture of grain sizes and is a result of glacial movement. Till chemistry is less susceptible to variation arising from anthropogenic sources than is the overlying soil layer. From a human health standpoint, the overlying soil (0- to 5-cm depth) is more relevant for exposure (HC 2011). Despite this, GSC data represent the best available information at this time.

Friske *et al*. (2014) reported GSC data from the 2008 and 2009 North American Soil Geochemical Landscape Project Field Surveys. The data include cadmium concentrations in the public health (PH) layer (0–5 cm) in addition to the 0–30-cm layer and the A, B and C horizons. Bioaccessibility data were not included in this study. The cadmium concentrations for the <2 mm fraction for the PH layer, 0- to 30-cm layer, and A, B and C horizons were 0.33 mg/kg (n = 363), 0.20 mg/kg (n = 157), 0.36 mg/kg (n = 329), 0.14 mg/kg (n = 336) and 0.11 mg/kg (n = 355), respectively. The results for the <63 µm unmilled fraction, for the B and C horizons, were 0.20 mg/kg (n = 335) and 0.16 mg/kg (n = 356), respectively.

Other studies (summarized in Appendix 1) provide concentrations in soil away from potential point sources. These studies were not used to calculate the estimate of typical concentration in soil in Canada.

Cadmium may be present in fertilizers as the result of recycling of by-products and waste materials (i.e., soil amendments). Agriculture and Agri-Food Canada (1997) provides a maximum acceptable cumulative metal addition to soil for soils and supplements of 4 kg/ha in 45 years, with maximum acceptable metal concentrations in products intended for use as fertilizer, which vary depending on the application rate (Canadian Food Inspection Agency [CFIA] 2020).

2.5.4 Surface Water

Cadmium concentrations in freshwater ranged from <0.002 µg/L in central Ontario lakes at least 70 km from smelter facilities to a mean of 122 µg/L in lakes within 20 km of Sudbury, Ontario (Lum 1987; Lum *et al*. 1991; Stephenson and Mackie 1988; Yan *et al*. 1990).

The concentration of cadmium in surface water was not included in determination of the EDI. A summary of concentrations of cadmium in surface water is presented in Appendix 1.

2.5.5 Groundwater

Although cadmium mobility may be enhanced under certain environmental conditions and, as such, pose a risk to groundwater quality (Section 3.2), reports on concentrations of cadmium in Canadian groundwater, including those near municipal landfills and contaminated sites, indicate that mean concentrations are well below 1 µg/L.

A summary of cadmium concentrations in groundwater is provided in Appendix 1. An average concentration of cadmium in Canadian groundwater was not determined for the purposes of setting a $SoQG_{HH}$.

Groundwater used as a source for drinking water is addressed in Section 2.5.6.

2.5.6 Drinking Water

HC (2011) estimated background cadmium concentration in Canadian drinking water at 0.165 ± 1.6 µg/L (arithmetic mean, n = 15,546), based on data obtained from the Ontario Ministry of Environment (1998 to 2007), Saskatchewan Ministry of Environment (2000 to 2009) and the Newfoundland and Labrador Department of Environment and Conservation (2000 to 2009). These data were used to derive the EDIs used to establish the $SoQG_{HHS}$. Data from other provinces were not available to include in the national background value estimate.

HC (2020) provides updated background concentrations of cadmium in raw water for the period between 2000 and 2016. As these data represent raw water and have a lower mean (0.07 µg/L) than that used to derive the EDIs, updating the EDIs based on this data was not warranted, as the values are still conservative.

The data included in the EDI, as well as additional Canadian background data, are presented in Appendix 1. The EDI methodology is further discussed in Section 5.2.

2.5.7 Sediment

The levels of cadmium found in sediment are not included in the determination of the SoQGs or EDIs. Canadian data on cadmium levels observed in sediment are presented in Appendix 1.

2.5.8 Biota Used as Human Food

A summary of concentrations in various tissues (most notably liver and kidney) of biota used as human food is provided in Appendix 1. Freshwater fish tend to have the lowest levels of cadmium (usually <0.5 mg/kg d.w.); oysters and clams are a bit higher at ≤20 mg/kg d.w.; and aquatic mammals (i.e., dolphins and whales) and terrestrial mammals (i.e., moose, hare and caribou) have the highest levels in renal tissues, reaching 138 and 106 mg/kg d.w., respectively.

Produce also contains high levels of cadmium, which are dependant on moisture content (Section 3.6). The highest concentrations were found in leafy plants (e.g., lettuce ≤668 mg/kg in 1973, but more recent (2009) data report ≤20 mg/kg), root vegetables (e.g., carrots ≤1.3 mg/kg) and grains (e.g., wheat or flax ≤1 mg/kg) (see Appendix 1 for details). Cadmium concentrations in biota used as food are included in the dataset used to generate the cadmium EDI from food.

2.5.9 Commercial Foods

Most foodstuffs consumed in Canada contain cadmium. HC's Food Directorate provides Canadian estimated daily cadmium intakes based on market basket surveys (Total Diet Studies [TDS]). The 2000 to 2007 TDS data (Dabeka *et al*. 2010) were considered the most appropriate to represent the Canadian population for EDI calculations since they were developed by HC in a methodical manner. The food groups that contribute the most to exposure in the general Canadian population are vegetables and grains (HC 2018). Populations that regularly eat food known to accumulate elevated amounts of cadmium (e.g., organ meats and shellfish from certain regions) may have greater background exposures to cadmium (HC 2018). The EDI methodology is further discussed in Section 5.2. Estimated daily cadmium intake through food ingestion (range = 0.177 to 0.486 µg/kg body weight per day [bw/d] for different age groups) is presented in Appendix 2.

A summary of cadmium concentrations in food from additional literary sources, including updated TDS data (HC 2018; 2020) and international data, is presented in Appendix 1. The EDIs were not updated based on the more recent TDS data, as estimated intake from foods (HC 2018) were in the same order of magnitude as those calculated from earlier TDS data (Dabeka *et al*. 2010).

2.5.10 Breast Milk

In estimating the average cadmium concentration in human breast milk, studies from other developed countries were considered due to limited Canadian data. Based on data from 11 human breast milk studies—two Canadian (Dabeka *et al*. 1986; Friel *et al*. 1999), three Italian (Coni *et al*. 2000; 1990; Turconi *et al*. 2004), one Swedish (Palminger Hallen *et al*. 1995), two Austrian (Krachler *et al*. 1998; 1999), one Japanese (Honda *et al*. 2003) and two Emirati (Abdulrazzaq *et al*. 2008; Kosanovic *et al*. 2008) (see Appendix 1)—HC (2011) calculated a mean cadmium concentration of 0.50 ± 1.71 µg/L (range = 0 to 16.8 µg/L; n = 896). These data were used to develop the cadmium EDI values which were used in $SoQG_{HH}$ calculations. The EDI methodology is further discussed in Section 5.2.

2.5.11 Human Tissues and Bodily Fluids

Several ongoing biomonitoring studies report the concentrations of chemicals, including cadmium, in human tissues and bodily fluids (AFN 2013; Arbuckle *et al*. 2016; HC 2019). These data do not figure in the development of $SoQG_{HHS}$ and are therefore not presented further herein.

2.5.12 Consumer Products

Contributions from consumer products to Canadian background exposures are not considered in $SoQG_{HH}$ development due to insufficient data. HC has set limits for cadmium in children's jewellery at 130 mg/kg to protect children who are more liable to mouth the jewellery and may therefore have higher exposures (HC 2013*a*). Leachate limits of 0.25 to 0.50 mg/L were set for ceramic and glassware (Department of Justice [DOJ] 1998) and limits were set for the coatings of children's toys (0.1% dissolving in 5% hydrochloric acid after 10 minutes stirring at 20ºC) (DOJ 2004).

Tobacco smoke is a major source of exposure for the general population. The estimated cadmium intake is approximately 1 µg/kg bw/d for people who smoke 20 cigarettes daily (Järup *et al*. 1998). Rickert and Kaiserman (1993) estimated that the mainstream smoke of Canadian cigarettes contained an average of 0.187 µg of cadmium per cigarette.

3.0 ENVIRONMENTAL FATE AND BEHAVIOUR

Cadmium exists in two oxidation states (0 and 2^+) in nature; however, the zero, or metallic, state is rare (National Research Council of Canada [NRCC] 1979). Cadmium does not break down in the environment, but it may be affected by physical and chemical processes that modify its mobility, bioavailability and residence time in different environmental media. Atmospheric cadmium compounds (e.g., cadmium oxide) are predominantly found in particulate form (fine particulates are more easily solubilized and more bioavailable than larger fractions), have relatively short tropospheric residence times, and are removed from air by wet and dry deposition. The mobility and bioavailability of cadmium in aquatic environments are enhanced under conditions of low pH, low hardness, low suspended matter levels, high redox potential and low salinity. The movement of cadmium in soil and potential accumulation by biota is enhanced by low pH, low organic matter content, large soil particle size and high soil moisture (EC/HC 1994).

3.1 Atmosphere

Cadmium has a boiling point of 765ºC, and therefore, it is not likely to volatilize except under extreme conditions. Volcanic activity (Nriagu 1980; 1989; Organisation for Economic Co-operation and Development [OECD] 1994; WHO 1992*b*; 2000) and forest fires (Nriagu 1980) are major natural sources of cadmium release to the atmosphere. Cadmium compounds emitted from high-temperature sources (>600ºC) (e.g., roasting of zinc ores, high-temperature incineration of sewage sludge, or burning of fossil fuels) oxidize rapidly to CdO (Nriagu 1980).

Most atmospheric cadmium is associated with respirable particulate matter (0.1 to 1 µm in diameter) (WHO 2000) and is subject to long-range atmospheric transport (Steinnes and Friedland 2006). Cadmium is removed from the atmosphere by dry deposition and by precipitation (WHO 1992*a*). Little information is available on atmospheric transformation processes. The cadmium compounds commonly found in air (e.g., CdO, $CdCl_2$ and $CdSO_4$) are resistant to photolytic degradation (ATSDR 2008). Cadmium may be dissolved in water vapour and subsequently removed by wet deposition (Fones and Nimmo 1993). In atmospheric aerosols measured in Ontario, water-soluble cadmium increased in areas with high-acidity air masses (Dvonch *et al*. 1993). Most of the cadmium released into the atmosphere is deposited within four weeks, and generally within 1,000 km of the source (Bewers *et al*. 1987).

3.2 Water

Weathering and erosion result in river transport of large quantities of cadmium to the world's oceans, with an estimated annual gross input of 15,000 tonnes (Joint Group of Experts on the Scientific Aspects of Marine Environmental Protection [GESAMP] 1987). The smelting of non-ferrous metal ores was estimated to be the largest human source of cadmium release into the marine environment (Nriagu and Pacyna 1988).

Gardiner (1974) and Vuceta and Morgan (1978) reported that a substantial proportion of the cadmium in rivers and lakes would be present as free Cd^{2+}; however, pH complexation by organic ligands and adsorption to particles would affect speciation. Most (up to 90%) of the cadmium present in freshwater systems occurs in the dissolved phase (i.e., <0.45 µm); however, at very high concentrations of suspended particulate matter (i.e., >200 mg/L), adsorbed cadmium predominates as a result of particle scavenging (Lum 1987). Cadmium entrained by particles and carried to bottom sediments is often released after oxidation or decomposition and is subsequently recycled into overlying waters. Concentrations of cadmium in lake waters are strongly dependent on pH and are consistently higher in acid lakes than in circumneutral systems (Steinnes 1990).

Most of the total cadmium entering the ocean from continental runoff is retained in estuaries, although 85% or more of dissolved cadmium may eventually enter the marine pelagic environment (Bewers *et al*. 1987). Dissolved forms of cadmium predominate (≤60%) in coastal waters (Lum 1987). The order of affinity for complexing ligands in most natural surface waters is humic acids > CO_3^{2-} > OH^- ≥ Cl^- ≥ SO_4^{2-} (US EPA 1979). In the dissolved state, cadmium is generally found as $Cd(H_2O)_6^{2+}$ in the water column (ATSDR 2012). At low salinity, free cadmium becomes more prevalent (Sprague 1986). The residence time for cadmium in the mixed layer of the Pacific Ocean is very short (<0.1 yr) compared to that of other metals (Bewers *et al*. 1987). Conversely, Wester *et al*. (1992) reported that cadmium had a mean residence time of four to 10 years in the waters of Lake Michigan.

3.3 Sediment

Cadmium enters sediment through precipitation and sorption to mineral surfaces, hydrous metal oxides and organic materials, of which humic acid is the main cadmium-absorbing component (ATSDR 2012). Depending on the type of sorption, cadmium may or may not be readily released or bioaccumulated (ATSDR 2012). For example, cadmium is less likely to be mobilized if linked with carbonate minerals or hydrous iron oxides, or formed as a stable solid, than if associated with mineral surfaces (e.g., clay or organic materials) (US EPA 1979). Sorption is directly proportional to pH (US EPA 1979) and cadmium may be released from sediments depending on the pH, salinity and redox potential of the aquatic system (Department of the Interior [DOI] 1985; Feijtel *et al*. 1988; Muntau and Baudo 1992; US EPA 1979) and the content of clay minerals, carbonate minerals, oxides, organic matter and oxygen in the sediment (McComish and Ong 1988). Bacteria may also aid in partitioning cadmium from water to sediment (Burke and Pfister 1988).

In seawater, much of the total cadmium (≤60%) is bound to or incorporated in organic matter, and as such, is constantly being removed from surface waters through biogenesis and sinking (Bewers *et al*. 1987). As a result, surface waters (<500 m) are typically depleted of cadmium. Upon decomposition at depth or through oxidation in sediments, much of the cadmium associated with organic matter is released into overlying waters or recirculated into the euphotic zone via vertical mixing (Bewers *et al*. 1987). Enhanced mobilization of cadmium from sediment, leading to increased cadmium water concentrations, may occur with reduced pH (WHO 1992*a*).

3.4 Soil

Soil pH appears to be the main factor controlling the solubility and availability of cadmium in soils, with numerous studies indicating that movement of cadmium within the soil matrix is more likely to occur under acidic conditions (Chanmugathas and Bollag 1987; Christensen 1989*a*; Eriksson 1989; Filius *et al*. 1998; Lodenius and Autio 1989; Sukreeyapongse *et al.* 2002). Suen-Zone *et al*. (1996) reported a linear increase in the log of the ratio of cadmium in soil to cadmium in solution from 0.8 for pH 3 to 3.7 for pH 10. Correspondingly, increased cadmium adsorption with increased pH was associated with decreased bioavailability (ATSDR 2008) (Section 3.6).

Soil type, including particle size and the presence of metal oxides, is another contributing factor in cadmium partitioning between dissolved and bound phases in soil. Generally, soil concentrations increase as particle size decreases (Rasmussen 2004*a*; Rasmussen and Hughes 2002). As such, clay soils have a higher affinity for cadmium than do silt or sand soils (Andersson 1979; Christensen 1984*a*; *b*; Inskeep and Baham 1983; McBride *et al*. 1981). Manganese and iron oxides play a role in reducing cadmium mobility in combination with an oxidizing redox soil environment (Benjamin and Leckie 1981; Bruemmer *et al*. 1988; Fu *et al*. 1991; Rieuwerts *et al*. 1998). Competition from other divalent cations, such as Ca^{2+}, can influence the adsorption of cadmium (Christensen 1984*a*) while the presence of anions, such as sulphate and phosphate, can create sparingly soluble cadmium salts (Farrah and Pickering 1977).

Organic matter in soils shows stronger sorption characteristics than clay minerals (Prokop *et al*. 2003) and can immobilize cadmium in soils (Blume and Brummer 1991; Liu *et al*. 2007; Suen-Zone *et al*. 1996). However, in some situations, the presence of organic matter can increase mobility; the formation of cadmium soluble complexes with inorganic ions (in particular with chloride ions) and organic ligands increases cadmium mobility in soils (Bollag and Czaban 1989; Christensen 1989*b*; McLean and Bledsoe 1992; Singh 1990).

Microorganisms may have either an inhibitory or a stimulatory effect on cadmium mobility in soil. Organic substances, such as various exudates and siderophores produced by some soil microorganisms, may chelate and effectively immobilize cadmium (Bollag and Czaban 1989). In addition, microbial production of hydrogen sulphide can result in the formation of very stable, insoluble cadmium sulphides (Bollag and Czaban 1989). On the other hand, microbial decomposition of organic matter or metal sulphides may result in the release of cadmium from stable complexes and, as such, increase its overall mobility (Cole 1979). The degree of mobilization is dependent on soil type, aeration and moisture content. Studies have shown that bacterial extracellular polymers can easily bind to metal ions and are very mobile in soil, making them a possible target for use in soil remediation (Jyh-Herng *et al*. 1995; Zhou *et al*. 2004).

Chemical precipitation can account for the loss of some metals from soil; however, cadmium precipitation is unlikely to occur in neutral or acidic soil conditions except where very high concentrations of carbonates, sulphates or phosphates occur (Beokhold *et al*. 1993).

Under certain circumstances, lateral transport, including aeolian and fluvial transport, has been shown to be an important environmental process affecting the fate of cadmium in soils. Nriagu and Pacyna (1988) calculated that wind erosion of soils constituted one of the largest natural cadmium fluxes into the atmosphere.

3.5 Indoor Dust

Concentrations of metals in indoor dust are commonly elevated relative to exterior dust and soil in ordinary urban environments (Rasmussen 2004*b*). This was partially attributed to the affinity of metals for the organic components of dust (Rasmussen 2004*a*), which is elevated in indoor dust relative to outdoor soil. The composition of indoor dust varies widely depending on many factors, including construction materials and architectural design, proximity to vehicular and industrial pollution sources, mode of heating and cooking, environmental factors (e.g., temperature, humidity) and variations in air exchange and particle infiltration rates in different climates and geographic regions (Rasmussen 2004*b*). There are also many indoor sources of particulate and gaseous air pollutants (Rasmussen 2004*a*). According to Hassan (2012), the most significant source of heavy metals in household dust was paint, especially yellow, which was associated with very high cadmium concentrations.

Quantitative information on the composition of indoor dust is currently limited. Metals occur in airborne particulate matter as both salts and complexed to inorganic and organic components (Rasmussen 2004*b*). Rasmussen and Hughes (2002) reported that the total metal content in dust increased with decreasing size fraction. Lidia (2004) reported that 58% of house dust particles ranged from 44 to 149 mm and that 6 to 35% were in the 30- to 63-mm size range (Hassan 2012). Cadmium in house dust also was much more bioavailable than cadmium in soil, likely due to the presence of inorganic compounds (Rasmussen and Hughes 2002).

3.6 Bioaccumulation and Bioconcentration

Plant uptake of cadmium from soils relies partly on soil characteristics such as soil type, pH, organic matter content, cation exchange capacity and soil nutrient status (Liu *et al*. 2007; Millennium 2013; Podar and Ramsey 2005; Shentu *et al*. 2008; Sun *et al.* 2007). Evidence suggests that plant uptake of cadmium decreases with increasing pH from acid to neutral (pH 1 to 7) soils

but is unchanged or increases in alkaline soils (pH >7) (Bolan *et al*. 2003; Podar and Ramsey 2005) in the presence of increased cadmium in soil solution (Tyler and Olsson 2001). The soil quality guidelines protocol (CCME 2006) does not explicitly address the uptake of metal contaminants into produce. However, a large body of literature exists to show that cadmium is among the most easily mobilized and assimilated metal contaminants in soil. Young, leafy plants with high transpiration rates tended to have higher cadmium uptake values than other plant tissues with high available moisture (Millennium 2013).

Bioaccumulation has been reported in the tissues of terrestrial wildlife. Cadmium concentrations in various waterfowl, rabbits, caribou and deer tissues are presented in Appendix 1. Generally, low concentrations (often undetectable) of inorganic metals are transferred from contaminated feed to muscle tissue; however, over time, concentrations of cadmium tend to accumulate in organs, particularly kidney and liver (Office of Environmental Health Hazard Assessment [OEHHA] 2012). The highest values (55.2 to 219.9 mg/kg d.w.) were reported in adult Arctic hare kidney (Pedersen and Lierhagen 2006). Long-lived ungulates, such as moose, caribou and elk, can accumulate significant levels of heavy metals, including cadmium, as they age (Danielsson and Frank 2008; Frøslie *et al*. 1986).

The bioavailability and bioaccumulation of cadmium in aquatic life have been linked to pH (uptake increases as pH declines), water hardness (higher uptake in softer water conditions), dissolved organic matter, and oxygenation (poorly oxygenated water environments related to higher cadmium uptakes by some aquatic species) (Australia and New Zealand Water Quality Guidelines [ANZWQG] 2000; Tran *et al*. 2001).

4.0 BEHAVIOUR AND EFFECTS IN HUMANS AND EXPERIMENTAL ANIMALS

4.1 Overview

Results from investigations into non-cancer effects, conducted in experimental animals (Section 4.4), indicate that exposure to cadmium is associated with a variety of effects including kidney, bone and liver injury as well as effects on reproduction and development. Pulmonary inflammation and tissue degeneration have been observed in inhalation experiments. Adverse renal and skeletal effects have been extensively documented in occupationally or environmentally exposed humans (Section 4.5), with some recent studies suggestive of adverse health effects on other organ systems as well.

Cadmium is identified as a multi-route (oral, inhalation, parenteral), multi-site and multi-species (mice, hamster, rats) carcinogen in experimental animals (Section 4.4.3). Epidemiological studies indicate that cadmium is carcinogenic to humans by inhalation and may also be carcinogenic via the oral route (Sections 4.5.2.3 and 4.5.2.4). The mechanisms involved in cadmium-induced carcinogenicity are not yet completely elucidated but they may include indirect genotoxicity and epigenetic mechanisms (Section 4.2).

It is not the role or the intention of this document to comprehensively re-evaluate the toxicology of cadmium. Although many reports were consulted, the information is presented below in a highly summarized format. The studies most relevant to the development of cadmium toxicological reference values (TRVs) are presented with greater detail than are supporting studies, which are summarized primarily to illustrate the range of health effects that may result from exposure to cadmium. For more information on dosing, exposure conditions and periods, the specific compounds administered, and the specific effects observed, the reader should consult the cited references. Note that no information related to the toxicology specific to cadmium-containing nanoparticles is presented in this report.

4.2 Mode of Toxicity

Cadmium (Cd^{2+}) can substitute for calcium and zinc ions in biological systems (e.g., many enzymes and sequence-specific DNA-binding factors that usually require zinc) (Beyersmann and Hartwig 2008), and the toxic effects of cadmium can be modulated by co-exposure to zinc.

Most cadmium is bound by MT, which enhances its long retention within tissues and decreases biliary excretion (Klaassen *et al*. 2009). Synthesis of MT in the liver, kidney and intestine is readily induced by metal ions (notably zinc, but also cadmium) and helps protect from cadmium toxicity (Klaassen *et al*. 2009; Coyle *et al.* 2002). This protective effect is mainly due to cadmium sequestration away from critical macromolecules (Klaassen *et al.* 2009).

The intracellular mechanisms thought to be involved in cadmium-induced toxicity are both broad and complex and have been the subject of several literature reviews (Cuypers *et al*. 2010; Moulis 2010; Thévenod 2010; Van Kerkhove *et al*. 2010). The most extensively investigated critical target organ of cadmium toxicity is the kidneys. Long-term exposure can lead to accumulation in the proximal tubules of the renal cortex, leading to morphological changes that can result in renal dysfunction followed by nephritis, necrosis and renal cancer (HC 2020; Joint Food and Agriculture Organization [FAO]/WHO Expert Committee on Food Additives [JECFA] 2001; WHO 1992*a*). Toxicity occurs when a threshold of cadmium is reached in the renal cortex and the kidney is no

longer able to neutralize intercellular cadmium with MT (Sabolić *et al*. 2010). The resulting damage has been reported to include disruption of ion transport homeostasis, impaired control of biological cations, and disruption of cell signalling pathways (HC 2020; Van Kerkhove *et al.* 2010). Respiration is inhibited and reactive oxygen species are generated in the mitochondria, which induce oxidative stress (Cuypers *et al*. 2020; Patra *et al.* 2011).

