CCME

Canadian Council of Ministers of the Environment | Le Conseil canadien des ministres de l'environnement

SCIENTIFIC CRITERIA DOCUMENT FOR CANADIAN SOIL QUALITY GUIDELINES FOR THE PROTECTION OF ENVIRONMENTAL AND HUMAN HEALTH:

NICKEL

PN 1540
ISBN 978-1-77202-019-9 PDF

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF APPENDICES

ABSTRACT

Canadian environmental quality guidelines 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 Guidelines 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 and the lowest value generated from the two approaches for each of the four land uses is recommended by the Canadian Council of Ministers of the Environment (CCME) as the Canadian Soil Quality Guidelines (CCME 2006).

This scientific criteria document provides the background information and rationale for the derivation of environmental and human health soil quality guidelines for nickel. This document contains a review of the chemical and physical properties of nickel, the sources and emissions in Canada, the distribution and behaviour of nickel in the environment, the toxicological effects of nickel on microbial processes, plants, invertebrates, livestock, wildlife, and the behaviour and effects in humans and mammalian species. This information is used to derive soil quality guidelines for nickel to protect human and ecological receptors in four types of land uses: agricultural, residential/parkland, commercial, and industrial.

The environmental soil quality guidelines for nickel for each of the four land uses are: 45 mg/kg soil for agricultural land use, 45 mg/kg soil for residential/parkland land use, 89 mg/kg soil for commercial land use, and 89 mg/kg soil for industrial land use. These guidelines are protective of ecological receptors and are optimised for soils within the pH range of 4.0 to 8.6 because the toxicological studies upon which they are based were conducted within this pH range. The environmental soil quality guidelines were selected from the following ecological exposure pathways developed for nickel: Soil Quality Guidelines for Soil Contact; Soil Quality Guideline for the Protection of Nutrient and Energy Cycling; Soil Quality Guidelines for Soil and Food Ingestion; and Off-site migration check.

The human health soil quality guidelines for nickel for each of the four land uses are: 200 mg/kg for agricultural land use, 200 mg/kg for residential/parkland land use, 310 mg/kg for commercial land use, and 1000 mg/kg for industrial land use based on an incremental lifetime cancer risk of 1 x 10^{-6} or 2500 mg/kg for industrial land use based on an incremental lifetime cancer risk of 1 x 10^{-5}. The human health soil quality guidelines were selected from direct human health-based soil quality guidelines for soil ingestion and dermal contact, direct human health-based soil quality guidelines for soil particulate inhalation (assessed for cancer and non cancer effects), and the Off-site migration check.

The Canadian Soil Quality Guidelines for the protection of environmental and human health, as recommended by the Canadian Council of Ministers of the Environment (CCME 2006) are based on the lowest of the environmental soil quality guidelines or the human health-based soil quality guidelines. Therefore, they are: 45 mg/kg soil for agricultural land use, 45 mg/kg soil for residential/parkland land use, 89 mg/kg soil for commercial land use, and 89 mg/kg soil for industrial land use. This revision to the Canadian Soil Quality Guideline for Nickel supersedes

the original nickel soil quality guideline derived in 1999 (CCME 1999; EC 1999), and the interim remediation criteria for nickel in soil (CCME 1991).

RÉSUMÉ

Les recommandations canadiennes pour la qualité de l'environnement sont des limites quantitatives ou descriptives recommandées dans le but d'assurer un écosystème sain, capable de supporter les utilisations actuelles et probables du site par les récepteurs écologiques et humains. Les recommandations canadiennes pour la qualité des sols peuvent être utilisées comme base pour l'uniformisation des processus d'évaluation et d'assainissement des terrains contaminés au Canada.

Les recommandations ont été élaborées selon les procédures décrites dans le *Protocole d'élaboration de recommandations pour la qualité des sols en fonction de l'environnement et de la santé humaine* (CCME 2006). Conformément à ce protocole, les recommandations pour la qualité des sols visant la protection de l'environnement et de la santé humaine sont développées et la plus petite valeur obtenue de ces deux procédures, pour chacune des quatre types de vocation des terrains, est recommandée par le Conseil canadien des ministres de l'environnement (CCME) comme étant la recommandation canadienne pour la qualité des sols (CCME 2006).

Ce document scientifique contient l'information pertinente sur les données de fond et la justification pour la détermination des recommandations pour la qualité des sols pour le nickel. Ce document contient une revue de l'information sur les propriétés chimiques et physiques du nickel, sur les sources et émissions au Canada, sur la distribution et le comportement du nickel dans l'environnement, sur ses effets toxicologiques sur les processus microbiens, les plantes, les invertébrés et les animaux et son comportement et ses effets chez les humains et les mammifères. Cette information est utilisée pour l'élaboration des recommandations pour la qualité des sols relatives au nickel afin de protéger les récepteurs écologiques et humains dans quatre types de vocation des terrains: agricole, résidentielle/parc, commerciale et industrielle.

Les recommandations pour la qualité des sols visant la protection de l'environnement établies pour le nickel pour chacune des quatre vocations des terrains sont de : 45 mg/kg pour les terrains à vocation agricole, 45 mg/kg pour les terrains à vocation résidentielle/parc, 89 mg/kg pour les terrains à vocation commerciale et 89 mg/kg pour les terrains à vocation industrielle. Ces recommandations sont protectrices des récepteurs écologiques et optimisées pour les sols ayant un pH entre 4,0 et 8,6 puisque les études toxicologiques utilisées pour leur élaboration ont été effectuées dans ces mêmes conditions de pH. Les recommandations pour