Bones are another sensitive target. Cadmium-induced bone injuries include osteopaenia, osteoporosis, osteomalacia and itai-itai disease (which also involves renal injury). Effects can result from both direct action (bone resorption and decrease in osteoblast bone formation) and indirect action (disturbance in vitamin D and calcium metabolism) (Bhattacharyya 2009; Brzóska and Moniuszko-Jakoniuk 2005*a*; HC 2018; Järup *et al*. 1998; JECFA 2004*a*; *b*). More recently, it has been demonstrated that cadmium chloride suppresses the osteogenesis of bone marrow mesenchymal stem cells by inhibiting the Wnt/β-catenin pathway, indicating another possible mechanism for cadmium-induced bone injury (Wu *et al*. 2019).

Considering that cadmium has shown clastogenic effects (ATSDR 2008) but is mutagenic only at high concentrations (Hartwig 2010) and does not form stable DNA adducts, a direct genotoxic mechanism is unlikely. In addition, since cadmium is not a redox active metal, it is unlikely that indirect oxidative DNA damage is a primary mechanism of toxicity. Consequently, indirect genotoxicity or epigenetic mechanisms (e.g., changes in gene activation, suppressed apoptosis, altered DNA repair) may be involved in cadmium-induced carcinogenesis (International Agency for Research on Cancer [IARC] 2012; Waalkes 2000; 2003).

4.3 Toxicokinetics

4.3.1 Absorption

4.3.1.1 Ingestion

Diet is the main source of exposure to cadmium within the general (non-smoking) population (ATSDR 2012; Olsson *et al.* 2002). The rate of gastrointestinal absorption of cadmium is lower in small experimental animals (0.5 to 3%) than in humans (1 to 10%) (JECFA 2011).

Cadmium absorption in the intestinal mucosa generally occurs in two phases: uptake from the lumen into the mucosa, followed by transfer into circulation (Foulkes 1980; 1985; Zalups and Ahmad 2003). Absorption is influenced by several factors related to physiological status (e.g., age, nutritional status) and diet (e.g., fiber level, type of food) (Ruoff *et al*. 1994). Age decreases apparent absorption (based on retention) in humans and rodents (Eklund *et al*. 2001; Horiguchi *et*

636 *al*. 2004*a*), with absorption rates higher in neonates or young rodents than in adults (Nordberg *et*
637 *al*. 1985; Sasser and Jarboe 1980). This may be due to longer retention in the small intestine (and
638 a prolonged absorption period) in early life, as shown in newborn rats (Eklund *et al.* 2001).
639 Elevated absorption (55%) was also reported in children (three months to 10 years of age), but
640 urinary excretion was higher than dietary intake (Alexander *et al*. 1974), suggesting that cadmium
641 may not accumulate in children. This absorption rate was consistent with values (4 to 37%)
642 reported in 12-month-old infants (Crews *et al*. 2000).

643 Cadmium absorption from dietary sources was enhanced in marginally zinc-, iron- and/or calcium-
644 deficient rodents (Flanagan *et al*. 1978; Nordberg *et al*. 1985; Reeves and Chaney 2001; 2002;
645 2008; Schäfer *et al*. 1990) but the presence of adequate levels of some competitors, such as zinc,
646 can independently minimize cadmium absorption (Reeves and Chaney 2001). Studies indicate that
647 absorption of cadmium is slightly higher in women than men (Olsson *et al*. 2002), which may be
648 explained by lower iron status in women. Cadmium uptake was also increased by 13 to 15% during
649 pregnancy (Kippler, Goessler *et al.* 2009).

650 The bioavailability of cadmium from various food sources will differ (Chunhabundit *et al*. 2011;
651 Eklund *et al*. 2001; 2004; Glaser *et al*. 1986; Reeves and Chaney 2008; Rusch *et al*. 1986).
652 Gastrointestinal absorption of soil-adsorbed cadmium is lower than for cadmium in solution
653 (Schilderman *et al*. 1997). Relative bioavailability (RBA) factors (bioavailability of Cd in soil
654 compared to that of $CdCl_2$ in solution) varied from 8 to 88% (stomach simulation) and 7 to 77%
655 (stomach and intestine simulation) and were validated by comparison with RBA factors obtained
656 *in vivo* in swine (9 to 89%) (Denys *et al*. 2012).

657 **4.3.1.2 Inhalation**

658 The fate and disposition of inhaled cadmium are governed by particle size. Larger particles
659 (>10 μm in diameter) will deposit in the upper airways whereas smaller particles (~0.1 μm) can
660 penetrate into alveoli, where the majority of absorption occurs (ATSDR 2012).

661 Human data on cadmium deposition, retention and absorption in the lung are very limited. Using
662 a human lung physiology model, deposition in the alveoli was estimated at 5 to 50%, and from 9
663 to 83% in the upper respiratory tract (particle size ≤1 to 10 μm) (Nordberg *et al.* 1985).

664 Studies in experimental animals showed that lung retention was greatest (5 to 20%) after short-
665 term exposures (15 minutes to two hours) (Barrett *et al*. 1947; Henderson *et al*. 1979; Moore *et al*.
666 1973; Rusch *et al*. 1986). Following cessation of exposure, the initial lung burden declined slowly

due to clearance and absorption (Barret *et al*. 1947; Henderson *et al*. 1979; Rusch *et al*. 1986). Slightly lower retention rates occurred with extended exposure (Glaser *et al*. 1986).

4.3.1.3 Dermal Absorption

Dermal absorption of cadmium is a slow process and would be of concern only in situations where concentrated solutions are in contact with the skin for prolonged periods of time (ATSDR 2012).

Cadmium absorption from water or soil vehicles differ. Wester *et al*. (1992) observed different partition coefficients in various skin compartments after application of $CdCl_2$ solution or cadmium in soil. After application of aqueous cadmium chloride solution (0.116 mg/L for 16 hours), 0.1 to 0.6% of cadmium entered the plasma, while 2.4 to 12.7% remained in epithelial cells and 74 to 93% remained unabsorbed on the skin surface. In comparison, retention levels were 0.02 to 0.07%, 0.06 to 0.13%, and 82 to 100% of the applied dose in plasma and epithelial cells, respectively, after application in soil.

4.3.2 Distribution and Accumulation

The distribution pattern is similar among animals and humans and seems to be dependent on the duration, but not the route, of exposure (ATSDR 2012). Once absorbed, cadmium is transported by both red blood cells and plasma. Cadmium is usually bound to MT (in the liver) or to other sulfhydril-rich proteins, peptides or amino acids (Goyer 1991; Zalups and Ahmad 2003).

Higher cadmium concentrations can initially be found in the liver but redistribution to the kidneys occurs over time (HC 2020; Massányi, Toman *et al.* 1995; Massányi, Uhrin et al. 1995). Cadmium was detected in virtually all tissues in post-mortem (JECFA 2011). *In vivo* analyses of adults from industrialized countries showed the highest concentrations in the kidneys, followed by the liver and muscles (ATSDR 2012; Christoffersen *et al.* 1988; Elinder 1985; Kjellstrom 1979; Salmela *et al*. 1983; Saltzman *et al.* 1990).

A human milk-to-plasma ratio of 3:4 indicates an apparent absence of a transfer barrier (Kippler, Lönnerdal *et al.* 2009). Concentrations in human milk were approximately 8% of the maternal blood concentration in non-smoking mothers (Radisch *et al.* 1987). A negative association with calcium levels suggested that cadmium inhibits calcium secretion into human milk.

Accumulation of cadmium is a function of age. In humans, the body burden of newborns was estimated to be less than 0.001 mg (Ellis *et al*. 1979) while the body burden in the general

population was in the range of 8 to 19 mg (Ellis *et al.* 1979; Salmela *et al*. 1983; Saltzman *et al*. 1990).

4.3.3 Metabolism

Cadmium is not metabolized in the human body (HC 2020). In plasma and tissues, cadmium ions (Cd^{2+}) can bind to anionic groups (e.g., sulfhydryl groups), which enables transport into plasma (ATSDR 2012; Carson 1984). Albumin-bound cadmium is largely taken up by the liver, which dissociates the cadmium-albumin complex and releases most of the MT-bound cadmium (European Food Safety Authority [EFSA] 2009*a*).

4.3.4 Elimination and Excretion

Most (90%) ingested cadmium (or inhaled and ingested from mucocilliary clearance) is excreted unabsorbed in the feces (JECFA 1972). Absorbed cadmium is excreted in very small amounts equally in feces and urine (ATSDR 2008; Nordberg *et al*. 2007). It is thought that fecal excretion involves the biliary excretion of a cadmium-glutathione conjugate and the sloughing of mucosal cells containing cadmium-MT.

Urinary excretion of cadmium increases with age and increasing cadmium body burden (JECFA 2004*a*; *b*; Nordberg *et al*. 2007). The biological half-life of cadmium ranges from several months to years in experimental animals and 10 to 30 years in humans (Kjellström and Nordberg 1978; Nordberg *et al*. 2007).

4.3.5 Concentrations in Human Biological Fluids

Blood and urine cadmium levels reported by various epidemiological studies are shown in Appendix 7. As they do not figure in the derivation of $SoQG_{HH}$, they are not discussed further.

4.3.6 Pharmacokinetic Modelling

Pharmacokinetic models are often used in human health risk assessment to estimate relationships between exposure (e.g., dietary intake or inhalation dose) and internal dose to critical organs, or between exposure and concentrations in blood, urine or other biological media used in biomonitoring. Two models have been used to relate urinary cadmium (UCd) concentrations and exposure:

- The modified Nordberg-Kjellström model (Kjellström and Nordberg 1978; Nordberg *et al.* 1985) is a linear multi-compartment model largely based on human data that describes cadmium distribution via the oral and inhalation routes.
- A simplified one-compartment model that describes the relationship between urinary cadmium and dietary intake (Amzal *et al.* 2009).

4.4 Mammalian Toxicology

4.4.1 Acute and Short-Term Toxicity

4.4.1.1 Oral Studies

Lethality (LD_{50}) occurred at oral doses of approximately 100 to 300 mg/kg bw in mice and rats (JECFA 2001*a*), with rats appearing less sensitive than mice, and the young more sensitive than adults, probably due to the greater fractional absorption of ingested cadmium in developing organisms (ATSDR 2012).

Common non-lethal effects of short-term oral exposure (<30 days) in experimental animals include reduced growth and body weight, necrotic changes to the kidneys, liver hemorrhages, reddening and ulcers of the intestinal tract and stomach, testicular atrophy, and other hormonal, hematological, neurological and immune system effects (ATSDR 2012; Borzelleca *et al*. 1989; Caride *et al*. 2010*a*, *b*; Government of Canada 1994; Höfer *et al.* 2009; 2012; Miler *et al.* 2010). The no-observed-adverse-effect levels (NOAELs) for these non-lethal effects range from 1.12 to 65.6 mg/kg bw/d (ATSDR 2012).

4.4.1.2 Inhalation Studies

Acute toxicity after inhalation exposure to cadmium fumes has been investigated in rodents and primates (Barrett *et al*. 1947; Friberg 1950*a*; *b*; National Toxicology Program [NTP] 1995; Rusch *et al*. 1986). LC_{50} doses vary with animal species, dosage and cadmium compound administered.

Non-lethal effects from acute or short-term inhalation exposure (<30 days) include inflammatory and degenerative lung effects (Boudreau *et al.* 1989; Buckley and Bassett 1987; Bus *et al.* 1978; Grose *et al.* 1987; Hart 1986; Henderson *et al.* 1979; NTP 1995; Palmer *et al.* 1986; Snider *et al.* 1973).

4.4.1.3 Dermal Studies

No studies investigating systemic health effects in animals following acute or short-term dermal exposures to cadmium were identified in the literature.

4.4.2 Sub-Chronic and Chronic Toxicity

4.4.2.1 Oral Studies

The most sensitive targets of cadmium toxicity appear to be the kidneys and skeletal system.

Renal effects were examined in a number of species, including mice, rats, rabbits, dogs and monkeys (ATSDR 2012; WHO 1992*b*), particularly in association with elevated cadmium concentrations in the renal cortex (JECFA 2001; WHO 1992*b*). Proteinuria, a renal effect characteristic of tubular dysfunction, is considered the first sign of cadmium-induced kidney damage (Consumer Product Safety Commission [CPSC] 2010; HC 2018). Reported NOAELs and lowest observed adverse effect level (LOAELs) range from 0.4 to 2.6 mg/kg bw/d and 1.5 to 14 mg/kg bw/d, respectively (JECFA 2011). Another indicator of changes in renal reabsorptive capacity is hypercalciuria, which was reported in rats (Bernard *et al*. 1982; Brzóska and Moniuszko-Jakoniuk 2005*a*; Prozialeck and Edwards 2010). If exposure to cadmium continues, impaired glomerular filtration may result, causing increases in serum creatinine and blood urea nitrogen concentrations (HC 2018; JECFA 2011).

Bone is another sensitive target of cadmium toxicity. Risk of bone disease may occur at the same dose range (or lower) than those associated with renal effects (Brzóska *et al*. 2005; HC 2018; Jarup *et al*. 1998). Cadmium can cause abnormal calcium homeostasis, which affects bone mineralization (Jarup *et al*. 1998; Yokota and Tonami 2008). Cadmium bone toxicity is greater in rapidly growing weanling rats than in adults (Ogoshi 1992) and is greater in females than in males (Bhattacharyya 2009; Brzóska and Moniuszko-Jakoniuk 2005*b*; Järup *et al*. 1998).

Long-term oral cadmium exposure also produced effects in rat liver, including biochemical changes (Sporn *et al.* 1970), alteration of zinc metabolism (Petering *et al*. 1979) and liver necrosis (Sutou *et al*. 1980). Other studies reported anemia, reduced weight, and peripheral neuropathy in rats exposed over periods of three to five months via food or drinking water (ATSDR 2012; Groten *et al.* 1990; Pleasants *et al.* 1993; Sato *et al*. 1978; Valois and Webster 1989; Watanabe *et al.* 1986).

4.4.2.2 Inhalation Studies

Pulmonary effects from subchronic cadmium inhalation exposures were similar to those observed for acute exposures, including immunological responses, tissue damage and increased relative lung weight (ATSDR 2012; Glaser *et al.* 1986; Kutzman *et al*. 1986; NTP 1995; Prigge 1978). Mortality was also observed after chronic exposure in rats (Oldiges *et al.* 1989).

4.4.2.3 Dermal Studies

No studies investigating the chronic dermal exposure of experimental animals to cadmium or cadmium compounds were identified in the available literature.

4.4.3 Carcinogenicity Studies

Reports have indicated that cadmium compounds are multi-tissue animal carcinogens via oral, inhalation and subcutaneous injection routes of exposure (IARC 1993; 2012). Long-term inhalation exposure resulted in a clear dose-response increase in lung tumours in rats and mice.

Long-term oral exposure resulted in increased incidence of leukemia and prostate and testicular tumours in rats at high doses; however, no clear dose-response relationship was observed (Waalkes and Rehm 1992). Another study showed that prostate tumours occur only at exposures below those that cause testicular tumours (Jarup *et al*. 1998), while other studies did not observe increased tumour incidence (Levy and Clack 1975; Levy *et al.* 1975; Löser 1980). The relevance of this endpoint to humans was questioned in other studies (JECFA 2011).

While most inhalation studies delineated a strong carcinogenic potential for cadmium in the lungs, there was no evidence of carcinogenicity in other tissues in rats exposed via inhalation (ATSDR 2012; IARC 2012; Takenaka *et al.* 1983). Concentrations associated with tumours varied with species, dosage and the cadmium compound administered (Glaser *et al.* 1990; Heinrich *et al.* 1989; 4; 1989; Pott *et al.* 1987).

4.4.4 Reproductive and Developmental Toxicity

A number of studies investigated the effects of cadmium on reproduction and development in animals, generally at higher doses than those associated with renal effects (see ATSDR 2012). Data from oral studies indicate that cadmium exerts toxic effects on the reproductive system, especially in males and in foetuses, particularly with respect to neurobehavioural development

(JECFA 2004). Neurobehavioural developmental and other measures of foetotoxicity and adverse reproductive effects have also been observed in inhalation studies, but at significantly higher doses than those resulting in increased tumour incidence (ATSDR 2012).

4.4.5 Genotoxicity

The genotoxic potential of cadmium was investigated in experimental animals and in epidemiological studies of occupationally exposed individuals and the general population (ATSDR 2012). Cadmium compounds generally did not demonstrate any direct genotoxic effects (EFSA 2009*a*; Hartwig 2010; JECFA 2011). However, there is evidence for clastogenic effects (induction of DNA damage, micronuclei, sister chromatid exchange and chromosomal aberrations) (ATSDR 2012; Beyersmann and Hartwig 2008; Çelik *et al.* 2009; Joseph 2009; Tapisso *et al.* 2009).

4.5 Human Toxicology

4.5.1 Acute, Short-term and Subchronic Toxicity: Case Reports

Numerous case reports identify skin and eye irritation as well as acute poisoning (including lethality) in humans following either inhalation or ingestion of high (unspecified) concentrations of cadmium (ATSDR 2012; Hazardous Substances Data Bank [HSDB] 2005; US EPA 1985; WHO 1992*b*). No studies examining the subchronic toxicity of cadmium in humans were identified (ATSDR 2012).

4.5.2 Chronic Exposure: Epidemiological Studies

Epidemiological studies of occupationally or environmentally exposed populations usually estimated cadmium exposure and kidney by measuring biomarkers (Section 4.5.2.1). The dose-response relationship derived from human data and a summary of some epidemiological studies are presented in sections 4.5.2.3 and 4.5.2.4. Additional studies are summarized in Appendix 7. Generally, environmental studies refer to oral (dietary) exposure to cadmium while occupational studies refer to inhalation exposure.

4.5.2.1 Biomarkers of Exposure to Cadmium

Blood (BCd) and urinary cadmium (UCd) concentrations and excretion rates are the most commonly used biomarkers to identify and estimate human exposure. Blood cadmium concentration is generally a good indicator of recent exposure; long-term exposure is better evaluated using UCd excretion, which is mainly influenced by cadmium body burden (Ghezzi *et al.* 1985; Lauwerys *et al.* 1994; Järup *et al.* 1988; Roels *et al.* 1989). Nevertheless, long-term exposure estimates, as determined by UCd, can be compromised by recent cadmium exposures (Bernard and Lauwerys 1986; Järup 2002) and reduced kidney efficiency in individuals above 60 years of age (Satarug *et al*. 2010).

As the cadmium body burden reaches levels that disrupt the tubular reabsorptive process, UCd increases in an almost linear manner; however, when renal cadmium concentrations are sufficient to cause tubular damage, UCd levels increase markedly (Prozialeck and Edwards 2010). Significant correlations have been established between total cadmium exposures and UCd concentrations in environmentally exposed populations (e.g., Ikeda *et al*. 2005*a*; b; Kido *et al*. 2004; Kobayashi *et al*. 2005; Shimbo *et al*. 2000). Modelization can be used to predict kidney and UCd concentrations reflective of dietary intake (e.g., Amzal *et al.* 2009; Choudhury *et al*. 2001).

Cadmium in hair has also been proposed as a potential biomarker of exposure; however, human hair may not be a reliable indicator of endogenous cadmium concentrations (Frery *et al.* 1993; Huel *et al*. 1984; Lauwerys *et al.* 1994; Shaikh and Smith 1984; Wilhelm *et al*. 1990).

MT levels can also indicate recent exposure; however, they can be affected by other factors, including exposure to other metals (Hochi *et al*. 1995; Kawada *et al*. 1990; Lu *et al*. 2001; Shaikh and Smith 1984; Tohyama *et al.* 1981; Waalkes and Goering 1990).

Cadmium in fecal matter has been used to estimate dietary intake, as cadmium is poorly absorbed in the gastrointestinal tract (Kjellström *et al.* 1978).

4.5.2.2 Biomarkers of Effects

A wide range of human enzymes, proteins and amino acids can be used to establish evidence of cadmium toxicity. Many are primarily located in the tissues most greatly affected by cumulative storage of cadmium (kidneys, bones and liver).

The presence of low molecular weight proteins (e.g., β_2-microglobulin (β_2MG) and retinol-binding protein (RBP) in urine are early signs of cadmium-induced renal toxicity (EFSA 2009*a*; HC 2018).

N-acytyl-β-D-glucosaminidase (NAG) is another reliable urinary biomarker of renal injury (Prozialeck and Edwards 2010).

4.5.2.3 Environmental Exposure

Using liver concentrations from individuals with cadmium-induced bone disease (from areas with elevated cadmium in soils used to grow rice) (Yamagata and Shigematsu 1970), Kjellström (1985) estimated their intake at 1 to 2 mg/d for many years. Chinese epidemiological data suggest that decreased bone mineral density correlates to previous cadmium-related kidney impairment, with a more marked relationship in women (Chen *et al.* 2011; Jin *et al.* 2004). Population data taken 10 years after cessation of elevated dietary exposure suggest that cadmium-related bone effects were irreversible (Chen *et al.* 2009). Renal damage caused by cadmium was also generally irreversible (Järup 2002; Kah *et al*. 2012; Kjellström 1985).

A limited number of epidemiological studies also suggest that cadmium may also contribute to diabetes, cardiovascular effects, hypertension, neurotoxicity, reproductive and developmental toxicity and macular degeneration (ATSDR 2012; EFSA 2009*a*; *b*; Järup and Åkesson 2009; JECFA 2004*a*; *b*; 2011; Satarug *et al.* 2010; 2017).

Associations between long-term exposure to cadmium and cancer or biomarkers of cancer were also suggested by epidemiological studies conducted in environmentally exposed populations (Huff *et al.* 2007; IARC 2012; Satarug *et al.* 2010). However, at present, investigations of environmental exposure to cadmium in relation to different cancers are limited and have not been used to derive TRVs (HC 2018).

Critical effect levels were derived for bone and kidney effects for those studies in which dose-response relationships were established. These levels were represented by a LOAEL or a lower limit of the 95% confidence interval for the benchmark dose (BMDL).

A summary of the analysis of cadmium effects on kidneys and bones is presented below. Representative studies are included in Appendix 7, with details on levels of exposure and the associations with biomarkers of effect.

Renal Effects

It is well established that inhalation or oral cadmium exposure can induce nephrotoxicity in humans (ATSDR 2008; EFSA 2009*a*; *b*; HC 2018; JECFA 2010), especially in subpopulations

that are more sensitive to cadmium-induced renal dysfunction, such as those with diabetes (Järup and Åkesson 2009; Nawrot *et al*. 2010). Numerous epidemiological studies on cadmium-induced nephrotoxicity have been thoroughly reviewed and summarized (ATSDR 2012; EFSA 2009*b*; HC 2020; JECFA 2001; 2004*a*; *b*; 2011; Nordberg *et al*. 2008; WHO 2011*b*).

For the purposes of health risk assessment, urinary β_2MG of >300 µg/g creatinine is considered an indicator of kidney damage and an adverse effect (ATSDR 2008; EFSA 2009*a*; *b*; JECFA 2011). JECFA (2011*a*) reviewed the epidemiological evidence for renal effects associated with cadmium exposure and chose to use a meta-analysis carried out by EFSA relating UCd and urinary β_2MG. The database for this meta-analysis covered 35 studies and approximately 30,000 non-occupationally exposed individuals. An analysis of group mean data for individuals over 50 years of age (i.e., age group considered to be at steady state) showed that β_2MG excretion in urine was relatively constant at levels of UCd less than 5.24 µg/g creatinine (EFSA 2009*a*). A lower 95% confidence limit on the $BMDL_{05}$ (benchmark dose for a 5% response) of 4.0 µg/g creatinine was identified based on the 300 µg/g creatinine cadmium urinary β_2MG indicator (EFSA 2009*a*).

Bone Disease

While cadmium exposure can alter calcium metabolism in bone and may increase the risk of osteoporosis, dose-effect and dose-response relationships have proven difficult to characterize due to confounding variables such as sex, age, nutrition and hormone status (JECFA 2003), and results have been inconsistent (HC 2018). Therefore, Health Canada deemed it premature to base risk assessments on bone effects (HC 2018) and EFSA did not include these effects in their meta-analysis of epidemiological data (EFSA 2009*a*). More recent studies were reviewed by HC (2020), which, once again, indicates that more research is needed before these effects can be used for risk assessments.

While bone effects have been observed in experimental animals at lower doses than those associated with renal effects, results from epidemiological studies are inconsistent (HC 2018).

4.5.2.4 Occupational Exposure

Occupational exposures are generally associated with higher concentrations in exposure media than for environmental exposures. Various investigators reported thresholds for tubular dysfunction and proteinuria, based on a number of urinary markers of renal dysfunction (Ellis *et al.* 1981; Falck *et al.* 1983; Järup *et al.* 1988; Kjellstrom *et al.* 1984; Mason *et al*. 1988; Roels *et al*. 1981; 1983; Roels, Lauwerys, Buchet and Bernard 1981; Smith *et al*. 1980; Thun *et al.* 1989).

End-stage renal disease did not appear to be a common cause of death in occupationally exposed individuals (ATSDR 2012); however, increased mortality from other renal diseases were reported in some studies (Armstrong and Kazantzis 1983; 1985; Elinder *et al.* 1985; Nakagawa *et al.* 1987). Increased mortality due to diabetes was also reported in environmentally exposed Japanese women (Nakagawa *et al.* 1987).

Respiratory and renal effects of occupational exposure were investigated in three different factories (Lauwerys *et al.* 1974). Women had higher UCd than the controls but there was no effect on respiratory function, proteinuria or other biological indices. Men had reduced respiratory function, changes in blood enzyme activity (increased β-galactosidase and lactate deshydrogenase, decreased red blood cell acetylcholinesterase), decreased hematocrit and abnormal electrophoretic pattern of urinary proteins.

Bone effects were also reported among cadmium-exposed workers. In a study of Belgian ex-workers, an association between UCd and decreased bone mineral density and a higher risk of osteoporosis in the absence of tubular renal dysfunction were observed (Nawrot *et al.* 2010).

Several studies also evaluated the possible association between occupational exposure and carcinogenicity (Huff *et al.* 2007; IARC 1993; 2012; Lemen *et al.* 1976; Stayner *et al.* 1992*a*; *b*; Thun *et al.* 1985). In spite of confounding factors, there is some evidence that prolonged inhalation exposure increased lung and prostate cancer-related mortality (IARC 1993; 2012; Stayner *et al.* 1993). Other studies also indicate an association with renal cancer (Huff *et al.* 2007; IARC 2012) and pancreatic cancer (Amaral *et al.* 2012; Schwartz and Reis 2000).

4.6 Overall Toxicological Evaluation for Humans

The current TRVs, or exposure limits for cadmium, are summarized in Appendix 8 (cancer-based values) and in Appendix 9 (non-cancer-based values).

4.6.1 Susceptible Populations

Some individuals may be more susceptible to the toxic effects of cadmium due to a higher absorption rate (e.g., children, women), the interaction of some factors with a mechanism of toxic cadmium action (e.g., hormonal status, nutrient status) or a genetic polymorphism (Miura 2009; Satarug *et al.* 2010). The subpopulations identified as susceptible include individuals with diabetes, low iron status (e.g., dietary deficiency, people with low ferritin) and possibly low zinc

intake (Åkesson *et al.* 2005; Edwards and Prozialeck 2009; Lin *et al*. 2013). Women are more at risk than men due to a combination of several risk factors (Nishijo *et al.* 2004).

4.6.2 Carcinogenicity Classification and Non-threshold TRVs

HC classifies cadmium as a Group II carcinogen ("probably carcinogenic to humans") (Government of Canada 1994). Similarly, the US EPA classifies cadmium as B1 ("probable human carcinogen") (US EPA 1989) and the European Commission classifies cadmium metal and oxide as Category 2 carcinogens ("may cause cancer") (European Chemicals Bureau 2007). IARC (1993; 2012) classifies cadmium and cadmium compounds as Group 1 ("carcinogenic to humans") and NTP (2016) classifies cadmium and cadmium compounds as "known to be human carcinogens" based on sufficient evidence human studies, including epidemiological and mechanistic studies.

In the case of cadmium, investigations have suggested that indirect genotoxicity and/or epigenetic mechanisms may be involved in carcinogenesis and that a direct genotoxic mechanism is unlikely (Section 4.2). However, no alternative biological models to describe the dose-response relationship for cadmium carcinogenicity at low, environmentally relevant exposures have been proposed or applied by agencies assessing cadmium risks.

The TRVs derived by national and international agencies for cancer risk assessment for cadmium inhalation are summarized in the following subsections. The rationale for the selection of the value to be used for the derivation of the cadmium direct contact human health-based soil quality guidelines ($SoQG_{DH}$) (non-threshold effects) is provided at the end of the present section.

Currently, carcinogenic risk estimates for cadmium via the oral route have not been developed (EFSA 2009*a*; European Chemicals Bureau 2007; JECFA 2011; WHO 2011*a*; *b*).

<u>Unit Risk (0.0018 $(\mu g/m^3)^{-1}$) Derived by US EPA (1989)</u>

US EPA concluded that the unit risk based on human data was more reliable than the value derived from animal data (US EPA 1985; 1989; Takenaka *et al.* 1983). The US EPA Integrated Risk Information System (IRIS) derived a unit risk of 0.0018 $(\mu g/m^3)^{-1}$ on the basis of lung, trachea and bronchus cancer mortality epidemiological data (Thun *et al.* 1985; US EPA 1989). US EPA used the approximate midpoints of the exposure intervals (provided personally by Thun), corresponding to the cumulative exposure categories used by Thun *et al.* (1985), to derive the standardized mortality ration (SMR). These median estimates were converted to 24-hour, accounting for the adequate number of days worked per year (US EPA 1985; 1989). The unit risk (0.0018 $(\mu g/m^3)^{-1}$)

was then estimated using a simple model, equivalent to a two-stage model with only the first stage affected by exposure.

An additional level of conservatism, such as the selection of the 95% upper bound (0.0035 $(\mu g/m^3)^{-1}$), was not deemed necessary because the model used inflated the risk estimate (US EPA 1985).

Unit Risk (0.0042 $(\mu g/m^3)^{-1}$) Derived by OEHHA (2009; 2011)

OEHHA (2009; 2011) derived a unit risk of 0.0042 $(\mu g/m^3)^{-1}$ on the basis of published epidemiological data (Thun *et al.* 1985) and additional information (median cumulative exposure estimates) provided by the study author (Thun *et al.* 1986). OEHHA specified that the SMR of 2.3 in workers with more than two years of cadmium exposure and the dose-response relationship based on the data reported by Thun *et al.* (1985) were unlikely to be explained by chance, bias or confounding factors related to smoking or arsenic exposure. It was thus concluded that the excess of lung cancer was best explained by exposure to high levels of cadmium.

The adjusted median cumulative exposures consider the adequate number of days worked per year and the corresponding equivalent lifetime (61.5 years) to provide dose rates of 2, 11.8 and 41 $\mu g/m^3$ (OEHHA 2009; 2011). Poisson regression was used to fit the data for cadmium carcinogenic potency (β) and the healthy worker effect (α) (mortality among workers in the low-exposure group was lower than in the general US white male population). The model was then applied to the Californian population to predict excess lung cancer deaths. The lung cancer death hazard was then estimated for a 1 $\mu g/m^3$ exposure, using the carcinogenicity potency factor (β = 0.0017 mg Cd-days/m^3) and suppressing the healthy worker effect. OEHHA (2009; 2011) thus derived a lifetime cancer unit risk based on the upper confidence limit of cadmium carcinogenic potential of 0.0042 $(\mu g/m^3)^{-1}$.

Unit Risk (0.0042 (µg Cd/m^3)$^{-1}$) Provided by HC (2021*a*)

The Health Canada Contaminated Sites Division (HC 2021*a*) provides an inhalation unit risk of 0.0042 $(\mu g/m^3)^{-1}$ as adopted from OEHHA (2011).

4.6.3 Rationale for the Selection of the TRV for the Derivation of the $SoQG_{DH}$ for Cadmium

The inhalation unit risk (0.0042 $(\mu g/m^3)^{-1}$) derived by OEHHA (2009; 2011) and proposed by HC (2021*a*) was considered appropriate for use in the development of non-threshold $SoQG_{DHS}$ for cadmium. This value was derived from the epidemiological results, where cumulative cadmium exposure was significantly associated with an increased incidence of mortality due to lung cancer (Thun *et al.* 1985). This value was preferred to the unit risk (0.0018 $(\mu g/m^3)^{-1}$) derived by the US EPA (1989) from the same epidemiological data because the OEHHA approach accounts for the healthy worker effect (OEHHA 2009; 2011). The use of epidemiological data instead of animal data for the derivation of a TRV is appropriate when the epidemiological data are of sufficient quality.

4.6.4 Threshold TRVs

4.6.4.1 Ingestion

Several agencies (ATSDR 2012; California Environmental Protection Agency [CalEPA] 2001; 2005; 2006; CPSC 2010; EFSA 2009*a*; *b*; JECFA 2011; National Institute of Public Health and the Environment [RIVM] 2001; US EPA 1989; WHO 2011*b*) have developed oral TRVs for cadmium (see Appendix 9). This summary focusses on the most recent TRVs established by the EFSA (2009*a*; *b*) and JECFA (2011*a*), which are both based on a meta-analysis of data collected from a comprehensive systematic review of epidemiological studies. The rationale for the selection of the value proposed for derivation of the $SoQG_{DH}$ for cadmium is provided at the end of the present section.

Tolerable Weekly Intake (TWI = 2.5 µg/kg bw/week) Developed by EFSA (2009*a*; *b*; 2011)

Following a comprehensive literature review of human epidemiological and clinical studies focused on dose-effect relationships between UCd and various biomarkers (including kidney and bone biomarkers), EFSA conducted a meta-analysis to determine the relationship between UCd and urinary β_2MG for the whole population and for non-occupationally exposed adults over 50 (i.e., the focus population) (EFSA 2009*b*).

EFSA estimated the $BMDL_5$ using the hybrid BMDL approach and the Hill statistical model to fit the dose-response relationship between urinary β_2MG excretion and UCd (EFSA 2009*b*; 2011). $BMDL_5$ values were derived for an increase in urinary β_2MG concentrations or on the basis of

observed reversible proteinuria. The average estimated $BMDL_5$ for a Caucasian population was a UCd of 4 µg/g creatinine (assuming a cut-off limit of 300 µg β_2MG/g creatinine), which was extrapolated from the shape of the curve for the Asian population since no Caucasian UCd data were as high as the Asian data (EFSA 2009*b*). EFSA elected to apply a chemical-specific adjustment factor (CSAF = 3.9) to account for any residual UCd variability. The reference value from which dietary intake could be estimated was set at a UCd of 1 µg/g creatinine ($BMDL_5$ ÷ CSAF) (EFSA 2009*a*; *b*).

The Amzal *et al*. (2009) one-compartment toxicokinetic model was used to determine the dietary exposure corresponding to a UCd of 1 µg/g creatinine (EFSA 2009*a*; 2011). Long-term cadmium intake and UCd information from a large population-based study provided sufficient data on inter-individual variability in absorption rates, particularly the high rates in women (EFSA 2009*a*; 2011). EFSA (2009*a*; 2011) estimated that the average daily dietary intake should not exceed 0.36 µg/kg bw/d, corresponding to a tolerable weekly intake (TWI) of 2.5 µg/kg bw. No further adjustments (e.g., uncertainty factor) were considered necessary since the data analysis used the most sensitive indicator of renal dysfunction (β_2MG) and a sensitive subpopulation (women) (EFSA 2009*a*).

EFSA (2011) reconfirmed their TWI for cadmium following the establishment of the JECFA pTMI (see the next subsection). They concluded that the 2.5 µg/kg bw/week TWI should be maintained in order to ensure a high level of protection for consumers, including subgroups such as children, vegetarians and people living in highly contaminated areas (EFSA 2011).

Provisional Tolerable Monthly Intake (pTMI = 25 µg/kg bw/month) Developed by JECFA (2011*a*; *b*)

Using the same 35 epidemiological study database as EFSA (2009*a*; *b*), JECFA compared the fit from three models: the Hill model (used by EFSA), an exponential model with a threshold, and a biexponential model with four parameters (JECFA 2011; WHO 2011*b*). They concluded that a BMD approach could not adequately model the variation in the cause-effect relationship. However, the biexponential model showed an obvious transition or breakpoint (i.e., the point where urinary β_2MG rises sharply with increased UCd) on the β_2MG *vs* UCd curve. From this model, a breakpoint of 5.24 µg/g creatinine (fifth to 95th percentiles: 4.94 to 5.57) was determined for the population of age 50 and up.

The same one-compartment toxicokinetic model (Amzal *et al.* 2009) was used to estimate dietary exposure associated with the calculated breakpoint, but with a probabilistic approach (JECFA

2011). JECFA also introduced a toxicodynamic variable to account for individual variability in the toxic response of the kidney. Using the toxicokinetic model with the additional parameter to adjust for toxicodynamic variability, JECFA constructed a two-dimensional Monte Carlo simulation to estimate dietary exposure equated to a UCd of 5.24 µg/g creatinine (1.2; fifth to 95th percentiles = 0.8 to 1.8) µg/kg bw/d. The lower bound of the confidence interval (0.8 µg/kg bw/d; equivalent to ≈25 µg/kg bw/month) was considered appropriate for establishing the TRV. Given cadmium's exceptionally long half-life, JECFA considered it appropriate to express the TRV on a monthly basis. The previous provisional tolerable weekly intake (pTWI) of 7 µg/kg bw/week (JECFA 2004*a*; *b*) was withdrawn and the provisional tolerable monthly intake (pTMI) was established at 25 µg/kg bw/month.

Tolerable Daily Intake (TDI = 0.8 µg/kg bw/d) Adopted by HC (2021*a*)

HC's Contaminated Sites Division (HC 2021*a*) provides a provisional TDI of 0.8 µg/kg bw/d. This value represents the lower bound (fifth percentile) of the JECFA (2011*a*; *b*) dietary exposure associated with the breakpoint for increased UCd.

4.6.5 Rationale for Selection of the TRV for Derivation of the SoQG$_{DH}$ for Cadmium (oral, non-cancer)

The pTDI (0.8 µg/kg bw/d), provided by HC (2021*a*) and based on JECFA (2011*a*; *b*), was considered appropriate for use in the development of the SoQG$_{DH}$s when cadmium is treated as a threshold contaminant. This value was selected among the existing values developed for risk assessment of ingested cadmium and whose derivations were sufficiently documented (ATSDR 2012; CPSC 2010; EFSA 2009*a*; *b*; 2011; JECFA 2011; US EPA 1989; WHO 2011*b*). Expressed on a per-day basis, these TRVs vary from 0.1 to 1.0 µg/kg bw/d. The variation can be explained by the use of different points of departure (PODs), different approaches for estimating the daily ingested dose corresponding to the POD, and the application (or not) of uncertainty factors to protect susceptible populations.

The difference between the EFSA (2009*a*; *b*; 2011) and JECFA (2011*a*; *b*) values (TWI of 2.5 µg/kg bw and pTMI of 25 µg/kg bw) relates primarily to choices in how to account for the fact that the meta-analysis was based on summary data (group means) rather than on individual data, and on the modelling approach used by the different agencies. EFSA's CSAF value had a large impact on the TRV, may not be appropriate for the Canadian population, and was considered overly conservative. A separate sensitivity assessment, using the conventional uncertainty factor

for inter-individual toxicodynamic variability and deterministic toxicokinetic modelling, resulted in a reference value comparable to that on which JECFA based its TRV.

4.6.5.1 Inhalation

While inhalation reference values are available for the threshold effects of cadmium, these values are greater than those for non-threshold effects. As the oral TRV is based on measures of total exposure (through all pathways), it is used to derive $SoQG_{HHS}$. Some agencies, however, have established values specific to the inhalation pathway, and these are summarized in the following subsections.

Minimal Risk Level (MRL = 0.01 µg/m^3) for Chronic Inhalation Developed by ATSDR (2012)

The ATSDR (2012) established a MRL of 0.01 µg/m^3 to protect the general population against the effects of chronic cadmium inhalation exposure. This MRL is based on the 95% lower confidence limit of the UCd concentration associated with a 10% increased risk ($UCDL_{10}$) of low-molecular-weight proteinuria in humans (0.5 µg/g creatinine), as identified in three studies conducted in environmentally exposed populations (Buchet *et al.* 1990; Järup *et al.* 2000; Suwazono *et al.* 2006). The internal dose corresponding to the $UCDL_{10}$ accounts for age-weighted exposure via both air and diet. The ambient air concentration corresponding to the $UCDL_{10}$ (0.1 µg/m^3) was divided by an uncertainty factor of three to account for human variability (protection of diabetics) and a modifying factor of three to account for the lack of adequate human data to compare the relative sensitivities of the respiratory tract and kidneys (ATSDR 2012).

Risk Exposure Level (REL = 0.02 µg/m^3) developed by CalEPA (2000)

The CalEPA (2012) REL for chronic cadmium exposure (0.02 µg/m^3) was derived on the basis of an epidemiological study (Lauwerys *et al.* 1974) of male and female workers (CalEPA 2000). A LOAEL of 21 µg/m^3 was established based on the NOAEL of 1.4 µg/m^3 for respiratory effects in men and a lack of effects in women, which was adjusted to 0.5 µg/m^3 for continuous exposure in the general population and with uncertainty factors of 10 (inter-individual variability) and three (less-than-lifetime [subchronic] exposure duration) (CalEPA 2000).

5.0 DERIVATION OF SOQG$_{HH}$S

5.1 Protocol

SoQG$_{HH}$S provide concentrations of contaminants in soil, at or below which no appreciable risks to human health are expected. As per the CCME (2006) protocol, SoQG$_{DH}$S are developed for three direct exposure pathways: soil ingestion, dermal contact with soil, and inhalation of suspended soil particles.

The strongest evidence for non-threshold effects (i.e., carcinogenicity) from cadmium in humans comes from occupational studies where inhalation is the primary exposure route. The non-threshold inhalation TRV is a unit risk (UR) (Section 4.6.2) based on evidence of increased lung tumours.

With respect to threshold effects, a guideline applicable to combined ingestion, dermal contact and inhalation exposure for each land use category is developed using the oral TRV. The oral TRV (Section 4.6.3.1) is based on the same critical effect (i.e., low-molecular-weight proteinuria) and derived from biomonitoring data representing total exposure to inorganic cadmium via all three routes of exposure.

For threshold toxicants, it is recognized that, exclusive of hazardous waste sites or other point sources of pollution, everyone is exposed to a "background" level of contamination. In setting SoQG$_{DH}$, the background estimated daily intake (EDI) is deducted from the TDI (CCME 2006). Twenty percent of the residual TDI is apportioned to each environmental medium, namely air, water, soil, food and consumer products (CCME 2006). This approach allows for the development of guidelines for other media without exceeding tolerable intakes.

HC considers an incremental risk of less than one in 10^5 to 10^6 (i.e., 1 in 1 000 000 or 1 in 100 000, respectively) above background risk levels to be "essentially negligible" (HC 2021*b*). Some provinces in Canada have adopted an acceptable incremental lifetime cancer risk (ILCR) of 10^{-5}, and others have chosen 10^{-6}. Therefore, SoQG$_{DH}$ for ILCRs of both 10^{-6} and 10^{-5} are presented in this document.

In addition to the SoQG$_{DH}$, the CCME (2006) protocol includes the derivation of two check values for inorganic substances: 1) consumption of produce, meat and milk and 2) off-site migration of contaminated soil. The check values are considered to be management adjustment factors and may or may not be included in the calculation of the overall SoQG$_{HH}$, based on professional judgement.

The CCME (2006) exposure assumptions used in the derivation of $SoQG_{HHS}$ are presented in Table 3 and Sections 5.6 and 5.7. Derivations were based on data for inorganic cadmium compounds, reported as total cadmium in this report because speciation information was not available. The available data on human and animal toxicity of cadmium pertain to those forms of inorganic cadmium for which exposure is most likely.

5.2 EDI for Canadians

The EDI is an estimate of the typical total concurrent background exposure (from uncontaminated environmental media) from all known or suspected sources via a multimedia exposure assessment for the average Canadian. It does not include exposures that may occur from a contaminated site or activities that may result in increased exposure to substances. The EDI calculation is illustrated in the equation below and expressed in units of µg/kg bw/d (CCME 2006):

$$EDI = \sum_{i=1}^{n} ED_i$$

The general population was subdivided into five age classes: infants (birth to six months), toddlers (seven months to four years), school-age children (five to 11 years), teenagers (12 to 19 years) and adults (20 years and older). The following media were considered in calculating the EDI: ambient air, indoor air, indoor dust, soil, drinking water, food and breast milk. For inorganic cadmium (as total Cd), background exposure arises primarily from food. Consumer products were not included in the EDI estimation because data are limited. The equation below illustrates the media and pathway-specific EDI calculation (CCME 2006).

$$ED_i = \frac{C \times CR \times BF \times EF}{BW}$$

where:

ED_i = exposure dose from pathway *i* (mg/kg bw/d)
C = contaminant concentration in medium (e.g., mg/L)
CR = media specific contact rate (e.g., L/d)
BF = bioavailability factor (unitless)
EF = exposure factor (unitless) which is the product of exposure frequency (events/year) and exposure duration (years/lifetime)
BW = body weight (kg)

Concentrations of cadmium in environmental media were obtained from government databases and scientific literature, as summarised in Section 2.4 and Appendix 1. Soil, ambient air, drinking water and food data were provided directly from Canadian government databases.

Probability distribution functions (PDFs) generated for concentrations in environmental media, receptor characteristics and intake rates were used to generate age-group EDI distributions for each media and a combined total EDI from all media and exposure routes, as described in HC (2011). PDFs were assumed to be lognormal except for human breast milk intake and time spent outdoors, for which a triangular distribution was used due to limited data availability. Receptor characteristics and intake rate distributions are presented in Appendix 4, Appendix 5, and Appendix 6.

Appendix 6 summarizes the EDI for cadmium via all media for the five age groups. The total cadmium EDIs for toddlers, children, teenagers and adults are 0.48, 0.436, 0.257 and 0.174 µg/kg bw/d, respectively (median values). Depending on whether or not infants are exclusively breast-fed, the EDI for infants are 0.0143 µg/kg bw/d (exclusively breast-fed) and 0.195 µg/kg bw/d (non-breast-fed). Food ingestion is the dominant cadmium exposure pathway for all age groups, whereas inhalation of ambient air contributes only negligibly to the total EDI.

Certain Canadian subpopulations may be exposed to higher levels of cadmium (in cigarette smoke, drinking water [due to plumbing] and individual activities [e.g., hobbies]). Consumption of food grown on soils containing high levels of cadmium could also possibly increase cadmium exposure above the levels calculated herein. In addition, people living near industrial areas associated with cadmium emissions could be exposed to higher concentrations via inhalation of ambient air. Due to insufficient data, it is not possible at this time to perform an exposure assessment for those groups. However, the current analysis does suggest that, compared to food consumption, the direct soil contact pathways (incidental ingestion, inhalation and dermal contact) are small contributors to total exposure.

For the purpose of soil quality guidelines derivation, the EDIs for toddlers and adults were used.

5.3 Exposure Limit for Human Receptors

The rationales for the selection of the TRVs selected to derive the $SoQG_{DH}$ were presented in Section 4.6. For threshold effects, the oral TDI (0.8 µg/kg bw/d) identified by HC (2021*a*) was selected for derivation of $SoQG_{DH}$ for threshold effects from combined oral, inhalation and dermal

exposures. For non-threshold effects, the inhalation UR (0.0042 µg/m^3) identified by HC (2021*a*) and OEHHA (2011; 2009) was selected for derivation of the inhalation SoQG$_{DH}$.

5.4 Relative Absorption Factors (RAF)

RAF may be applied when the critical toxicological study used to develop the TRV is based on exposure via a different medium than that under investigation. RAFs account for the difference in a substance's absorption by the body when absorbed from different media.

For cadmium, the critical study for the oral TRV was a meta-analysis of 35 epidemiological studies, in which exposure occurred primarily through the environment. The inhalation unit risk was based on lung cancer in occupationally exposed workers (mainly inhalation). Based on this, no RAFs are recommended to derive the SoQG$_{DHS}$ for the oral and inhalation routes.

The available information indicates that little cadmium is likely to be absorbed through human skin (US EPA 1995). For the purposes of this assessment, HC (2011) recommends a dermal soil relative absorption factor of 0.01 (i.e., 1%) based on the data-derived absolute absorption factor recommended by the Ontario Ministry of the Environment (OMOE 2009).

5.5 SoQG Input Parameters

Table 3 lists and describes the parameters used to calculate the SoQGs.

Table 3. SoQG calculation input parameters

Acronym	Description	Land use		
		Agricultural and residential/ parkland	Commercial	Industrial
TDI	Tolerable daily intake (µg/kg bw/d) per oral route of exposure (HC 2018; HC 2021*a*)	0.8	0.8	0.8
TILCR	Target incremental lifetime cancer risk	10^{-6} and 10^{-5}	10^{-6} and 10^{-5}	10^{-6} and 10^{-5}
DC	Dust concentration from resuspension of soil g/m^3 (HC 2021*b*)	7.6×10^{-7}	7.6×10^{-7}	7.6×10^{-7}
UR	Inhalation unit risk (µg/m^3)$^{-1}$ (HC 2021*a*)	0.0042	0.0042	0.0042
AF_L	RAF for lungs (unitless) (UR derived from an inhalation study. No adjustment necessary.)	1	1	1
EDI	Estimated daily intake (µg/kg bw/d) (Section 5.2)	0.48	0.48	0.174
SF	Soil allocation factor (default—unitless) (CCME 2006)	0.2	0.2	0.2
BW	Body weight (kg) (CCME 2006)	16.5	16.5	70.7
AF_G	Relative absorption factor for Cd across the gut (unitless)	1	1	1
SIR	Soil ingestion rate (kg/d) (CCME 2006)	8×10^{-5}	8×10^{-5}	2×10^{-5}
AF_S	Relative absorption factor for Cd across the skin (unitless)	0.01	0.01	0.01
SR	Soil dermal contact rate (kg/d) (CCME 2006)[a]	6.9×10^{-5}	6.9×10^{-5}	1.14×10^{-4}
AF_L	Relative absorption factor for Cd across the lung (unitless)	1	1	1
IR_S	Soil inhalation rate (kg/d)[b]	6.3×10^{-9}	6.3×10^{-9}	1.3×10^{-8}
ET_1	Exposure term 1 (default—unitless) (CCME 2006)	1	0.66	0.66
ET_2	Exposure term 2 (default—unitless) (CCME 2006)	1	0.42	0.42
Off-site migration default	Depth of soil to which the material is deposited (D_m = 2 cm) ÷ depth of deposited material (D_d = 014 cm). D_m is assumed by CCME (2006). D_d is estimated from the soil mass calculated using the EPIC model (13.9 T/ha) (Williams *et al*. 1990) and an assumed soil bulk density of 1 kg/m^3 (CCME 2006).	14.3	14.3	14.3
Off-site migration default	$(D_m\text{-}D_d)/D_d$	13.3	13.3	13.3
BSC	Background soil concentration (mg/kg—assumed)	0.24	0.24	0.24
$SoQG_A$	Soil quality guideline for agricultural land use (mg/kg—calculated) (Section 5.6.1)	13	13	12

Notes:
[a] Soil dermal contact rate = (hands surface area × soil loading to exposed skin of the hands) + (arms surface area × soil loading to exposed skin of the arms) + ([toddler only] legs surface area × soil loading to exposed skin of legs).
[b] Value derived from the daily inhalation rate (Allan *et al*. 2008) for the critical receptor, assuming the airborne concentration of suspended soil particulate above a contaminated site is 7.6×10^{-10} kg/m^3.

5.6 Ingestion, Inhalation and Dermal Pathways

5.6.1 Agricultural and Residential/Parkland Uses—Threshold Effects

To determine agricultural and residential/parkland soil guidelines, the toddler is the most appropriate receptor due to a large exposure per unit mass.

In accordance with CCME guideline derivation procedures (CCME 2006), a guideline for soil ingestion, dermal contact and inhalation, which applies to agricultural (residential use of farm property only) and residential/parkland soil, is derived using the following equation:

$$\mathrm{SoQG_{DH}} = \frac{(\mathrm{TDI} - \mathrm{EDI}) \times \mathrm{SAF} \times \mathrm{BW}}{[(\mathrm{AF_G} \times \mathrm{SIR}) + (\mathrm{AF_S} \times \mathrm{SR}) + (\mathrm{AF_L} \times \mathrm{IR_S} \times \mathrm{ET_2})] \times \mathrm{ET_1}} = \mathrm{BSC}$$

Therefore, using this approach, the $\mathrm{SoQG_{DH}}$ for cadmium at agricultural and residential/parkland sites is **13 mg/kg**.

5.6.2 Commercial Land Use—Threshold Effects

No manufacturing activities are expected to take place at commercial sites, and neither is residential occupancy. A commercial site is fully accessible to all ages, but it is used with less intensity, duration and frequency than a residential site. An example of a commercial site would be an urban shopping mall.

For threshold contaminants such as cadmium, the toddler is assumed to be the most sensitive receptor, with access restricted to 10 hours per day, five days per week and 48 weeks per year.

Therefore, using the above approach, the $\mathrm{SoQG_{DH}}$ for cadmium in dry soil at commercial sites is calculated to be **20 mg/kg**.

5.6.3 Industrial Land Use—Threshold Effects

As industrial sites typically have limited or restricted access to the public, occupational exposure will predominate and only adult receptors are considered. The typical adult exposure period is assumed to be 10 hours per day, five days per week and 48 weeks per year.

Therefore, using the equation presented in Section 5.6.1 along with the above adult receptor characteristics and exposure terms, the $\mathrm{SoQG_{DH}}$ for commercial use is 634 mg/kg, which is rounded to **630 mg/kg**.

5.7 All Land Uses—Non-Threshold Effects

As previously discussed (Section 5.1), for the purpose of deriving SoQGs, the non-threshold effects of cadmium are evaluated for the inhalation pathway (in this case inhalation of particles) using the inhalation UR. Adults are considered the most appropriate receptor for evaluating lifetime cancer risk for non-threshold substances. The CCME (2006) default exposure term (ET) for all land uses is 1. The non-threshold $SoQG_{DH}$ for cadmium, based on inhalation of soil particles, is calculated as follows:

$$SoQG_{DH-PI} = \frac{TILCR}{(DC \times UR \times AF_L) \times ET} + BSC$$

(This is a mathematical rearrangement of the CCME equation for estimation of soil quality guidelines for non-threshold effects when the cancer potency factor is expressed as an inhalation unit risk factor.)

Using this equation, the $SoQG_{DH\text{-}PI}$ ($SoQG_{DH}$-particulate inhalation) is 314 mg/kg for an excess cancer risk of 10^{-6} and 3,133 mg/kg for an excess cancer risk of 10^{-5}. These values were rounded down to **300 mg/kg** and **3,000 mg/kg** for excess cancer risks of 10^{-6} and 10^{-5}, respectively.

5.8 Protection of Groundwater Used as a Source of Raw Water for Drinking

No guideline for the protection of groundwater used as a source of raw water for drinking was derived for inorganic cadmium compounds due to constraints on the mathematical model when applied to inorganic compounds (CCME 2006). HC provides a maximum acceptable concentration of cadmium in drinking water of 0.007 mg/L (HC 2020). This value should be used to assess cadmium levels in water used as drinking water at contaminated sites.

5.9 Off-site Migration Guidelines for Commercial and Industrial Land Uses

Transfers of contaminated soil, from one property to another, are possible by environmental occurrences such as wind and water erosion (CCME 2006).

The Universal Soil Loss Equation and the Wind Erosion Equation are utilized to estimate the transfer of soil from one property to another. The following equation allows us to calculate the concentration in eroded soil from the site that can raise contaminant concentration to the agricultural guideline level in receiving soil at another site, within a specific time frame. This concentration is referred to as the human health soil quality guideline for off-site migration

(SoQG$_{OM-HH}$). If the guidelines for commercial or industrial sites are found to be above SoQG$_{OM-HH}$, the potential arises for the contamination of adjacent properties from off-site deposition (CCME 2006). SoQG$_{OM-HH}$ is calculated using the following equation:

$$SoQG_{OM-HH} = 14.3 \times SoQG_A - 13.3 \times BSC$$

The resulting SoQG$_{OM-HH}$ is 183 mg/kg, which is rounded to 180 mg/kg, which is greater than the SoQG$_{DH}$ for commercial land uses but lower than the SoQG$_{DH}$ for industrial land uses. Therefore, the industrial land use SoQG$_{HH}$ is set at the SoQG$_{OM-HH}$ of **180 mg/kg**.

5.10 Produce, Meat and Milk Check

The produce, meat and milk check (SoQG$_{FI}$) was not retained due to high variability in some of the modelled parameter values used to derive the check value. This resulted in a check value that was unrealistically low (µg/kg) and would not be reasonable or workable as required for setting an SoQG.

5.11 Final SoQG$_{HH}$s

SoQG$_{HH}$s were derived for cadmium at agricultural, residential/parkland, commercial and industrial sites based on ingestion, dermal absorption and inhalation of soil. Cadmium was assumed to behave as a threshold substance via the ingestion, inhalation and dermal contact pathways as well as a non-threshold substance via the inhalation pathway. Separate SoQG$_{HH}$ were calculated based on the evidence of different toxic effects, dependent on the exposure route. The SoQGs calculated for each land use are presented in Table 4.

The overall SoQG$_{HH}$s are set as the lowest of the human health guidelines and checks derived for each land use. Based on this, the overall SoQG$_{HH}$s are based on the ingestion, inhalation and dermal direct contact pathways for non-cancer effects for agricultural land use (13 mg/kg), residential/parkland land use (13 mg/kg) and commercial land use (20 mg/kg). For industrial land use, the SoQG$_{HH}$ is 180 mg/kg based on the off-site migration check mechanism. The SoQG$_{DH}$ for non-threshold effects associated with inhalation exposures were higher than those calculated for threshold effects (Section 5.7).

With the above in mind, the SoQG$_{HH}$s are protective of human health at most sites.

6.0 RECOMMENDED CSoQG

According to the CCME protocol (2006), both $SoQG_E$ and $SoQG_{HH}$ are developed for four land uses: agricultural, residential/parkland, commercial and industrial. The lowest value generated by the environmental and human health approaches for each of the four land uses is recommended by CCME as the CSoQG. The $SoQG_E$s for cadmium developed in 1999 (CCME 1999; EC 1999) were considered along with the $SoQG_{HH}$s in selecting the final SoQGs for the protection of environmental and human health. The recommended SoQGs for the protection of environmental (CCME 1999; EC 1999) and human health are presented in Table 4.

Cadmium intake via food represents the highest contributing source to total cadmium exposure in Canada. At sites where appreciable amounts of garden produce are consumed, a lower $SoQG_{HH}$ may be required for consideration. Drinking water consumption was not evaluated in the development of the $SoQG_{HH}$. It may be necessary to consider alternative limits to daily intake at sites where drinking water is sourced from nearby wells.

Table 4. SoQGs and check values for cadmium ($mg \cdot kg^{-1}$)

	Land use			
	Agricultural	**Residential/ parkland**	**Commercial**	**Industrial**
Guideline (SoQG)	3.8	10	20	22
Human health guidelines or check values				
$SoQG_{HH}$[a,b,c]	13	13	20	180
Direct contact $SoQG_{DH}$ (threshold)	13	13	20	630
Direct contact $SoQG_{DH}$ (non-threshold):				
Incremental target risk level = 10^{-5}	3,000	3,000	3,000	3,000
Incremental target risk level = 10^{-6}	300	300	300	300
Inhalation of indoor air check[d]	NC	NC	NC	NC
Off-site migration check	NC	NC	NC	180
Groundwater check (drinking water)[e]	NC	NC	NC	NC
Produce, meat and milk check[f]	NC	NC	NC	NC
1999 Environmental health guidelines or check values (CCME 1999; EC 1999)				
$SoQG_E$[a]	3.8[g]	10[h]	22[h]	22[h]
Soil contact guideline	10	10	22	22
Soil and food ingestion guideline	3.8	-	-	-
Nutrient and energy cycling check	54	54	195	195
Off-site migration check	-	-	-	132
Groundwater check (aquatic life)	NC[e]	NC[e]	NC[e]	NC[e]

Notes: NC = not calculated; ND = not determined; $SoQG_E$ = soil quality guideline for environmental health; $SoQG_{HH}$ = soil quality guideline for human health; $SoQG_{DH}$ = soil quality guideline for human health-direct contact. The dash indicates a guideline or check value that is not part of the exposure scenario for this land use and therefore is not calculated. Soil guidelines and the data used to calculate them are, by convention, always expressed on a dry weight (d.w.) basis to allow the data to be standardized. In case of doubt and if the scientific criteria document does not specify whether wet or d.w. is used, readers are advised to check the references provided.

[a] Data are sufficient and adequate to calculate an updated $SoQG_{HH}$. Data were sufficient and adequate to calculate an $SoQG_E$ (CCME 1999; EC 1999), which are included here to allow for the selection of final SoQGs for each land use.

[b] The $SoQG_{HH}$ is the lowest of the human health guidelines and check values.

[c] The $SoQG_{HH}$ is based on direct exposure to soil ingestion, dermal contact and particulate inhalation (agricultural, residential/park and commercial land uses) and the off-site migration check value (industrial land uses).

[d] The "inhalation of indoor air" check applies to volatile organic compounds and is not calculated for non-volatile contaminants.

[e] Applies to organic compounds and is not calculated for metal substances. Concerns about metal substances should be addressed on a site-specific basis.

[f] This check is intended to protect against chemicals that may biomagnify in human food. Variability in model parameters was high and resulting check values were excessively low (µg/kg) and therefore unreasonable and unworkable, as required for application as SoQGs. This pathway should be assessed on a site-specific basis, as applicable.

[g] The $SoQG_E$ is based on the soil and food ingestion guideline.

[h] The $SoQG_E$ is based on the soil contact guideline.

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APPENDIX 1. SUMMARY TABLES OF CADMIUM CONCENTRATION IN ENVIRONMENTAL MEDIA

Ambient / outdoor air

Location	Year	Concentration (ng/m^3)	Range (ng/m^3)	Comments	Reference
Canada					
British Columbia, Alberta, Ontario, Québec, New Brunswick, Nova Scotia	2012–16	0.05 (median)	0.02–14.89	NAPS data, $PM_{2.5}$ analyzed by ICP-MS; acid digestion.	ECCC 2017
British Columbia, Ontario, Québec, New Brunswick	2003–09	0.153 (mean)	0.000573–18.5	NAPS data, $PM_{2.5}$ analyzed by ICP-MS; acid digestion.	EC 2011
Alberta					
Edmonton	2010	0.03 (median)	0.005–1.3	50 non-smoking homes. Winter and summer. GC-MS	Bari et al. 2015
Ontario					
Windsor	2000 1999 1998 1997 1996	1.39 (1.93) 1.16 (1.16) 2.17 (2.17) 1.55 (1.55) 3.45 (3.45)		98th percentile (maximum).	OMOE 2007
Toronto	2000 1999 1998 1997 1996	3.30 (3.44) 1.51 (2.79) 2.86 (2.86) 2.15 (2.15) 2.04 (2.38)			
Hamilton	2000 1999 1998 1997 1996	1.95 (2.51) 1.95 (1.95) 1.72 (1.72) 2.23 (2.23) 2.65 (2.65)			
Ottawa	2000 1999 1998 1997 1996	1.97(2.12) 0.95 (0.98) 2.05 (2.55) 0.97 (1.00) 1.01 (1.04)			
Windsor	1990–2000	0.003–0.006 (annual mean)	0.003–0.027 (max. 24-hr value)	Cd concentrations in PM_{10}.	IAQAB 2004

Windsor	2004	9.5 ng/g (median)	2.9–24.2 ng/g (n=8)	$PM_{2.5}$	Rasmussen *et al.* 2007
Canadian Arctic					
Resolute and Coral Harbour, Nunavut	1973–2000	0.2–0.05		Average Cd concentrations in surface air particulate from two Arctic sites.	Li *et al*. 2003

Note: [a] DL=detection limit

Indoor air

Location	Year	Concentration (ng/m3)	Range (ng/m3)	Comments	Reference
Canada					
Ontario					
Ottawa	Winter 1993	4.42	1.12–34.94	Nitric hydrofluoric acid digestion and ICP-MS, n = 48	Rasmussen *et al*. 2001
Windsor	Summer 1992	0.8 0.35 0.7	0.2–2.6 0.05–0.25 0.1–4.5	Smoking n = 15 Non-smoking n = 22 Smoking and non-smoking n = 37	Bell *et al*. 1994
Windsor	2004	6.1 ng/g media	2.2–23 ng/g	PM2.5 n = 8	Rasmussen *et al*. 2007
Alberta	May–June 1997	0.1 0.05		PM10 n = 20 PM2.5 n = 20	Alberta Health 1998
USA					
Minneapolis/St. Paul, MN,	April–November 1999	0.3		Non-smoking PM2.5. n = 235	Adgate *et al*. 2007
Towson, MD	1998	0.041 (median) 0.044 (median)		Indoor – PEM (non-smoking); n = 10 Indoor – VAPS (non-smoking); n = 10	Graney *et al*. 2004
Chicago, IL	June 1994–April 1995	0.045	nd–6	Non-smoking; n = 48	Van Winkle and Scheff 2001
Region V (IL, IN, OH, MI, MN and WI)	1995–97	0.36 ± 0.7	0.1–7.7		NHEXAS 2003
Minnesota		0.20 ± 0.50	0.002–6.42		
Arizona		<DL (median)		n = 119; 100% samples <DL	O'Rourke *et al*. 1999
Other countries					
Austria (Vienna)	April–June, Aug–Sept 2003	0.59 ± 0.37 0.32 ± 0.31		Indoor (day); n = 12 Indoor (night); n = 12 PM2.5	Komarnicki 2005

Indoor air

Location	Year	Concentration (ng/m3)	Range (ng/m3)	Comments	Reference
Singapore (Choa Chu Kang)	May 12–23, 2004	0.7 0.6 0.03		Indoor (living room) n = 2 Indoor (master bedroom) n = 2 Indoor (bedroom) n = 2 PM2.5	Balasubramanian and Lee 2007

2596 **Notes:** DL = detection limit, ICP-MS = inductively coupled plasma-mass spectrometry; nd = not detectable; PEM = personal exposure monitor; VAPS = versatile air pollutant sampler

Indoor dust

Location	Year	Concentration (mg/kg)	Range (mg/kg)	Comments	Reference
Ontario					
Ottawa	1993	4.42	1.12–34.94	Analysed by ICP-MS n=48	Rasmussen *et al*. 2001
Ottawa	Not reported	24.3 25.6 1.9		<53 µm indoor dust (urban); n = 1 53–100 µm indoor dust (urban); n = 1 <100 µm indoor dust (suburban); n = 1	Rasmussen 2004*a*
USA					
Arizona		4.6 (median)	3.6–16.6	N = 135; 43% samples <DL	O'Rourke *et al*. 1999
Region V (Illinois, Indiana, Ohio, Michigan, Minnesota and Wisconsin)	1995–97	11.38 (GM)	0.69–8383	All surfaces; n = 325	NHEXAS 2003
Arizona		4.3 (GM)	1.795–16.57	Floor. n = 117	
Maryland		3.47 (GM)	0.01–249.10	N = 260	
Other countries					
Germany	1990–92	0.86 (GM)	Max 220	N = 3,900	Seifert *et al*. 2000
Australia (Sydney)	1999	1.9 ± 12.7	0.3–109	82 homes in 6 suburbs	Chattopadhyay *et al*. 2003
Australia (Sydney)	1997 and 1999	13 (GM) 2.9 (GM) 2.2 (GM)	2–52 1–19.9 2–3	Attic (ceiling) dust <500 m from industrial building; n = 10 500–1,500 m from indust. building; n = 19 >1,500 m from industrial building; n = 8	Davis and Gulson 2005
New Zealand (Christchurch)	September–October 1987	4.24 (GM)	0.557–21	PM2.5 Carpet; n = 120	Kim and Fergusson 1993
United Kingdom (regional)		1.2 (GM)	0.6–4.9	Indoor dust (vacuum cleaner canisters); n = 32	Turner and Simmonds 2006

Indoor dust

Location	Year	Concentration (mg/kg)	Range (mg/kg)	Comments	Reference
Kingdom of Bahrain	Not reported	1.9	0.3–6.7	Indoor dust (non-residential); n = 76	Madany *et al*. 1994
Egypt (Aswan City)	Not reported	3.72 ± 1.99	1.30–8.80	N = 40	Rashed 2008
Turkey (Kayseri)		3.1 ± 1.16		Indoor dust (doormat); n = 27	Turkoglu *et al* 2004
United Kingdom (regional)		1.2 (GM)	0.6–4.9	Indoor dust (vacuum cleaner canisters); n = 32	Turner and Simmonds 2006

2597 **Notes:** DL = detection limit; GM = geometric mean

Soil

Location	Number of samples	Sample depth (cm)	Concentration mean mg/kg (± SD)	Range	Analytical technique	Reference
Canada						
Compilation of data from across Canada as collected by the Geological Survey of Canada and New Brunswick Department of Natural Resources	14 812	Till samples (<63 µm fraction)	0.24 ± 0.41	0.005–33.7	Partial analysis (ICP or AAS)	HC 2011
Geological survey (five regions, soils away from ore bodies and contamination sources)	173	A, B and C horizons	All determinations <0.3		$HNO_3/HF/HClO_4$ digestion, flame AAS	McKeague and Wolynetz 1980
Newfoundland						
St. John's (urban)	260	Surface soils	0.5 (median)		ICP-ES	Bell 2003
Nova Scotia						
Agricultural soils	864 (total)				0.1N HCl	Baker and Matheson 1980
• North shore		0–15	0.120	0.012–0.430		
		15–30	0.069	0.012–0.376		
• Annapolis Valley		0–15	0.099	0.012–0.469		
		15–30	0.065	0.012–0.349		
Sydney					U.S.EPA-3050A	JDAC 2001*a*; *b*
• Urban reference sites	90	0–5	0.32	0.075–1.0		
• Rural reference sites	91	0–5	0.23	0.15–1.2		
New Brunswick						

Soil

Location	Number of samples	Sample depth (cm)	Concentration mean mg/kg (± SD)	Range	Analytical technique	Reference
1983–84 survey of different regions	40 sites	surface soils: 0–20	0.40	0.10–0.80	H_2O_2 and HNO_3 digestion, ICP-MS	MacMillan 1985
1992: urban garden soils • East St. John • West St. John • Fredericton	24 18 4 2	surface soils	0.1–0.8 (overall) 0.3±0.2 0.3±0.1 0.1±0.0		No data	Pilgrim and Ecobichon 1992
Québec						
Survey of 12 agricultural regions	76 dupl.	Ap horizon	1.10; 98th percentile = 2.0	0.05–3.38	Hot aqua regia; ICP/AAS	Giroux *et al.* 1992
Uncontaminated agricultural soils	296	0–15	0.56 ± 0.89; 0.43 (median)	0.10–8.1	HNO_3 digestion; AAS	Frank *et al.* 1976
Montreal urban soil			0.35	0.22–0.66	26 urban gardens	Hendershot and Turmel 2007
Ontario						
Ottawa • Garden soil	50		0.27 (GM)	0.11–0.75	ICP-MS	Rasmussen *et al*. 2001
Old urban parklands	60	0–5	0.30; 98th percentile = 0.84	0.03–1.16	HNO_3/HCl (aqua regia) ICP/AAS	OMEE 1994
Rural parklands	101		0.26; 98th percentile = 0.71	0.03–1.06		
Essex County, • Agricultural soils • City of Windsor • Roadside soils	131 (39 sites)	Not reported Not reported	0.38 ± 0.02 0.62 ± 0.07		HCl digestion flame AAS	Weis and Barclay 1985
Halton region agricultural soils • No sludge treatment • With sludge treatment	252 57	0–15	<0.5 (median); 0.95; 0.68 (median)	<0.5–2.4 0.19–4.3	H_2O_2 and HNO_3/HF/ $HClO_4$ flame AAS	Webber and Shamess 1987
Agricultural soils[a] • No sludge treatment (10 locations) • With sludge treatment		0–15	0.44 1.06	0.13–1.06[b] 0.62–1.94[b]	H_2O_2 and HNO_3/HF/$HClO_4$ flame AAS	Webber *et al.* 1983
Agricultural soils, southern Ontario	26 sites	Ap horizon B horizon C horizon	(<0.6–1.0) (<0.6–1.7) (<0.6–1.0)		HNO_3/HF/$HClO_4$, flame AAS	Whitby *et al.* 1978
1990: Windsor area[c] • Urban (12 sites) • Rural (18 sites)		0–5 0–5	0.79 0.49	0.41–1.70 0.06–1.06	Not reported	Gizyn 1994

Soil

Location	Number of samples	Sample depth (cm)	Concentration mean mg/kg (± SD)	Range	Analytical technique	Reference
Manitoba, Saskatchewan and Alberta						
Surface soils	1273	Ap horizon	0.28 ± 0.1788; 0.3 (median)	<0.2–3.8	$HF/HClO_4/HNO_3$, flame AAS	Garrett 1994
Manitoba						
Urban (Winnipeg)	11	0–15	1.09 ± 0.26 (0.7–1.7)	1.0–1.22[b]	$HNO_3/HClO_4$, AAS	Mills and Zwarich 1975
Southwest Manitoba highways (ditch, 100 m from highway)	24					
Alberta						
Background concentration	78	A horizon C horizon	No mean reported 0.34	0.08–1.1	Graphite furnace AAS	Dudas and Pawluk 1980
Northwestern Alberta agricultural soils	52 11	0–20 20–35	0.3 0.2	<0.1–0.9 <0.1–0.6	$HF/HClO_4/HNO_3$ extraction, ICP-AES	Soon and Abboud 1990
British Columbia						
Kootenay area, near trail		50–330	0.61	0.11–7.23	$HNO_3/HF/HClO_4$, AA	John, VanLaerhoven and Cross 1975
Fraser River Valley (agricultural soils)			0.88	<0.5–4.67		John 1975
Nelson (reference site)	100[d]	0–2.5	5 3		$HF/HNO_3/HClO_4$, $HNO_3/HClO_4$, ICP/AES ICP/AES	Lynch *et al.* 1980
Near Burnaby municipal incinerator (1987–90):		0–10			$HNO_3/HClO_4$, ICP	Soilcon 1991
Delta, residential garden	48		0.55	0.1–1.3		
Richmond, dairy pasture	48		0.235	0.1–0.7		
Burnaby, residential garden	48		0.77	0.11–1.91		
Richmond, blueberry farm	48		0.48	0.1–1.01		
Burnaby, produce farm	48		3.685 (fertilizer used)	2.4–4.9		
Richmond, cranberry farm	48		0.703	0.1–1.81		
Richmond, bog	36		0.887	0.38–1.33		
Burnaby, woodland park	36		0.183	0.1–1.0		
Various regions: Vancouver Island Lower Mainland Greater Vancouver Southern Interior Kootenay Cariboo Skeena	Not reported	Not reported	95th percentile values: 0.35 0.40 0.55 0.55 1.5 0.45		Aqua regia digestion	BCWLAP 2000

Soil

Location	Number of samples	Sample depth (cm)	Concentration mean mg/kg (± SD)	Range	Analytical technique	Reference
Omineca Peace			0.60 0.90			

Notes: AAS = atomic absorption spectrometry; AES = atomic emission spectrometry; DL = detection limit; GM = geometric mean; ICP = inductively coupled plasma; INAA = instrumental neutron activation analysis; MS = mass spectrometry; SD = standard deviation; wt = weight

[a] Twenty cores per composite sample from four areas per location.

[b] Range of means.

[c] Three replicates per site.

[d] Duplicate samples analyzed using different digestion procedure.

Concentrations of cadmium (µg/g dry wt) in Canadian surface soils in the vicinity of known sources of Cd pollution

Location	Number of samples	Sample depth (cm)	Cadmium concentration mean (±SD) (range)	Analytical technique	Reference
New Brunswick					
Belledune smelter vicinity (1989)		0–5		Not reported	Brunswick Mining & Smelting 1990 *In:* Pilgrim 1995
0.2–0.8 km from smelter	5		(10.5–28.8)		
1.4–2.4 km from smelter	7		(1.0–7.3)		
2.4–8.0 km from smelter	6		(1.5–4.5)		
14.5 km from smelter	1		0.8		
59.0 km from smelter	1		0.5		
Belledune smelter vicinity (7 km)	Not reported	0–10	1.6	Not reported	MacMillan 1990
Charlo	Not reported	0–15	1.8	Not reported	Sergeant and Westlake 1980
Bathurst			1.6		
Tabusintac			1.0		
Belledune smelter vicinity			(5–66.3)		Murphy 1991
Québec					
Rouyn-Noranda peat samples				HNO_3/HF/$HClO_4$, flame AAS	Dumontet *et al*. 1990
1–3.7 km from smelter		0–15	(54–66)		
(pH 4–4.4)		5–30	(4.2–11)		
5–15 km from smelter		0–15	(13–19)		
(pH 3–3.4)		5–30	(0.7–3.5)		
25–43 km from smelter		0–15	(5.5–7.8)		
(pH 2.9–3.1)		5–30	(0.3–2.6)		
Peat samples within 15 km of Noranda smelter			9		Azzaria and Frechette 1987

Concentrations of cadmium (µg/g dry wt) in Canadian surface soils in the vicinity of known sources of Cd pollution

Location	Number of samples	Sample depth (cm)	Cadmium concentration mean (±SD) (range)	Analytical technique	Reference
Duparquet					Azzaria and Frechette 1987
Humus near former gold roasting plant			110		
Peat samples within a few km of roasting site			1,000 (max)		
Ontario					
Sudbury, within a 26 km radius from a nickel or copper smelter			10 (3–47)		McGovern and Balsillie 1975
Near urban secondary Pb smelter	4 sites	0–10		AAS	Bisessar 1982
15 m from smelter			151		
90 m from smelter			102		
150 m from smelter			33		
180 m from smelter			26		
1,000 m from smelter			5		
Near urban smelter	65 sites	0–2.5	2.3	AAS	Linzon *et al*. 1976
		10–15	2.1		
Port Colborne	17 sites,	≤ 20	1.2 (0.0–35.3)	MOE E30731	OMEE 2002
Residential	27 cores each		2.2 (90th percentile)		
Manitoba and Saskatchewan					
Near East Selkirk Coal Generation Station	66	0–7.5	(0.11–0.37)[a]	EPA3051 (3-Acid digestion)	AXYS 2001
Near Flin Flon smelter			(65–280)	Cold-vapour/AES	Zoltai 1988
Flin Flon and vicinity	11	10	3.9 (0.3–10.5)	Strong acid (HCl and HNO_3), ICP/MS	Jones and Henderson 2006
Flin Flon, MN	93 sites	0–2.5	(0.7–70.9)	HCl/HNO_3 digestion, ICP/MS	Manitoba Conservation 2007
Creighton, SK (<3 km from smelter)	13 sites		(0.9–20.8)		
British Columbia					
Vicinity of Pb/Zn smelter in trail; 12.4–197 km from smelter	26	Litter surface horizons	3.51 (GM) (0.99–22.26)	$HNO_3/HF/HClO_4$ digestion, AAS	John, VanLaerhoven and Bjerring 1975
Vicinity of Pb/Zn smelter in trail; ≤ 9.7 km from smelter	13 sites	0–5	17.1 (1.8–36.1)	1N HNO_3, AAS	John, VanLaerhoven and Cross 1975
Vicinity of Pb/Zn smelter in trail; 1.5–25.7 km from smelter	22 sites	0–10	(0.6–16.0)	$HNO_3/HF/HClO_4$ digestion, ICP/MS	Goodarzi *et al*. 2002; 2006

Notes: AAS = atomic absorption spectrometry; GM = geometric mean; ICP = inductively coupled plasma; MS = mass spectrometry; SD = standard deviation; wt = weight

[a] Range of means

Surface water

Location	Year	Mean concentration (µg/L)	Range (µg/L)	Comments	Reference
British Columbia		0.2	<0.1–8.6	N = 2399	NAQUADAT/ENVIRODAT 1992
Yukon		0.1	<0.1–1.3	N = 359	
Northwest Territories		0.4	<0.1–15.4	N = 903	
Alberta		0.3	<0.1–112	N = 652	
Saskatchewan		0.1	<0.1–0.4	N = 388	
Manitoba		0.2	<0.1–2.2	N = 481	
Québec		0.3	<0.1–10.8	N = 750	
Nova Scotia	2009		<1–3		NSE 2010
Belledune Harbour, NB	1984		0.09–0.17	N = 7	Uthe *et al*. 1986
St. Lawrence River, QC	1987		0.007–0.018[a]	N = 9	Lum *et al*. 1991
Saguenay Fjord, QC	1974		0.044–0.074	N = 47	Yeats 1988
Ontario (70 lakes)	1980–87	0.011 (central Shield lakes) 4.78 µg/L (Wavy Lake, Sudbury)		n>100	Alikhan *et al.* 1990; Keenan and Alikhan 1991; Lum 1987; Stephenson and Mackie 1988
Sudbury, ON		122		≤20 km of Sudbury, Ontario; n = 7	Stephenson and Mackie 1988
Central ON		10.8		Elsewhere in central Ontario; n = 57	
Central Ontario lakes			0.051–0.587[a]	≤20 km of smelter	Lum 1987; Lum *et al.* 1991; Yan *et al*. 1990
			<0.002–0.12	70–360 km from smelter	
Lake Ontario, 29 central Shield lakes, and the St. Lawrence River			0.01–0.041	N = 100	
BC				dissolved Cd	
Vancouver Island	2001–10		0.005–0.09	n = 130; 74.6% <DL	BCMOE 2015
Cariboo	1999–2012		0.005–0.145	n = 142; 73.9%<DL	
Omineca–Peace	2002–06		0.01–0.03	n = 32; 87.5%<DL	
Lower Mainland	2007–08		0.01–0.07	n = 25; 96%<DL	
Thomson-Okanagan	2007–08		0.01–0.03	n = 22; 77.3%<DL	
Kootenay	2003–04		0.003–0.009	n = 3; 0%<DL	
Baffin Island, Northwest Territories	1977–78		0.029–0.071	N = 68	Campbell and Yeats 1982; Moore 1981
Baffin Bay		0.31		sea ice	Campbell and Yeats 1982

Notes: [a] Range of mean concentrations

The average cadmium content in the world's oceans was reported at as low as <5 ng/L (WHO 1992*a*) and 5–20 ng/L (Jensen and Bro-Rasmussen 1992; OECD 1994), as high as 110 ng/L (CRC 1996), 100 ng/L (Cook and Morrow 1995) and 10–100 ng/L (Elinder 1985). Higher concentrations were noted around certain coastal areas (Elinder 1985) and variations in cadmium concentration with the ocean depth, presumably due-patterns of nutrient concentrations, were also measured (WHO 1992*a*; OECD 1994).

Groundwater

Location	Year	Mean Concentration (µg/L)	Range (µg/L)	Comments	Reference
Atlantic provinces	1985–88		nd–1	N = 150	EC 1989
Nova Scotia			<0.2–0.74 (mean concentrations)	55 private wells Selected from four communities that represent tjree bedrock types: granite—Hacketts Cove (14 homes) and East Dalhousie (15 homes); quartzite—Cole Harbour (16 homes); limestone—Pleasant Valley (10 homes)	Maessen *et al*. 1985
New Brunswick		0.592 ± 1.834; 0.50 (median)	≤DL -58	N = 1,002; 98% samples <DL of 1µg/L	Boyle *et al*. 1994

Note: DL = detection limit; nd = not detectable

Sediment

Location	**Year**	**Concentration (mg/kg dry wt)**	**Range (mg/kg dry wt)**	**Comments**	**Reference**
Yukon, Québec, New Brunswick, Labrador and BC	1975–91	0.35	0.2–110	Stream sediments (n = 50,000)	GSC 1991
Ontario, Saskatchewan, Northwest Territories, Manitoba, New Brunswick, Labrador and BC		0.38 (GM)	0.2–23.7	Lake sediments	
Baynes Sound, BC	2004	1.15 2.4 2.36		Winter (n=8) Spring (n=16) Summer (n=15)	Widmeyer and Bendell-Young 2008
Port Hawkesbury, NS Sydney, NS Belledune Harbour, NB Entrance—Chedabucto Bay, NS		5.4 0.1	0.45–0.64 0.1–1.3	(International piers) (180 m depth)	Sharp *et al.* 1988.
Yukon		2.28 ± 6.09		N = 15,639; summary of GSC/Yukon Geological Survey database. Stream sediments	Gamberg *et al.* 2005
Tadenac Lake, ON		<3	Not specified	Surface samples from 14 sites, different depths	Wren *et al*. 1983
Canadian Arctic and Subarctic Western streams Eastern streams		 102 ± 03 314 ± 335		 N = 5 N = 6	Evans *et al.* 2005

Sediment

Location	Year	Concentration (mg/kg dry wt)	Range (mg/kg dry wt)	Comments	Reference
Lake, offshore of streams		156 ± 96		N = 6 (depths 5–15 m)	
Lake outflow, 3 m		1,205		N = 1	

Notes: GM = geometric mean; wt = weight
Average concentrations of cadmium in ocean sediments are in the 1 μg/g range (ICdA 2004).

Biota used as human food

Type of food	Mean concentration (mg/kg dry wt)		Range (mg/kg dry wt)	Comment	Reference
Oysters: Desolation Sound	10.2 ± 0.68			Pacific north-west coast, 2003	Christie and Bendell 2009
Barkley Sound	6.0 ± 0.6		26.1 (max)		
American lobster (*H. americanus*)				n = 15; NB (Heron Island), 1992	Chou and Uthe 1993
digestive gland (hepatopancreas)	3.5		2.31–6.97		
cooked meat	0.017		0.01–0.02		
Cisco and walleye	<1 μg/g			Canadian Arctic and Subarctic	Evans *et al*. 2005
Lake trout	≤1 μg/g				
Char			1–2 μg		
Burbot: Muscle	0				
Liver	0.18				
Kidney	0.012				
Pike: Muscle	0				
Liver	0.09				
Kidney	0.18				
Stomach	0.03				
	Liver	Muscle		BC uncontaminated lakes.1982–87	Rieberger 1992
Cutthroat trout	0.29 ± 0.22 (n = 75)	0.22 ± 0.02 (n = 54)		Fish collected from 54 lakes	
Rainbow trout	0.31 ± 0.22 (n = 110)	0.23 ± 0.03 (n = 112)			
Dolly Varden	0.27 ± 0.1 (n = 49)	0.23 ± 0.05 (n = 51)			
Lake trout	0.28 ± 0.09 (n = 19)	0.29 ± 0.22 (n = 75)			
Arctic grayling	0.24 ± 0.09 (n = 13)	0.20 ± 0.02 (n = 22)			
Mountain whitefish	0.25 ± 0.0 (n = 24)				

Biota used as human food

Type of food	Mean concentration (mg/kg dry wt)		Range (mg/kg dry wt)		Comment	Reference
	0.24 ± 0.03 (n = 20)					
Northern pike (n = 20)	nd				Tadenac Lake, ON: undeveloped Precambrian shield watershed 50 km south of Parry Sound.	Wren *et al.* 1983
Rainbow smelt (n = 20)	nd					
Small mouth bass (n = 20)	nd					
Lake char (n = 20)	nd					
Clams (n = 20)	5.8		3.1–9.2			
Bluntnose minnow (n = 6)	0.22		0.16–0.29			
Lake trout (liver) (n = 15)	0.25		0.20–2.9		Northern QC	Langlois and Langis 1995
Ascoohvllum nodosum	0.6 ± 0.2				Pumpkin Island, NS	Sharp *et al.* 1988.
Chondrus criseus	0.5 ± 0.1					
Laminaria diqitat	0.4 ± 0.1					
Laminaria Ionaicruris	0.8 ± 0.1					
Harbour seal (*Phoca vitulina*)					Newfoundland and Labrador	Veinott and Sjare 2006
Kidney			0.34–20.25a			
Liver			0.15–9.6a			
Muscle			0.003–0.032a			
Harp seal (Phoca groenlandica)	Mothers (n = 20)	Pups (n = 20)			Gulf of St. Lawrence. Determined by DCAPES (0.5 g liver and kidney, 1 g muscle). 1984.	Wagemann *et al.* 1988
Liver	22.2 ± 0	<002				
Kidney	105 ± 40	<002				
Muscle	0.15 ± 0.09	<002				
White-beaked dolphin:					Newfoundland	Muir *et al.* 1988
Kidney (n = 25)	13.6 ± 12.4		2.52–43.8		Analyzed by flame AAS	
Liver (n = 26)	2.41 ± 2.46		0.2–8.42			
Muscle (n = 26)	0.09 ± 0.07		0.02–0.24			
Atlantic pilot whale *(G. melaena)*	Grand Beach	Point Leamington	Gr Beach	Pt. L.	Newfoundland	Muir *et al.* 1988
Blubber (n = 14; n = 26)	0.03 ± 0.02	0.03 ± 0.03	0.001–0.07	0.001–0.17	Analyzed by flame AAS	
Kidney (n = 15; n = 26)	138 ± 90.5	77.6 ± 63	0.04–255	0.03–190		
Liver (n = 13; n = 26)	73.9 ± 47.3	42.7 ± 34.3	0.05–162	0.02–102		
Muscle (n = 15; n = 26)	0.19 ± 0.11	0.08 ± 0.07	0.01–0.35	0.004–0.27		

Biota used as human food

Type of food	Mean concentration (mg/kg dry wt)		Range (mg/kg dry wt)		Comment	Reference
Minke whale: Kidney (n = 13)	3.72		1.71–5.62		Baffin Island, NT, 1980–1986	Hansen *et al.* 1990
Liver (n = 17)	0.90		0.50–1.45			
Muscle (n = 16)	0.02		0.01–0.03			
Beluga: Kidney (n = 36)	10.3		0.015–28.7			
Liver (n = 40)	2.21		0.015–8.54			
Muscle (n = 41)	0.03		0.015–0.12			
Narwal: Kidney (n = 93)	39.1		0.015–125			
Liver (n = 90)	10.8		0.015–73.7			
Muscle (n = 85)	0.11		0.015–1.68			
Beluga whale (liver) (n = 5)	4.4		1.2–9.1		Northern Québec	Langlois and Langis 1995
Caribou (Rangifer tarandus):					15 different herds across NU, NT, YK monitored during the 1990s	INAC 2003
Canadian Arctic (liver)	22.5					
Beverly herd	45.6					
Bluenose herd	15.3					
Porcupine herd	17.5					
Tay herd	47.3					
Caribou (*Rangifer tarandus*) kidney	11.5 5				Québec Manitoba	HC 1994
Mainland caribou: Kidney			9.68–42.6			Larter and Nagy 2000
Moose: Kidney (n = 384)	28.11 ± 18.37				Yukon,1994 and 2001	Gamberg *et al*. 2005
Liver (n = 56)	4.94 ± 3.52					
Muscle (n = 37)	0.03 ± 0.03					
Red deer: Muscle	1					Swiergosz *et al*. 1993
Kidney	27					
Wild boar: Muscle	19.8					
Kidney	89.8					
Wild boar: Kidney	2.358					Wolkers *et al*. 1994
Farmed boar: Kidney	1.274					
Snowshoe hare (liver) (n=10)	0.29		<0.02–1.70		Northern QC. 20%<DL	Langlois and Langis 1995
Arctic hare (*Lepus arcticus*)	Adult; n = 9	Juvenile; n = 7	Adult	Juvenile	Nunavut, 2003	Pedersen and Lierhagen 2006
Kidney	106.6	1.73	55.2–219.9	0.29–4.41		
Liver	4.58	0.196	1.68–10.90	0.021–0.44		

Biota used as human food

Type of food	Mean concentration (mg/kg dry wt)		Range (mg/kg dry wt)		Comment	Reference
Muscle	0.032	0.005	0.035–0.201	0.002–0.009		
Willow ptarmigan (liver) (n=2)	8.9		5.9–12.0		Northern QC	Langlois and Langis 1995
Surf scoters (Melanitta perspicillata):			3.7–172 (n=48)		Strait of Georgia, BC, four sites: Baynes Sound, Esquimalt Harbour, Howe Sound, Vancouver Harbour	Harris *et al*. 2007
Adult females (kidney)	18.1					
Adult males (kidney)	37.9					
Canadian Arctic: East Bay:					Concentrations thought to be due to diet of mussels and bottom-dwelling invertebrates.	INAC 2003
Common eider (liver and kidney)			17–25			
King eider (liver and kidney)			32.1–40.8			
Holman (Uluqsaqtuuq)			25.1–32.0			
Common and King eider (liver and kidney)						
Sea bird liver			1.8–21.8 (n=6; fresh wt)		Northern Baffin Bay, three auk (*Alcidae*), four gull (*Laridae*) and one petrel (*Procellariidae*) species, 1988.	Borga *et al*. 2006
Sea bird muscle			0.04–1.2 (n=8; fresh wt)			
Adult pheasants: Liver	3.53					Toman *et al*. 2005
Kidney	9.6					
Muscle	0.03					
Calf: Liver	0.0078					Alonso *et al*. 2000
Muscle	0.0008					
Kidney	0.0543					
Cow: Liver	0.0833					
Muscle	0.0009					
Kidney	0.338					
Cow: Liver (background)	0.21					Cai *et al*. 2009
Liver (mild pollution)	1.31					
Liver (heavy pollution)	2.47					
Muscle (background)	0.002					
Muscle (mild pollution)	0.005					
Kidney (background)	2.15					
Kidney (mild pollution)	6.64					
Kidney (heavy pollution)	38.3					

Biota used as human food

Type of food	Mean concentration (mg/kg dry wt)	Range (mg/kg dry wt)	Comment	Reference
Cow: Liver		0.99–7.00		Smith *et al*. 1991
Muscle		0.09–0.19		
Kidney		0.99–64.19		
Colostrum		0.061–0.072		
Milk		0.032–0.038		
Cow: Liver (background)	0.642			Waegeneers *et al*. 2009
Liver (polluted)	2.655			
Muscle (background)	0.012			
Muscle (polluted)	0.019			
Kidney (background)	4.22			
Kidney (polluted)	15.3			
Cow: Meat	0.004			Doganoc 1996
Liver	0.094			
Kidney	0.373			
Pig: Meat	0.01			
Liver	0.088			
Kidney	0.393			
Pig kidney cortex	0.0678			Lindén *et al*. 1999
Sheep iver		0.14–0.32		Zantopoulos and Nikolaidis 1999
Sheep kidney	3.34			Morcombe *et al*. 1994
Sheep: Liver	0.252			Beresford *et al*. 1999
Kidney	0.3			
Chicken: Crop		0.12–0.22		Hinesly *et al*. 1985
Liver		0.61–2.83		
Muscle		<DL–0.056		
Kidney		4.03–29.5		
Laying hen: Liver		14.2–86.4		Leach *et al*. 1979
Muscle		0.071–2.7		
Kidney		116.3–300.8		
Lettuce grown in urban gardens	0.017 µg/g (fresh weight)	0.003–0.040 µg/g; n = 26 (fresh wt)	Montreal, QC, 2006	Hendershot and Turmel 2007
Durum wheat		0.0017–0.498	Regina and Waitville, SK	Cieśliński *et al*. 1996
Flax		0.1217–1.092		

Biota used as human food

Type of food	Mean concentration (mg/kg dry wt)	Range (mg/kg dry wt)	Comment	Reference
Lettuce		51.1–667.7	Fraser Valley, BC	John 1973
Spinach		207.5–239.3		
Broccoli		36–268.5		
Cauliflower		185.5–198.6		
Peas		9.5–28.2		
Oats		20.8–33.6		
Radish		54.6–123.3		
Carrot		26.8–29.8		

Notes: AAS = atomic absorption spectrophotometry; DCAPES = direct current argon plasma emission spectrometry; DL = detection limit; wt = weight; nd = not detected
[a] Range of mean concentrations

Commercial foods*

Location and food type	Year	Concentration (mean)	Range	Comment	Reference
Canada					
	1995–96				Dabeka *et al*. 2002
Water (µ g/L):					
- Mineral (n = 42)		0.27	<0.10–0.77	21% of samples <DL	
- Spring (n = 102)		0.22	<0.10–1.29	37% of samples <DL	
- Distilled/reverse osmosis (n = 25)		0.22	<0.10–0.40	36% of samples <DL	
- Soda (n = 19)		0.14	<0.10–0.36	58% of samples <DL	
Bottled water (mg/L; MB) (n = 40)		0.2 ± 0.04	<0.1 –1.1	13 ozonated samples: 11 carbonated; five both ozonated and carbonated; 11 neither ozonated nor carbonated.	Pip 2000
Cereals and grains (ppm)	2009–10	0.025	0,003–0.126	Method not provided.	CFIA n. d. a
Confectionary (ppm)		0.074	0.006–0.435		
Dairy (ppm)		0.014	0.002–0.073		
Fish and seafood (ppm)		0.015	0.007–0.024		
Legumes (ppm)		0.025	0.003–0.124		
Meat (ppm)		0.007	0.003–0.014		
Nuts and seeds (ppm)		0.009	0.004–0.023		
Processed fruits and vegetables (ppm)		0.019	0.002–0.130		
Biscuits (ppm)	2010–11	0.020	0.005–0.051	Method not provided.	CFIA n. d. b
Cereals (ppm)		0.016	0.005–0.044		
Cereal bars (ppm)		0.016	0.008–0.046		
Dairy (ppm)		0.011	0.006–0.015		

Commercial foods*

Location and food type	Year	Concentration (mean)	Range	Comment	Reference
Fruit and vegetable snacks (ppm)		0.008	0.002–0.012		
Fruit or vegetable juice		0.007	0.007–0.007		
Meat combinations (ppm)		0.007	0.002–0.019		
Pasta and vegetables (ppm)		0.012	0.005–0.020		
Pureed fruits (ppm)		0.004	0.001–0.047		
Rice snacks (ppm)		0.023	0.001–0.047		
Apple sauce (ppm)	2011–12	0.002	0.002–0.002	Method not provided	CFIA n. d. c
Breakfast cereals (ppm)		0.030	0.005–0.284		
Candy (ppm)		0.040	0.007–0.091		
Cheese (ppm)		0.003	0.002–0.004		
Cookies, crackers, cakes (ppm)		0.024	0.004–0.095		
Dried fruit (ppm)		0.013	0.002–0.025		
Fruit drinks (ppm)		0.009	0.002–0.042		
Fruit or vegetable products (ppm)		0.014	0.002–0.104		
Milk-based drinks (ppm)		0.002	0.002–0.002		
Pasta (ppm)		0.034	0.008–0.122		
Rice-based products (ppm)		0.022	0.004–0.184		
Tomato-based products (ppm)		0.021	0.009–0.088		
Snack food (ppm)		0.017	0.003–0.098		
Nut-based products (ppm)		0.053	0.002–0.210		
Milk-based formula (ppm)	2012–13	0.002	0.001–0.009	Method not provided	CFIA n. d. d
Soy-based formula (ppm)		0.008	0.004–0.044		
Specialized formula (ppm)		0.003	0.002–0.009		
Assorted foods (algae-based, chocolate, legumes) (n = 379) (ppm)	2011–13	1234	0.025–6401	Analysed as-bought; 11 Canadian cities	CFIA n. d. e.
Vegetable- and nut-based foods (n = 613) (ppm)		0.119	0.004–2483	LD=0.002 ppm; LQ=0.007 ppm	
Cereal-based foods (n = 813) (ppm)		0.031	0.002–0.296		
Dairy	2013–14		0.010–0.010	Method not provided	CFIA n. d. f.
Meat			0.002–0.328		
Processed products			0.002–0.056		
Fresh fruit and vegetables			0.002–0.411		
Formula (ng/g)	1986–87				Dabeka 1989
- Evaporated milk (n = 21)		(0.38)	0.017–3.4		
- Ready-to-use milk formula (n = 33)		(0.35)	0.032–3.04		
- Ready-to-use soy formula (n = 16)		(3.39)	1.87–6.7		
- Milk-based liquid formula (n = 34)		(0.71)	0.07–6.5		
- Soy-based liquid formula (n = 16)		(6.84)	3.12–14.8		
- Milk powdered formula (n = 36)		(0.85)	0.33–1.41		
- Soy powdered formula (n = 28)		(10.83)	2.2–32.7		

Commercial foods*

Location and food type	Year	Concentration (mean)	Range	Comment	Reference
Milk-based preparations (ng/g):	2002				HC 2002
- Vancouver (2002)		0.09			
- Montreal (2003)		0.13			
- Winnipeg (2004)		0.16			
- Toronto (2005)		0.43			
- Halifax (2006)		0.40			
- Vancouver (2007)		0.19			
Soy-based formula (ng/g)					
- Vancouver (2002)		1.3			
- Montreal (2003)		1.09			
- Winnipeg (2004)		0.77			
- Toronto (2005)		1.23			
- Halifax (2006)		0.54			
- Vancouver (2007)		0.55			
Cows' milk (ng/g; n = 67)		0.10; 0.039 (median)	0.005–0.74		Dabeka and McKenzie 1988
Dry infant cereals (ng/g; n = 39)		33.6; 28 (median)	11.1–92.5		
Ready-to-use milk-based formula (ng/g)		0.23	0.03–1.26	n=437	Dabeka *et al*. 2012
Soy-based formula (ng/g)		1.18	0.71–2.95		
Lettuce (µg/g; n = 2)		0.015 (fresh wt)	0.003–0.040 (fresh wt)	Montreal, QC, from local grocery stores.	Hendershot and Turmel 2007
USA: Arizona					O'Rourke *et al*. 1999
Drinking water (µg/L; n = 73)		<DL	0.1–0.4	92% <DL	
Beverages (µg/kg; n = 154)		0.6	0.2–9.2	29% <DL	
Food (µg/kg; n = 159)		16.3	3.2–166	0 <DL	

Notes:
DL = detection limit; DW = drinking water; wt = weight
*See Appendix 2 for EDIs based on TDS data (Dabeka *et al*. 2010).

Human breast milk

Location and tissue/fluid	Concentration (mean) µg/L	Range	Comment	Reference
Breast milk				
Canada	0.063 ng/g (GM)	0.001–4.05 ng/g	Assumed mature milk (not specified); n = 210	Dabeka *et al*. 1986
Newfoundland	mg/L			Friel *et al*. 1999
Colostrum (full-term gestation)	<1		N = 17	
Mature milk (full-term gestation)	<1		N = 119	
Colostrum (preterm gestation)	<1		N = 24	
Mature milk (premature gestation)	<1		N = 128	
Austria (Graz)	0.5 µg/kg	0.09–5 µg/kg	Mixed milk (1–293 days postpartum) n = 55	Krachler *et al*. 1998
Austria (Graz)	0.6 ± 0.5	0.09–1.9	Colostrum (2–3 days after delivery) n = 27	Krachler *et al*. 1999
Austria (Graz)	01.68 ± 2.37		Colostrum (3–4 days after delivery) n = 134	Turconi *et al*. 2004
Italy	µg/g	µg/g		Coni *et al*. 1990
All	6	1–65	N = 36	
Rural non-smoker	3	1–6	n = 9	
Rural smoker	12	1–65	n = 9	
Urban non-smoker	6	1–35	n = 9	
Urban smoker	2	1–3	n = 9	
Italy (Turin)	0.8 ± 0.2 ng/ml		Mature (second month lactation)	Coni *et al*. 2000
Sweden (mature milk)	0.06 ± 0.04		Control area relative to exposed smelter area; n=29	Palminger Hallen *et al*. 1995
Japan (mature milk)	0.277	0.07–1.22	5–8 days postpartum, n = 68	Honda *et al*. 2003
United Arab Emirates (mature milk)	0.003 ± 0.008	0.004–0.115	Mothers with children aged 4–80 weeks; n = 205	Abdulrazzaq *et al*. 2008
United Arab Emirates	0.27 ± 0.04	0.023–1.19	N = 120	Kosanovic *et al*. 2008

APPENDIX 2. CANADIAN YEARLY AVERAGE INTAKE OF CADMIUM VIA FOOD INGESTION (WEIGHT-ADJUSTED)

	µg/kg bw/d (males and females)				
	0–6 mo	**7 mo–4 yr**	**5–11 yr**	**12–19 yr**	**20+ yr**
2000	0.1878	0.5036	0.4591	0.2699	0.1815
2001	0.1971	0.4591	0.4215	0.2452	0.1675
2002	0.1755	0.5201	0.4815	0.2873	0.1889
2003	0.2466	0.5126	0.4711	0.2770	0.1888
2004	0.2085	0.5471	0.5048	0.3058	0.2081
2005	0.1845	0.4690	0.4275	0.2493	0.1783
2006	0.1550	0.3358	0.3005	0.1739	0.1097
2007	0.2033	0.5387	0.4819	0.2858	0.1912
Mean	0.1948	0.4858	0.4435	0.2618	0.1767
Standard deviation	0.0269	0.0679	0.0642	0.0408	0.0295

Notes:
mo = months; yr = years
Source: Dabeka *et al*. 2010

APPENDIX 3. TYPICAL ENVIRONMENTAL CONCENTRATIONS USED TO CALCULATE EDIS

Media	Units	Distribution	Statistics	Cadmium
Drinking water[a]	µg/L	Lognormal	Arithmetic mean Standard deviation Minimum Maximum	0.165 1.59 0 1.0
Outdoor air[b]	µg/m^3	Lognormal	Arithmetic mean Standard deviation Minimum Maximum	0.000153 0.000418 0.00000 0.00421692
Indoor air[c]	µg/m^3	Lognormal	Arithmetic mean Standard deviation Minimum Maximum	0.000301 0.000631 0 0.0063684
Surface soil[d]	µg/g	Lognormal	Arithmetic mean Standard deviation Minimum Maximum	0.0240 0.0411 0 4.05
Settled dust[e]	µg/g	Lognormal	Arithmetic mean Standard deviation Minimum Maximum	6.983 141 0 500
Breast milk[f]	µg/L	TRI	Arithmetic mean Standard deviation Minimum Maximum	0.5 1.71 0 16.8

Notes:
EDI = estimated daily intake
[a] Based on average cadmium concentrations of drinking water from Ontario (1998–2007), Saskatchewan (2000–2009) and Newfoundland and Labrador (2000–2009) (HC 2011).
[b] Outdoor air $PM_{2.5}$ concentrations NAPS data collected from 2003 to 2009 from British Columbia, Ontario, Québec and New Brunswick from urban and rural centres (HC 2011).
[c] Indoor air concentrations based on NHEXAS (2003) and the following additional literature sources: Adgate *et al*. 2007, Alberta Health 1998, Balasubramanian and Lee 2007, Bell *et al*. 1994, Graney *et al*. 2004, Komarnicki 2005, and Van Winkle and Scheff 2001 (as cited in HC 2011).
[d] Based on Geological Survey of Canada data; Grunsky 2010 (as cited in HC 2011).
[e] Based on NHEXAS (2003) as well as the following additional literature sources: Chattopadhyay *et al*. 2003, Davis and Gulson 2005, Kim and Fergusson 1993, Madany *et al*. 1994, Rashed 2008, Rasmussen 2004*a*, Rasmussen *et al*. 2001, Seifert *et a*l. 2000, Turkoglu *et al*. 2004, and Turner and Simmonds 2006 (as cited in HC 2011)
[f] Based on cadmium concentration in human breast milk from various literature sources: Abdulrazzaq *et al*. 2008, Coni *et al*. 1990, 2000, Dabeka *et al*. 1986, Friel *et al*. 1999, Honda *et al*. 2003, Kosanovic *et al*. 2008, Krachler *et al*. 1998 and 1999, Palminger Hallen *et al*. 1995, and Turconi *et al*. 2004 (as cited in HC 2011).

APPENDIX 4. CANADIAN GENERAL POPULATION RECEPTOR CHARACTERISTICS USED TO CALCULATE EDIS[A]

Parameter	Statistic	Breast-fed infant (0–6 mo)	Non-breast-fed infant (0–6 mo)	Toddler (7 mo–4 yr)	Child (5–11 yr)	Teen (12–19 yr)	Adult (20+ yr)
Body weight (kg)	Minimum	2.8	2.8	7.1	14.2	30.0	38.1
	Maximum	21.5	21.5	35.9	71.5	112.2	126.5
	Mean	8.2	8.2	16.5	32.9	59.7	70.7
	SD	2.9	2.9	4.5	8.9	13.5	14.5
	Distribution	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Skin surface area: hands (cm^2)	Minimum	242	242	299	396	556	614
	Maximum	416	416	614	863	1,142	1,262
	Mean	320	320	430	590	800	890
	SD	30	30	50	80	100	110
	Distribution	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Skin surface area: arms (cm^2)	Minimum	200	200	396	797	1,409	1,588
	Maximum	1,367	1,367	1,882	2,645	3,465	3,906
	Mean	550	550	890	1,480	2,230	2,510
	SD	180	180	240	300	340	360
	Distribution	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Skin surface area: legs (cm^2)	Minimum	539	539	907	1,604	3,042	3,753
	Maximum	1,496	1,496	3,012	5,655	7,945	8,694
	Mean	910	910	1,690	3,070	4,970	5,720
	SD	160	160	340	660	810	760
	Distribution	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Soil loading-exposed skin[b] (kg/cm^2/event): Hands Other skin surfaces	Mean	1.0×10^{-7} 1.0×10^{-8}	1.0×10^{-7} 1.0×10^{-8}	1.0×10^{-7} 1.0×10^{-8}	1.0×10^{-7} 1.0×10^{-8}	1.0×10^{-7} 1.0×10^{-8}	1.0×10^{-7} 1.0×10^{-8}
Time spent[c] outdoors (hr/d)	Minimum	0	0	0	0	0.13	0.11
	Maximum	3	3	3	4	9.45	10.76
	Mean/mode	1.25	1.25	1.25	2.2	1.42	1.43
	SD					1.17	1.28
	Distribution	Triangular	Triangular	Triangular	Triangular	Lognormal	Lognormal

Notes:
mo = months; SD = standard deviation; yr = years
[a] Mean receptor characteristics from Richardson (1997) and CCME (2006) unless otherwise stated.
[b] Soil loadings from Kissel *et al.* (1996; 1998) as cited in CCME (2006).
[c] Time spent outdoors by an infant, toddler or child is assumed to be equivalent to that of an adult if child or infant is assumed to be accompanied by an adult.

APPENDIX 5. TYPICAL AIR, WATER AND SOIL INTAKE RATES FOR THE CANADIAN GENERAL POPULATION

Intake rates[a]	Statistic	Breast-fed infant (0–6 mo.)	Non-breast-fed infant (0–6 mo)	Toddler (7 mo–4 yr)	Child (5–11 yr)	Teen (12–19 yr)	Adult (20+ yr)
Air inhalation (m^3/d)	Minimum	1.1	1.1	4.6	8.3	9	9.5
	Maximum	4.4	4.4	15.6	25	28.9	33
	Mean	2.18	2.18	8.31	14.52	15.57	16.57
	SD	0.59	0.59	2.19	3.38	4.00	4.05
	Distribution	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Water ingestion[b] (L/d)	Minimum	-	0.1	0.2	0.2	0.2	0.2
	Maximum	-	0.7	0.9	1.1	2	2.7
	Mean	-	0.3	0.6	0.8	1	1.5
	SD	-	0.2	0.4	0.4	0.6	0.8
	Distribution	Not available	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Soil ingestion[c] (g/d)		0.02	0.02	0.08	0.02	0.02	0.02
Soil inhalation[d] (m^3/d)		1.66×10^{-9}	1.66×10^{-9}	6.32×10^{-9}	1.10×10^{-8}	1.18×10^{-8}	1.26×10^{-8}
Indoor settled dust Ingestion (g/d)	Minimum	8.00×10^{-5}	8.00×10^{-5}	0	0	0	0
	Maximum	1.77	1.77	0.94	0.8.33	0.0339	0.0620
	Mean	0.0374	0.0374	0.0406	0.0317	0.00207	0.00251
	SD	0.0833	0.0833	0.0522	0.0458	0.00232	0.00306
	Distribution	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Food[e] (µg/kg bw/d)	Minimum	Breast milk	0.1142	0.2821	0.2508	0.1395	0.08824
	Maximum		0.2754	0.6894	0.6362	0.3840	0.2652
	Mean/Mode		0.1948	0.4858	0.4435	0.2618	0.1767
	SD		0.02688	0.06789	0.06422	0.04076	0.02950
	Distribution	Triangular	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal

Notes:
mo = months; SD = standard deviation; yr = years
[a] Probability distribution function curves for receptor intake rates from HC (2011) unless otherwise stated.
[b] Breast-fed infants are assumed to be exclusively breast-fed for six months and are not given drinking water. Infants that are not breast-fed are assumed to consume 0.3 L of drinking water based on HC (2004).
[c] Soil ingestion rates from CCME (2006).
[d] Soil inhalation rates based on Allan *et al*. (2008) and a PM_{10} concentration of 0.76 µg/m^3 (CCME 2006).
[e] Breast-fed infants are assumed to be exclusively breast-fed for six months and non-breast-fed infants are assumed to be fed a mixture of milk, formula and food.

APPENDIX 6. EDI FOR CADMIUM BY AGE CLASS FOR THE CANADIAN GENERAL POPULATION[A]

Medium of exposure	Daily cadmium intake (µg/kg bw/d)					
	BF Infant (0–6 mo)	**NBF Infant (0–6 mo)**	**Toddler (7 mo–4 yr)**	**Child (5–11 yr)**	**Teen (12–19 yr)**	**Adult (20 yr+)**
AIR						
Ambient air (inhalation)	7.67×10^{-7}	7.67×10^{-7}	1.40×10^{-6}	1.82×10^{-6}	6.23×10^{-7}	5.50×10^{-7}
Indoor air (inhalation)	0.0000329	0.0000329	0.0000613	0.0000518	0.0000310	0.0000281
DRINKING WATER						
Drinking water (ingestion)	Not available	0.000549	0.000485	0.000337	0.000237	0.000301
Indoor settled dust						
Settled dust (ingestion)	0.000671	0.000671	0.000540	0.000198	8.27×10^{-6}	8.03×10^{-6}
Settled dust (dermal)	0.0000207	0.0000207	0.0000148	0.0000111	6.05×10^{-6}	5.68×10^{-6}
SOIL						
Soil (ingestion)	0.00031	0.00031	0.000601	0.0000756	0.0000413	0.0000348
Soil (inhalation)	1.32×10^{-9}	1.32×10^{-9}	2.44×10^{-9}	3.21×10^{-9}	1.09×10^{-9}	9.63×10^{-10}
Soil (dermal)	7.16×10^{-6}	7.16×10^{-6}	5.14×10^{-6}	3.93×10^{-6}	2.11×10^{-6}	1.97×10^{-6}
FOOD						
Food (ingestion)	0.0131[b]	0.190	0.474	0.433	0.255	0.172
TOTAL EDI[c]	0.0143	0.195	0.480	0.436	0.257	0.174

Notes:
EDI = estimated daily intake; mo = months; yr = years
[a] Median values of EDI values for each age class were modeled based on receptor characteristics details listed in Appendix 4 and Appendix 5 and the probability distribution functions of typical concentrations of air (indoor and outdoor), drinking water, indoor settled dust, soil and food based on details in Appendix 3. The probabilistic modeling of the EDI was completed as described in Health Canada (HC 2011). The median value (50th percentile) was chosen to represent the EDI values for the Canadian population.
[b] Human breast milk
[c] Since a probabilistic method was used to develop the EDIs, the total EDI is not the sum of all sub-EDIs for each age category. The total EDI and each sub-EDI have individual probability distribution functions. The 50th percentile (median) for each distribution is displayed in the above table.

2646 **APPENDIX 7. SUMMARY OF EPIDEMIOLOGICAL STUDIES REVIEWED (2004–2012)**

Population studied	Urinary/blood cadmium levels	Effect biomarker	Results	Reference
Cadmium smelter workers (exposed) and health care workers (unexposed), Zhuzhou, Hunan Province, China (n = 114)	Geometric means Non-exposed (non-smokers, n = 15): • UCd = 1.14 µg/g creatinine • BCd = 1.82 µg/L Non-exposed (smokers, n = 14): • UCd = 1.65 µg/g creatinine • BCd = 6.89 µg/L Exposed (non-smokers, n = 25): • UCd = 2.52 µg/g creatinine • BCd = 3.86 µg/L Exposed (smokers, n = 60): • UCd = 3.53 µg/g creatinine • BCd = 13.38 µg/L	Biomarkers of tubular and glomerular dysfunction: • Urinary ß$_2$-microglobulin (ß$_2$-UMG), N-acetyl-ß-D-glucosaminidase (UNAG); albumin (UALB) Relationship between urinary MT (UMT) also compared against exposure biomarkers and effect biomarkers	• Significant UMT increase at UCd ≥2 µg/g creatinine and BCd ≥5 µg/L • Significant correlation of UMT with UCd and BCd • ß$_2$-UMG, UALB, UNAG significantly positively correlated with UMT • Dose-response relationship with UCd and indicators of renal tubular dysfunction • $BMDL_{10}$ (estimated from UCd): 3.11 µg/g creatinine for UMT (used as an indicator of renal dysfunction) • 2.72 µg/g creatinine for UNAG • 3.37 µg/g creatinine for ß$_2$-UMG • 4.23 µg/g creatinine for UALB • Conclusion: UMT can be used as a biomarker of renal tubular dysfunction	Chen *et al.* 2006*a*
Middle-aged Japanese women (35–60 yrs old) (data from previously collected datasets; no occupational exposure) (n = 10,753)	• UCd (GM±SD): 1.26 ± 2.099 µg/g creatinine, range: <DL–20.9 µg/g creatinine	• Urinary microglobulins • (α1-UMG; ß2-UMG) • Urinary Ca, urinary Mg, urinary Zn	• α1-UMG possibly associated with increased UCd. However, there is no clear-cut evidence showing environmental exposure to Cd induced tubule dysfunction. • No thresholds for UCd with the other elements measured in the urine (Ca, Mg, Zn).	Ezaki *et al.* 2003
Rural, elderly Chinese (>65 yrs old); Sichuan and Shandong, China (n = 2,000)	• Mean BCd level: 1.75 µg/L • Median BCd: 0.05 µg/L • BCd range: 0.05–10.96 µg/L	• Composite cognitive score from cognitive assessment tests • Cd, Al, Ca, Cu, Fe, Pb, and Zn measured in the plasma of 188 participants	• Increasing BCd and BCu associated with a lower composite score ($p<0.0044$ and $p<0.0121$, respectively), while increasing BCa associated with a higher composite score ($p<0.0001$).	Gao *et al.* 2008
Non-ferrous metal smelter workers (male) (occupational Cd and Pb exposure); France (n = 57)	Control • UCd (mean ± SD) = 0.67 ± 0.45 µg/g creatinine (range: 0.08–2.43) • BCd (mean ± SD) = 0.84 ± 0.63 µg/L (range: 0.16–2.95) Exposed • UCd (mean ± SD) = 2.51 ± 1.89 µg/g creatinine (range: 0.26–6.80) • BCd (mean ± SD) = 3.26 ± 2.11 µg/L (range: 0.36–9.46)	Markers of oxidative stress: • Malondialdehyde (MDA), superoxide dismutase, glutathione peroxidase, selenium, glutathione reductase Proximal tubule markers: • Retinol binding protein (RBP), α-glutathione-S-transferase (α-GST), total N-acetyl-ß-D-glucosaminidase (NAGtotal), NAG (isoforms A and B) Distal tubular marker: • π- glutathione-S-transferase General markers: • Urinary protein • 8'-hydroxy-2'-desoxyguanosine	• Markers of oxidative stress (MDA), proximal tubular damage (RBP, α-GST), and total urinary protein correlated with Cd (MDA, GST and protein also correlated with Pb). • Overall, α-GST is correlated with early changes in proximal tubular integrity after exposure to relatively low levels of Cd (and Pb).	Garçon *et al.* 2007
Torres-Strait Islanders, Australia; mix of Australian and	GM: All groups • UCd = 0.93 µg/g creatinine	• Albumin creatinine ratio (ALBCreat); normal if <3.4 g/mol	• Higher UCd in non-diabetics with albuminuria (GM = 1.21 µg/g creatinine) compared to individuals with normal ALBCreat (GM = 0.81 µg/g creatinine).	Haswell-Elkins *et al.* 2008

Population studied	Urinary/blood cadmium levels	Effect biomarker	Results	Reference
aboriginals, males and females (n = 182)	With diabetes • UCd = 1.20 µg/g creatinine No diabetes • UCd = 0.86 µg/g creatinine		• Higher UCd in those with diabetes and albuminuria (GM = 1.91 µg/g creatinine) than those with diabetes and normal ALBCreat (GM = 0.74 µg/g creatinine). • UCd and ALBCreat are significantly linked and the association is stronger in people with diabetes.	
Individuals (16–80 yrs old) vicinity of a battery plant in Sweden (n = 492)	UCd (nmol/mmol creatinine): median (10th–90th percentile) • Males: 0.33 (0.16–0.74) • Females: 0.46 (0.21–0.99)	• Environmental Cd-exposure index reflecting exposure via ambient air and consumption of food grown on contaminated soil. • Dietary intakes based on home grown vegetable or potato consumption, other factors such as smoking compared to UCd levels.	• Increased UCd levels (UCd >1.0 nmol/mmol creatinine) are associated with various factors, including home-grown vegetable or potato consumption, high environmental Cd-exposure index, female gender, age >30 years, and smoking >1 pack for at least 10 years. • Consumption of locally grown potatoes and vegetables estimated to increase UCd by 18 to 38%.	Hellstrom *et al.* 2007
Rural Japanese women living in a polluted area with environmental exposure near the pTWI (7 µg/kg bw/week), including women with diabetes mellitus or anemia (n = 38)	GM: • UCd (whole group): 4 µg/g creatinine Diabetes control • UCd = 5.16 µg/g creatinine, • BCd = 4.98 µg/L Diabetes • UCd = 4.90 µg/g creatinine, • BCd = 2.18 µg/L Anemia control • UCd = 2.72 µg/g creatinine, • BCd = 2.71 µg/L Anemia • UCd = 2.92 µg/g creatinine, • BCd = 3.56 µg/L	• Dietary absorption calculated from the total cadmium intake during experiment (440–511 µg/d) and total fecal excretion of cadmium.	• Determined factors affecting absorption of Cd. • Multiple regression analysis showed that age was the only independent factor affecting Cd absorption (greater absorption rates in younger women).	Horiguchi *et al.* 2004*b*
Southeastern China, cross-sectional study, three groups: a) worked in smelter and lived in Cd-polluted area (n = 44) b) never worked in smelter and lived in Cd-polluted area (n = 88) c) never worked in smelter or lived in Cd-polluted area (n = 88)	UCd (µg/g creatinine) (GM) • Group A = 11.86 • Group B = 9.51 • Group C = 1.81 BCd (µg/L) (GM) • Group A = 9.66 • Group B = 7.82 • Group C = 1.53	• Indicators of renal tubular dysfunction: ß2-microglobulin (ß2-UMG) and N-acetyl-ß-D-glucosaminidase (NAG) • Indicator of renal glomerular function: urinary albumin (ALB)	ß2-UMG (mg/g creatinine) (GM) • Group A = 0.521 • Group B = 0.346 • Group C = 0.170 NAG (U/g creatinine) (GM) • Group A = 10.35 • Group B = 7.10 • Group C = 2.20 ALB (mg/g creatinine) (GM) • Group A = 6.4 • Group B = 5.0 • Group C = 2.9 Overall, results showed a higher rate of renal dysfunction in the occupationally and environmentally exposed group.	Jin, Kong *et al.* 2004
Male lung cancer patients aged 40–70 yrs, Sindh, Pakistan, current or ex-smokers	BCd (µg/L) (mean) • Non-smokers: 5.42 (control), 9.53–13.62 (patients—all stages)	• Association: Cd concentration, cigarette smoking and lung cancer risk	• Positive associations between Cd concentrations, cigarette smoking and lung cancer risk. • Cd concentrations greater in lung cancer patients at different stages compared to controls.	Kazi *et al.* 2008

Population studied	Urinary/blood cadmium levels	Effect biomarker	Results	Reference
(n = 120 lung cancer patients, n = 150 controls)	• Smokers: 8.6 (control), 14.61–15.94 (patients—all stages) Scalp hair (µg/g) (mean) • Non-smokers: 1.4 (control), 2.13–4.34 (patients—all stages) • Smokers: 2.52 (control), 3.35–3.72 (patients—all stages)		• Smoker controls have a greater blood and hair Cd concentration than non-smoker controls.	
Post-menopausal Japanese women (n = 164)	UCd distributions (µg/g creatinine) • <1 (2.4%) • 1–1.99 (27.4%) • 2–2.99 (42.7%) • 3–3.99 (17.7%) • 4–5.35 (9.8%)	• Estrone, estradiol, testosterone, and dehydroepiandroesterone (DHEAS) serum hormone levels	UCd = 0–2 µg/g creatinine • Estrone = 17.8 pmol/L; testosterone = 0.25 nmol/L; DHEAS = 1,971 nmol/L UCd = 2.01–3 µg/g creatinine • Estrone = 24.4 pmol/L; testosterone = 0.32 nmol/L; DHEAS = 2,523 nmol/L UCd = >3 µg/g creatinine • Estrone = 21.5 pmol/L; testosterone = 0.32 nmol/L; DHEAS = 2,592 nmol/L • Overall, significant association between UCd and serum testosterone even after adjustment for smoking, alcohol and reproductive factors including known risk factors for breast cancer (high testosterone levels could be linked to breast cancer).	Nagata *et al.* 2005
Flemish adult population (northeast Belgium) (n = 994) living near Zn smelters and a reference group (low Cd exposure)	Baseline measurements (1985–1989) (GM) • BCd (nmol/L) = 10.5 (low exposure), 11.9 (high exposure) • UCd (nmol/d) = 7.7 (low exposure), 12.3 (high exposure)	• Population follow-up for (median) 17.2 years (until 2004) • Used Cox regression to calculate hazard ratios relating internal (urinary) and external (soil) exposure to Cd	• Significant association between lung cancer and environmental Cd exposure. Lung cancer, hazard ratio (HR) adjusted for smoking: • HR = 1.70 (1.13–2.57, p = 0.011) for a doubling of 24-h UCd excretion • HR = 4.17 (1.21–14.4, p = 0.024) for residence in the high- vs low-exposure area • HR = 1.57 (1.11–2.24, p = 0.012) for a doubling of soil Cd concentration	Nawrot *et al.* 2006

Flemish women (northeast Belgium) (mean age = 49.2 yrs), environmental exposure (n = 294)	Arithmetic mean
	Pre-menopausal women
	• UCd = 5.7 nmol/d
	• BCd = 6.9 nmol/L
	Menopausal women
	• UCd = 9.8 nmol/d
	• BCd = 8.5 nmol/L
		• Forearm density (proximal, distal)
		• Biomarkers of bone resorption:
		  • Urinary hydroxylysylpyridinoline (HP)
		  • Urinary lysylpyridinoline (LP) urinary Ca
		  • Serum total Ca
		  • Parathyroid hormone (serum)
		  • Calcitonin
		  • Bone-alkaline phosphatase
		• Marker of renal effect:
		  • Urinary-retinol binding protein
			• Environmental exposure to Cd increases bone resorption in women in the absence of tubular renal dysfunction.
			• Increased UCd excretion correlated (among quartiles of 24-h urinary excretion) with increased urinary excretion of HP and Ca, and with a decreased level of parathyroid hormone in serum.
				Schutte *et al.* 2008

Adults (>35 yrs), males and females, in southern China; metal smelter area	GM UCd (µg/g creatinine): • 1.83 (control) • 3.55 (moderate) • 11.18 (high)	• Renal dysfunction • ß2-microglobulin (ß2-MG) • N-acetyl-ß-D-glucosaminidase (NAG) • Retinol-binding protein (RBP)	• UCa higher in the high exposure group. • Association between increased prevalence of osteoporosis and greater Cd exposure and with biomarkers of renal tubule damage.	Jin, Wu *et al.* 2004

Population studied	Urinary/blood cadmium levels	Effect biomarker	Results	Reference
(n = 294 high exposure, n = 243 moderate exposure, n = 253 control)		• Urinary calcium (UCa) • Glomerular dysfunction • Albumin • Osteoporosis (Z score <-2) • Forearm bone mineral density	• Prevalence of renal dysfunction also present in individuals with osteoporosis. • No association of osteoporosis with glomerular dysfunction.	
Mixed population (environmental exposure) (16–60 yrs), Bangkok, Thailand (n = 200)	Arithmetic mean • BCd (nM) = 4.2 (female non-smoker), 5.4 (male non-smoker), 7.6 (male smoker) • UCd (nM) = 3.5 (female non-smoker), 2.7 (male non-smoker), 6.0 (male smoker)	• Total protein • ß2-microglobulin (ß2-MG) • N-acetyl-ß-D-glucosaminidase (NAG) • Blood pressure (systolic, diastolic)	• Increased Cd concentrations associated with an increases probability of developing high blood pressure. • Individuals with renal dysfunction resulting from high Cd exposure may have an even higher probability of developing high blood pressure.	Satarug *et al.* 2005
Women in southern Sweden (54–63 yrs old) (n = 820)	Median (5th–95th percentiles) values • BCd = 0.38 (0.16–1.8) µg/L • UCd = 0.67 (0.31–1.6) µg/g creatinine • UCd = 0.52 (0.24–1.3) µg/L	• Serum cystatin C for calculation of the glomerular filtration rate (GFR) • Creatinine clearance (marker of glomerular function) • Urinary human complex-forming protein (protein-HC, α1-microglobulin), N-acetyl-ß-D-glucosaminidase (NAG), and Ca for tubular damage	• Overall, concentrations of BCd and UCd showed significant associations with renal tubule and with glomerular effects, as per the biomarkers (human complex-forming protein, NAG, GFR and creatinine clearance). • Significant effects for tubular function at 0.8 µg UCd/g creatinine (0.6 µg/L), corresponding to ~20 µg/g kidney cortex. Significant effect on glomerular function seen at 1.0 µg/g creatinine (0.86 µg/L). • Tubular renal effects seen at lower Cd levels than previously observed	Åkesson *et al.* 2005
Women southern Sweden (54–63 yrs old) (n = 820)	• BCd = 0.38 µg/L (median) • UCd = 0.52 µg/L (median)	• Bone metabolism • Parathyroid hormone (PTH), osteocalcin, bone alkaline phosphatase (bALP) in serum, deoxypyridinoline (U-DPD) and Ca in urine • Forearm bone mineral density (BMD)	• After multivariate adjustments, BMD, TH and U-DPD (bone resorption) adversely associated with Cd urinary excretion, even in non-smokers. • Negative effects of low-level Cd exposure (cause osteoporosis) • Increased bone resorption (greater after menopause)	Åkesson *et al.* 2006
Human Biological Monitoring (HBM) project (2001–2003), Czech Republic: n = 1,188 adults (blood), n = 657 adults (urine), n = 333 children (blood), n = 619 children (urine)	• Median BCd adult = 0.5 µg/L (total) • Smoker BCd = 1.3 µg/L vs non-smoker BCd = 0.4 µg/L • BCd child 65% <LD • Median UCd adult = 0.31 µg/g creatinine • Women Ucd = 0.39 µg/g creatinine vs. Men Ucd = 0.29 µg/g creatinine • No Ucd difference between smokers and non-smokers	• Compared BCd and Ucd levels against smoking status, age and sex	• Updating levels in the Czech Republic (baseline) • Reference values recommended for 2001–03: • BCd = 1.1 µg/L • Ucd = 1.2 µg/g creatinine	Batariova *et al.* 2006
Cross-sectional European study (France, Czech Republic, Poland) children aged 8.5–12.3	France • BCd (µg/L): female = 0.47 (control), 0.5 (exposed); male = 0.46 (control), 0.52 (exposed) • Ucd (µg/g creatinine): female = 0.91 (control), 1.07 (exposed);	Renal and dopaminergic Renal biomarkers: • Serum creatinine, urinary creatinine, • Serum cystatin C, serum ß2-microglobulin (ß2-SMG), urinary	• Consistent increase of URBP, urinary Clara cell protein and UNAG with BCd and Ucd, even at low Cd levels. • Heavy metals may have an effect on the renal and dopaminergic systems in children (no clear threshold)	de Burbure *et al.* 2006

Population studied	Urinary/blood cadmium levels	Effect biomarker	Results	Reference
yrs, Cd-polluted areas (n = 804)	male = 1.02 (control), 1.15 (exposed) Czech Republic • BCd (µg/L): female = 0.20 (control), 0.24 (exposed); male = 0.20 (control), 0.29 (exposed) • Ucd (µg/g creatinine): female = 0.22 (control), 0.25 (exposed); male = 0.22 (control), 0.24 (exposed) Poland • BCd (µg/L): female = 0.08 (control), 0.19 (exposed); male = 0.07 (control), 0.19 (exposed) • Ucd (µg/g creatinine): female = 0.45 (control), 0.56 (exposed); male = 0.44 (control), 0.68 (exposed)	retinol-binding protein (URBP), N-acetyl-ß-D-glucosaminidase (UNAG) in urine Dopaminergic biomarkers: • Urinary homovanillic acid • Serum prolactin		
Women (50–90 yrs) (NHANES studies) (n = 3,207) 1998–94, (n = 1,051) 1999–2004	Ucd (arithmetic mean) (µg/g creatinine) • 0.96 (all women) • 1.12 (women with osteoporosis) • 0.92 (no osteoporosis)	• Hip bone mineral density (BMD)	• Evidence that increased Cd body burden may be linked to prevalence of osteoporosis. • Risk of osteoporosis increased by 43% in women aged ≥50 yrs with Ucd between 0.50 and 1.0 µg/g creatinine compared to ≤0.50 µg/g creatinine (OR = 1.43, 95% CI: 1.02–2.00, p = 0.04) (after adjustment for confounders). • Null findings among smokers suggest increased Cd body burden linked to dietary Cd intake and that current dietary exposure in the US (11 µg/person/d) may be too elevated.	Gallagher *et al.* 2008
Flemish adult population (northeast Belgium) (n = 473)	GM (5th–95th percentile) Low exposure area (8–13.6 km from a smelter) • BCd = 6.2 (1.8–21.4) nmol/L • UCd = 7.0 (2.2–19.6) nmol/24 hr High exposure (0.4–2.1 km from a smelter) • BCd = 9.2 (2.7–27.6) nmol/L • UCd = 10.5 (2.8–32.7) nmol/24 hr	• Compared biomarkers of exposure with metal loading rates (house dust, vegetable index)	• Concluded that house dust can contribute significantly to metal uptake; therefore, it should be considered in risk assessments.	Hogervorst *et al.* 2007

Japanese women from five districts (four contaminated and one non-contaminated) (n = 1,380 total)	GM
	• BCd = 2.54 µg/L (all)
	• UCd by district: 2.6 (non-contaminated), 3.5, 3.2, 3.2 and 4.1 (contaminated) µg/g creatinine
	• UCd = 3.46 µg/g creatinine (all)
	• UCd by subgroup (<2.5, 2.5–<3.5, 3.5–<5.0, ≥5.0 µg/g creatinine): 1.66, 2.98, 4.17, 6.75 µg/g creatinine
		• Luteinizing hormone
		• Renal effects: α1-MG, ß2-MG, Ca, creatinine (urine)
		• Bone effects:
		  • Serum bone-specific alkaline phosphatase (BALP) and bone Gla protein (BGP)
		  • Urinary N-telopeptide crosslinked collagen type 1
			• Dose-related changes of most renal and bone biomarkers (UCa, BALP, NTx, α1-MG, ß2-MG, BMD)
			• Concluded that Cd-induced bone injury is a secondary effect of renal dysfunction.
				Horiguchi *et al.* 2005

Population studied	Urinary/blood cadmium levels	Effect biomarker	Results	Reference
		(NTx) and deoxypyridinoline (DPD) • Forearm BMD		
Swedish OSCAR study (osteoporosis; Cd as a risk factor) (n = 1,021), occupationally and environmentally exposed and controls	• No data reported	• Indicator of renal tubular damage: protein HC (α1-MG) • Forearm bone mineral density (BMD)	• Tubular proteinuria can occur at Cd levels much lower than previously seen. • Negative dose effect between UCd and BMD (60 years+), increased forearm fractures with increased Cd levels. • Odd ratios (OR) for low bone mineral density (Z-score <-1), compared to UCd <0.5 nmol/mmol creatinine. • UCd ≥0.5–<3 nmol/mmol creatinine: OR = 1.12 (95%CI: 0.81–1.56) • UCd ≥3 nmol/mmol creatinine: OR = 3.2 (95% CI: 1.72–5.9)	Järup and Alfvén 2004
Females (20–69 yrs) Wisconsin, U.S. (n = 254)	• Mean UCd concentrations for all women in study = 0.08–2.64 µg/g creatinine	• Compared UCd levels against various possible determinants such as smoking, age, multivitamin/multimineral use, Zn supplements, etc.	• Smoking status and age are the strongest determinants of UCd levels.	McElroy *et al.* 2007
Male and female (50+ yrs), Kakehashi river basin, Japan (Cd polluted) (n = 3,119) follow-up	GM • Men (50 + years old) = 4.55 µg/g creatinine • Women (50 + years old) = 7.16 µg/g creatinine	• Dose-response relationship between UCd and mortality (mortality risk calculated)	• Causal association between Cd body burden (UCd ≥3 µg/g creatinine) and mortality.	Nakagawa *et al.* 2006
US adults (general population) ≥20 yrs old (NHANES 1999–2004) (n = 10,991 BCd, n = 3,496 UCd)	GM (all participants) • BCd = 3.77 nmol/L • UCd = 2.46 nmol/L	• Systolic and diastolic blood pressure measurements	• BCd positively associated with slight increases in blood pressure levels. • Association is stronger in never-smokers than current smokers. • No association between UCd and blood pressure levels nor between UCd or BCd and the prevalence of hypertension.	Tellez-Plaza *et al.* 2008
Adults exposed or not to Cd as children (vicinity of a Zn smelter) (n = 172 unexposed, n = 136 exposed)	GM Unexposed group • BCd (µg/L) = 1.37 (1993), 1.6 (2000) • UCd (µg/g creatinine) = 1.28 (1993), 2.23 (2000) Exposed group • BCd (µg/L) = 0.6 (1993), 0.87 (2000) • UCd (µg/g creatinine) = 0.86 (1993), 0.97 (2000)	• Renal tubular dysfunction • Urinary ß2-microglobulin (ß2-UMG), urinary retinol binding protein (URBP), N-acetyl-ß-D-glucosaminidase (NAG) and isoforms A and B (NAG-A, NAG-B) • Glomerular dysfunction • Albumin in urine (ALB-U) • ß2-microglobulin in serum (ß2-SMG)	• Early signs of renal effects may occur at UCd ≥2 µg/g creatinine. • Cd exposure in childhood may be more significant for causing effects than exposure in adults.	Trzcinka-Ochocka *et al.* 2004
Flemish adult population (northeast Belgium), low exposure area (n = 476) or high exposure area (near Zn smelters) (n = 480).	Follow-up of the BCd (1985–2003) and UCd (1985–96) (GM) BCd (nmol/L), low exposure • = 10.6 (1985–89) • = 6.3 (1991–96)	• Follow-up for mortality until 2007 • Hazard ratios • 1985–89 biochemical measurements	• Increased mortality (total and from cardiovascular disease) resulting from increased environmental Cd exposure.	Nawrot *et al.* 2008

Population studied	Urinary/blood cadmium levels	Effect biomarker	Results	Reference
Last smelter closed in 2002.	• = 7.4 (2001–03) UCd (nmol/d), low exposure • = 7.7 (1985–89) • = 6.7 (1991–96) BCd (nmol/L), high exposure • = 11.5 (1985–89) • = 8.8 (1991–96) • = 8.2 (2001–03) UCd (nmol/d), high exposure • = 11.7 (1985–89) • = 9.1 (1991–96)			
Pregnant Bangladeshi women (n = 890)	UCd (median, 10th–90th percentile) = 0.59 (0.22–1.53) µg/L	• Plasma ferritin and plasma Zn	• Determined how stores of Fe and Zn affected Cd uptake and accumulation. • Low Fe and adequate Zn associated with significantly higher UCd. No significant association for women with adequate Fe and Zn stores or low Fe and Zn stores.	Kippler *et al.* 2007
Bangladeshi mothers and newborns from a rural area (n = 1,916), non smokers.	UCd at the 8th wk of gestation (µg/L, adjusted for mean specific gravity): • Mean ± SD = 0.81 ± 0.67 • Range: 0.044–7.0 • Median: 0.63 • 25th–75th percentile: 0.38–1.0	• not available	• A 1 µg/L increase in maternal UCd associated with a decrement of 45 g (95% CI: -82.5–7.3) in mean birth weight, 0.26 cm in mean head circumference (95% CI: -0.43–0.088) and 0.24 cm (95% CI: -0.44–0.030) in mean chest circumference in girls.	Kippler *et al.* 2012
Japan (male and female), Cd-polluted areas (n = 3,103) and non-polluted areas (n = 2,929)	UCd (GM, range) • Male = 3.0 (0.01–49.6) µg/g creatinine • Female = 4.2 (0.02–57.6) µg/g creatinine	• ß2-microglobulinuria	ß2-MG (GM and range) • Male = 157 (1–107,922) µg/g creatinine; n = 2,578 • Female = 195 (2–186,668) µg/g creatinine; n = 3,454 • Calculated threshold levels for UCd based on ß2-microglobulinuria using a benchmark dose approach (multiple regression analyses) and using various cut-off values. Determined that threshold levels should be age-specific.	Kobayashi *et al.* 2008
Men working in Cd pigment factory (n = 11)	1st year–4th year • UCd (mean) = 14.2–7.8 µg/g creatinine • BCd (mean) = 2.15–1.56 µg/100 g • ambient air (Cd) concentrations changed from year 1 to year 2.	• Markers of renal tubular function: • ß2-microglobulin in the serum (ß2-SMG) • ß2-microglobulin in the urine (ß2-UMG)	• Strong association between markers of renal tubular function and UCd and BCd. ß2-SMG & ß2-UMG increased as UCd and BCd increased.	Kawasaki *et al*. 2004
England (male and female, 18–86 yrs), Cd-polluted area (≤7 km of a (closed) Zn smelter) (n = 180 among which 15 exposed occupationally)	UCd (median; non-smokers/smokers) • Men (n = 58) = 0.18/0.40 µg/g creatinine • Women (n = 102) = 0.31/0.46 µg/g creatinine • Men and women combined: 0.25/0.44 µg/g creatinine	Three urinary biomarkers of tubular damage: • N-acetyl-ß-D- glucosaminidase (UNAG) • Retinal-binding protein (URBP) • α-1-microglobulin (α1-UMG)	• Significant dose-response relationship between UCd and the prevalence of UNAG above reference level • OR = 2.64 (95% CI: 0.70–9.97) at 0.3–<0.5 µg/g creatinine • OR = 3.64 (95% CI: 0.98–13.5) at ≥0.5 µg/g creatinine • No change in the dose-response trend without smokers.	Thomas *et al.* 2009
Poland (male and female, 18–76 yrs), Cd-	GM±SD • UCd (women) = 1.08 ± 2,15 µg/g creatinine	• Tubular damage: • Albuminuria (UALB)	Simple dose-effect analysis indicated: • a significant increase of low-molecular protein excretion at UCd levels ≥1 µg Cd/g creatinine.	Trzcinka-Ochocka *et al*. 2010

Population studied	Urinary/blood cadmium levels	Effect biomarker	Results	Reference
polluted area (Zn smelter) (n = 270)	• UCd (men) = 0.88 ± 2.33 µg/g creatinine • BCd (women) = 1.27 ± 2.15 µg/L • BCd (men) = 1.15 ± 2.64 µg/L	• Urinary ß2-microglobulin (ß2-UMG) • Urinary retinol-binding protein (UBRP) • Urinary N-acetyl-ß-D-glucosaminidase (UNAG) • Bone effects: • Bone mineral density (BMD) • Bone mineral content • Urinary Ca • Serum bone alkaline phosphatase • Serum C-terminal telopeptide fragment of collagen type 1	• a statistically significant reduction of bone mineral density from 2 µg Cd/g creatinine. However, multivariate analysis did not indicate an association between Cd exposure and bone mineral density.	
US general population (males and females) (third NHANES) (n = 10,978 subjects aged 30–90 yrs)	• UCd (mean) = 0.55, 0.77 and 1.16 µg/g creatinine in the normal population (n = 6,811), osteopenic population (n = 3,417) and osteoporotic population (n = 750), respectively	• Bone mineral density	• Analysis of data from the third US NHANES indicated Cd exposure may be a risk factor for osteoporosis independent of age, sex, ethnicity and smoking status. • After adjustment for age, sex, ethnicity, body mass index, Ca intake and physical activity, OR were (for UCd concentrations of 1.00–1.99 and for ≥2.00 µg Cd/g creatinine, respectively): • Osteopenia, OR =1.49 (95%CI: 1.24–1.80) and 2.05 (95%CI: 1.52–2.78) • Osteoporosis, OR = 1.78 (95%CI: 1.26–2.52) and 3.80 (95%CI: 2.36–6.14)	Wu *et al.* 2012
Women, general population (non-polluted area), aged 39–77 yrs (mean 54.6 yrs) (n = 389)	• BCd: 1.57 ± 2.11 µg/L (GM±SD) • UCd: 1.93 ± 2.05 µg/g creatinine (geometric mean ± SD)	Renal biomarkers: • Urinary ß2-microglobulin (ß2-UMG), • Urinary N-acetyl-β-D-glucosaminidase (UNAG) Bone metabolism: • Serum bone alkaline phosphatase (SBAP) • Urinary cross-linked N-telopeptide of type I collagen (UNTx) • Urinary free deoxypyridinoline (DPD) • Quantitative ultrasound bone measurements	• Positive correlations between Cd exposure and biomarkers of altered bone metabolism: • DPD and UCd or Cd intake • UNTx and UCd or Cd intake • No significant correlation between parameters of ultrasonic bone evaluation and Cd-associated biomarkers. • Possibility of bone metabolic disorder induced by environmental low-grade Cd exposure (21.6 µg/d, corresponding to 3.6 µg/kg bw/d). • Long-term follow up recommended.	Osada *et al.* 2011
General population (males and females), all ages, industrial area in Korea (n = 804)	UCd, GM±SD • Males: 0.48 ± 2.67 µg/g creatinine • Females: 0.64 ± 2.84 µg/creatinine	• Bone mineral density (BMD) at the non-dominant heel	• BMD significantly decreased with UCd in adults but not in children or teenagers. • Increased risk of osteopenia in adults with UCd excretion >0.5 µg/g creatinine, OR = 2.92 (95% CI: 1.51–5.64) in females and 3.37 (95% CI: 1.09–10.38) in males. OR in median exposure group = 1.18 (95%CI: 0.57–2.44) in females and 1.29 (95% CI: 0.49–3.36) in males.	Shin *et al.* 2011

Population studied	Urinary/blood cadmium levels	Effect biomarker	Results	Reference
			• Similar results in smokers (similar odd ratios). • Environmental exposure may present a risk.	
Schoolchildren (males and females) aged 8–12 yrs, Pakistan (n = 155) Elevated air Cd concentrations	UCd (arithmetic mean, 5th–95th percentile) • Male: 0.41 (0.15–1.58) nmol/mmol creatinine • Female: 0.65 (0.20–1.63) nmol/mmol creatinine	• Urinary Ca • Urinary deoxypyridinoline (DPD)	• Association between UCd and urinary DPD when adjusted for UCa. • Doubling UCd associated with an increased urinary DPD (by 1.72-fold) and an increased UCa excretion (by 1.21-fold).	Sughis *et al.* 2011
Ex-workers (males) from a radiator industry in Belgium with exposure th Cd fumes, aged 24–64 yrs (n = 83)	• UCd geometric mean (5th–95th percentile): 1.02 (0.17–5.51) µg/g creatinine UCd in tertiles (n = 27 each) of the distribution • Low: <0.51 • Medium: 0.51–1.88 µg/g creatinine • High: ≥1.88 µg/g creatinine	• Urinary ß2-microglobulin (ß2-UMG) • Urinary Ca • Bone mineral density (forearm, hip and lumbar spine) (BMD) • Osteoporosis (T-score <2.5)	• After adjustment, doubling the UCd inversely and significantly associated with lower BMD of forearm and hip, but not of the lumbar spine. • ORs: risk of osteoporosis increased 4.8-fold (95%CI: 0.88–29.1, p = 0.09) and by 9.9-fold (95% CI: 1.8–55.2, p = 0.009) in the middle and highest tertiles, respectively, compared to the lower tertile. • Each doubling of UCd associated with a 1.47-fold (95% CI: 1.03–2.10, p = 0.032) increase in the risk of osteoporosis. Similar result after adjustment for urinary β2-microglobulinuria (four men with >300 µg/g creatinine). • Similar associations within smokers only.	Nawrot *et al.* 2010
Population (males and females) with elevated dietary exposure, Thailand (n = 420)	BCd (mean ± SD, range) • Men: 7.20 ± 1.80 (1.44–28.65) µg/L • Women: 5.54 ± 1.94 (0.80–33.12) µg/L UCd (mean ± SD, range) • Men: 6.71 ± 1.92 (0.84–41.82) µg/g creatinine • Women: 7.32 ± 1.89 (1.19–42.41) µg/g creatinine	Renal biomarkers: • Urinary ß2-microglobulin (ß2-UMG) • Urinary N-acetyl-β-D-glucosaminidase (UNAG) Bone biomarkers: • Serum osteocalcin (bone formation) • Urinary cross-linked N-telopeptides of type I collagen (NTx) (bone resorption) • Urinary deoxyyridinoline (DPD) (bone resorption) • Serum Ca • UCa • Fractional excretion of calcium (FECa)	• In both genders, elevated UCd and BCd and elevated markers for both renal dysfunction and bone resorption with a dose-response relationship. • Excretion of bone resorption markers positively correlated to the ratio of excreted Ca and UCd. • Bone resorption accelerated by impaired Ca reabsorption in renal tubules.	Nambunmee *et al.* 2010
Post-menopausal women aged 49–62 yrs (n = 2,676), dietary Cd exposure: mean and median: 13 µg/d, range: 3.3–29 µg/d, corresponding to 1.4 (0.36–3.6) µg/kg bw/d)	• Low exposure group (<13 µg/d): mean ± SD dietary exposure = 11 ± 1.3 µg/d • High exposure group (<13 µg/d): mean ± SD dietary exposure = 15 ± 2.1 µg/d • Median UCd: 0.34 (5th–95th percentile: 0.15–0.79) µg/g creatinine	• Bone mineral density (BMD) at the total body, femoral neck and lumbar spine. • Osteoporosis (T score <-2.5)	• 15% of women had osteoporosis (hip or spine). • Dietary Cd associated with decreased BMD in total body and lumbar spine (not in femoral neck). Association more pronounced after adjustment for the intake of Ca, Mg, Fe and fibre. • Estimate not attenuated after exclusion of smokers. • Increased risk of osteoporosis (32%, 95% CI: 2–71%) and first fracture (31%, 95% CI: 2–69%) in high-exposure group compared to low-exposure group.	Engstrom *et al.* 2012

Population studied	Urinary/blood cadmium levels	Effect biomarker	Results	Reference
			• After combining high dietary Cd intake and high UCd excretion in never-smokers, ORs ratios were 2.65 (95% CI: 1.43–4.91) for osteoporosis and 3.05 (95% CI: 1.66–5.59) for fractures. • Low-level dietary Cd exposure is associated with low BMD and increased risk of osteoporosis and fractures.	
Workers (males and females), smelter area, east Hunan Province, China (n = 103) Non-occupationally exposed controls (n = 36)	UCd (GM, 95% CI on the GM) • Control: 1.67 (1.26–2.22) µg/creatinine • Exposed: 3.09 (2.49–3.84) µg/creatinine BCd (GM, 95% CI on the GM) • Control: 3.22 (2.31–4.47) µg/L • Exposed: 7.58 (6.24–9.23) µg/L	Renal biomarkers: • Urinary ß2-microglobulin (ß2-UMG) • Urinary N-acetyl-β-D-glucosaminidase (UNAG) • Urinary albumin (UALB) Biomarkers of the pancreatic function: • Serum insulin • Serum amylase • Blood glucose	• Insulin and amylase inversely correlated with UCd. • Serum insulin increased from 5 µg/g creatine and serum amylase increased from 10 µg/g creatinine. • All renal biomarkers increased from 5 µg/g creatine. • BMDL10 estimated for each biomarker and varied from 3.7 µg/g creatinine (insulin) and 5.8 µg/g creatinine (UALB).	Amaral *et al.* 2012
Patients (males and females) with type II diabetes, Shangai city, China, aged 44–87 yrs (n = 229)	GM (range) • BCd = 0.61 (0.03–5.54) µg/L • UCd = 0.38 (0.05–4.17) µg/g creatinine	• Urinary albumin (UALB) • Urinary ß2-microglobulin (ß2-UMG) • MT antibody (MT-Ab)	• Percentage of individuals with high levels of MT-Ab significantly elevated in subjects with high ß2-UMG (both sexes), with significant positive correlation. OR for tubular dysfunction: • OR = 3.34 (95%CI: 1.17–9.53) group with ≥1 µg/g creatinine compared with group <1 µg/g creatinine • OR = 5.56 (95%CI: 2.25–13.73) high compared to low-level MT-Ab. Elevated MT-Ab may increase susceptibility for tubular damage.	Chen *et al.* 2006*b*
Prospective cohort of 30,210 post-menopausal women in Sweden with 16 years follow-up (n = 378 cases of endometrial cancer)	Tertiles of Cd intake (dietary, based on a 96-item food frequency questionnaire) • 1st tertile (<13.7 µg/d): mean = 12.3 µg/d • 2nd tertile (13.7–16.0 µg/d): mean = 14.8 µg/d • 3rd tertile (≥16.0 µg/d): mean = 17.7 µg/d	• 378 cases of endometrial cancer • Relative risk (RR) estimated using Cox proportional hazards regression models. Adjustment for age, education, parity, age at menarche, age at menopause, leisure time physical inactivity.	• Average estimated dietary intake: 15 µg/d. • Cd intake significantly associated with increased risk of endometrial cancer. • Risk of endometrial cancer significantly associated with Cd intake in all women, comparing highest versus lowest tertile (RR: 1.39, 95% CI: 1.04–186). • Association more significant among never-smoking women with body mass index <27 kg/m2 (RR = 1.86, 95% CI: 1.13–3.08). • 2.9-fold increase risk (95% CI: 1.05–7.79) associated with long-tem Cd intake consistently above the median at baseline in never-smoking women with low bio-available estrogen. Concluded these findings support the hypothesis that Cd may exert estrogenic effects and increase risk of hormone-related cancers.	Åkesson *et al.* 2008

Notes: BCd = blood cadmium; UCd = urinary cadmium; B = bone; S = serum; U = urinary; ALB = albumin; ALP = alkaline phosphatase; BMD = bone mineral density; CI = confidence interval; DHEAS = dehydroepiandroesterone; DPD = deoxypyridinoline; GFR = glomerular filtration rate; GM = geometric mean; GP = Gla protein; HP = hydroxylysylpyridinoline; HR = hazard ratio; LP = lysylpyridinoline; MG = microglobulin; MT = metallothionein; NAG = N-acetyl-ß-D- glucosaminidase; NTx = N-telopeptide crosslinked collagen type 1; OR = odds ratio; PTH = parathyroid hormone; pTWI = provisional tolerable weekly intake; RBP = retinol-binding protein; RR = relative risk; SD = standard deviation

[a] 1 nmol Cd/mmol creatine ~1 µg Cd/g creatinine

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Agency	Exposure limit	Limit type	Extrapolation method		Critical effect and description of study	Derivation date
			High to low dose	Animal to human		
Health Canada (HC 2021*a*)	0.0042 (µg/m^3)$^{-1}$	Inhalation unit risk	See OEHHA (2009)		Based on selection of OEHHA assessment as most appropriate for the derivation of a TRV (OEHHA 2009). The inhalation SF, in (µg Cd/kg bw/d)$^{-1}$, was converted from cancer inhalation UR, in (µg Cd/m^3)$^{-1}$,using a 15.8 m^3/d inhalation rate and a 70.7 kg adult body weight (HC 2010).	
	0.0188 (µg/kg-bw day)$^{-1}$	Inhalation slope factor				
US EPA (1985; 1989)	0.0018 (µg/m^3)$^{-1}$	Inhalation unit risk	Two-stage model with only the first phase affected by exposure; extra risk	-	Based on evidence of lung, tracheal and bronchus cancer deaths in workers exposed to Cd in the Cd production industry. White males hired after January 1926 and employed for a minimum of six months. (Thun *et al.* 1985). Unit risk (0.0018 (µg Cd/m^3)$^{-1}$) estimated using a simple model equivalent to a two-stage model with only the first stage affected by exposure. Extra risk based on the US white male population.	1989
OEHHA (2009)	0.0042 (µg/m^3)$^{-1}$	Inhalation unit risk	Poisson regression model, extra risk	-	Based on evidence of lung, tracheal and bronchus cancer deaths in workers exposed to Cd in the Cd production industry. White males hired after January 1926 and employed for a minimum of two years. Overall twofold increase in the risk of developing lung cancer in these workers (Thun *et al.* 1985). A Poisson regression model was fitted to the data. The model was then applied to the California population to predict excess lung cancer deaths induced by Cd exposure (continuous, lifetime). The inhalation SF, in (µg Cd/kg bw/d)$^{-1}$, is converted from cancer UR, in (µg Cd/m^3)$^{-1}$, using a 20-m^3/d inhalation rate and a 70-kg adult body weight. OEHHA default values are slightly different from those used by Health Canada (HC 2010).	1986; 1990
	0.015 (µg/kg bw/d)$^{-1}$	Inhalation slope factor				

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APPENDIX 9. NON-CARCINOGENIC TRVS FOR CADMIUM

Agency	Inhalation exposure limit ($\mu g/m^3$)	Duration/ limit type	Critical effect level (corresponding concentration or daily intake)		UF	Critical effect and description of study	Date derived
			Value	Basis			
CalEPA (2000; 2008; 2012)	0.02	Chronic / REL	0.5 $\mu g/m^3$ (continuous)	NOAEL	30	Based on kidney and respiratory effects in human occupational exposure. A LOAEL (21 $\mu g/m^3$) for respirable cadmium for renal and respiratory effects (proteinuria, reduction in forced vital capacity and peak expiratory flow rate). NOAEL (1.4 $\mu g/m^3$) established for an average 4.1-yr exposure (adjusted to 0.5 $\mu g/m^3$ for continuous exposure in the general population) (Lauwerys *et al.* 1974). A UF of 10 applied for inter-individual variability and of 3 for short (subchronic) exposure duration.	2000
ATSDR (2008; 2012)	0.01	Chronic / MRL	0.5 µg/g creatinine in urine (0.1 $\mu g/m^3$)	$UCDL_{10}$	9	$UCDL_{10}$ of the UCd concentration associated with extra risk of low molecular weight proteinuria, estimated from meta-analysis of environmental exposure data (Buchet *et al.* 1990; Järup *et al.* 2000; Suwazono *et al.* 2006). Using biokinetic models and assuming a dietary Cd intake of 0.3 µg/kg bw/d, a 0.1 $\mu g/m^3$ air concentration was estimated to result in the $UCDL_{10}$. Intake divided by a UF for human variability (3) and a modifying factor (3) for lack of adequate human data that could be used to compare the relative sensitivities of the respiratory tract and kidneys.	2008
WHO (2000)	0.005	Chronic/AQG	100 µg Cd/m^3-years (occupational) (approx. 0.3 $\mu g/m^3$; continuous)	LOAEL	See next column	Lowest estimate of critical cumulative exposure to airborne Cd, based on proteinuria associated with proximal tubular dysfunction in workers (Thun *et al.* 1991). Permissible concentration extrapolated for continuous lifetime exposure estimated at ~0.3 $\mu g/m^3$. Note: WHO (2000) considered that the Cd body burden of the general population in some parts of Europe cannot be further increased without endangering renal function and set the guideline to a value similar to the current airborne concentrations in urban or industrialized areas.	1999
European Commission (2000)	0.005	Chronic/AQG	100 µg Cd/m^3-years (occupational) (0.27 $\mu g/m^3$ continuous)	LOAEL	50	Lowest estimate of critical cumulative exposure to airborne Cd, based on proteinuria associated with proximal tubular dysfunction in workers (Thun *et al.* 1991). UFs for derivation of the NOAEL from the LOAEL (5) and inter-individual variability (10). LOAEL extrapolated for a continuous lifetime (75 years) exposure estimated at 0.27 $\mu g/m^3$.	2000
OMOE (2006; 2007; 2008)	0.005	Chronic (annual) AAQC	100 µg Cd/m^3-years (occupational) (0.27 $\mu g/m^3$ continuous)	LOAEL	50	Based on the value derived by the European Commission (2000).	2006

Agency	Inhalation exposure limit ($\mu g/m^3$)	Duration/ limit type	Critical effect level (corresponding concentration or daily intake)		UF	Critical effect and description of study	Date derived
			Value	Basis			
	0.025	Acute (24-h avg.) AAQC	-	-	5	From annual ambient air quality criterion using a conversion factor of 5 (AAQC).	2006
ORAL (µg Cd/kg bw/d)							
Health Canada (2018; 2020)	0.8	Chronic/ pTDI	5.24 µg/g creatinine in urine	POD		pTDI corresponding to the pTMI of JECFA (2011), see below.	
JECFA (2011); WHO (2011*a*)	0.8 (25 µg/kg bw/month)	Chronic/PTMI	5.24 µg/g creatinine in urine	POD	-	Highest urinary excretion of Cd not associated with increased urinary excretion of β_2-microglobulin in individuals aged ≥50 years (JECFA 2011) based on data from a meta-analysis of human studies (EFSA 2009*b*). Dietary exposure corresponding to the POD estimated using a one-compartment toxicokinetic model and Monte-Carlo simulation (5th percentile = 0.8 µg/kg bw/d).	2010
EFSA (2009*a*; 2011)	0.4 (2.5 µg/kg bw/week)	Chronic/TWI	1 µg/g creatinine in urine (0.36 µg/kg bw/d)	POD	-	Highest urinary excretion of Cd not associated with increased urinary excretion of β_2-microglobulin in individuals aged ≥50 years based on human study meta-analysis (EFSA 2009*b*). POD corresponds to the $BMDL_5$ (4 µg/g creatinine) divided by a CSAF (3.9) to account for inter-individual variability.	2009
ATSDR (2008; 2012)	0.1	Chronic/MRL	0.5 µg/g creatinine in urine (0.33 µg/kg bw/d)	$UCDL_{10}$	3	Lower confidence limits of UCd excretion corresponding to 10% excess risk of low-molecular-weight proteinuria at age 55 ($UCDL_{10}$) based on meta-analysis of human cohort studies examining the relationship between UCd and the prevalence of elevated renal function biomarker levels in environmentally exposed European populations. (Buchet *et al.* 1990; Järup *et al.* 2000; Suwazono *et al.* 2006). Daily dose corresponding to the $UCDL_{10}$ estimated using pharmacokinetic models (5% absorption rate for males; 10% for females). Application of UF of 3 to the lowest value (0.33 µg/kg bw/d; females) for protection of diabetics.	2008
US EPA (1989)			200 µg/g renal cortex tissue (w.w.)			Highest Cd level in the human renal cortex not associated with significant proteinuria (US EPA 1985). Corresponding daily intake (NOAEL) was calculated using a toxicokinetic model (absorption rates: 2.5% from food and 5% from water). The UF accounts for inter-individual variability.	1985
	0.5	Chronic RfD (water)	(5 µg/kg bw/d)	NOAEL	10		
	1.0	Chronic RfD (food)	(10 µg/kg bw/d)	NOAEL	10		
RIVM (2001)	0.5 (3.5 µg/kg bw/week)	Chronic TDI and TWI	2.5 µg/g creatinine in urine (1 µg/kg bw/d)	Previous TDI	2	UCd concentration corresponding to a renal cortex of 50 µg/g cortex after continuous exposure for 40 to 50 years associated with adverse effects in 4% of the population. Exposure at the previous TDI (1 µg/kg bw/d) for 40 to 50 years anticipated to lead to the critical renal cortex Cd concentration (50 µg/g cortex), so a UF of 2 was applied. The TDI should preferably be expressed on a weekly basis.	1999 / 2000

Agency	Inhalation exposure limit ($\mu g/m^3$)	Duration/ limit type	Critical effect level (corresponding concentration or daily intake)		UF	Critical effect and description of study	Date derived
			Value	Basis			
CalEPA (2005)	0.011	Child-specific reference dose (chRD)	Urinary excretion of 2 µg/24 h (1 µg/kg bw/d)	LOAEL	90	TRV developed in the context of use in risk assessments for proposed or existing school sites. Lowest Cd excretion rate associated with renal tubular dysfunction, based on Buchet *et al.* (1990) conducted on Belgian adults with high or low environmental Cd exposure. Daily intake corresponding to the critical excretion rate (LOAEL) estimated by Buchet *et al.* (1990) for non-smokers using a 5% absorption rate and a 0.005%-per-day elimination rate. The global UF accounts for the adult UF (30) multiplied by a child protective factor (3) to account for difference in gastrointestinal absorption between adults and children.	2005
CalEPA (2001)	4.1 µg/d	MADL (safe harbour level)	0.706 mg/kg bw/d	LOEL	10,000	Safe harbour levels are based on carcinogenicity or reproductive effects. Developmental effects (reduced weight gain and altered locomotor activity) in rats (Ali *et al.* 1986). Adjusted dose for human based on a 58 kg bw. LOEL divided by 10 and by an additional factor of 1,000.	2001
CPSC (2010)	0.1	Chronic / ADI	0.5 µg/g creatinine in urine (0.33 µg/kg bw/d)	$BMDL_5$	3	$BMLD_{05}$ for excess risk of renal effects based on a cohort study in 280 Swedish women aged 53 to 64 years (Åkesson *et al.* 2005; Suwazono *et al.* 2006). Dietary intake (0.33 µg/kg bw/d) corresponding to the $BMDL_5$ (0.5 µg/g creatinine) taken from ATSDR (2008) and application of a UF of 3.	2009

Notes: AAQC = ambient air quality criteria; ADI = adequate daily intake; AQG = air quality guideline; BMDL = benchmark dose level; chRD = child-specific reference dose; CSAF = chemical-specific adjustment factor; HEC = human equivalent concentration; LOAEL = lowest-observed-adverse-effect level; LOEL = lowest-observed-effect level; MADL = maximum allowable daily level (Proposition 65); MRL = minimal risk level; NOAEL = no-observed-adverse-effect level; POD = point of departure; PTMI = provisional tolerable monthly intake; REL = reference exposure levels; RfD = reference dose; TDI = tolerable daily intake; TWI = tolerable weekly intake; UCDL = lower confidence limit of the urinary cadmium level; UF = uncertainty factor; URT = upper risk threshold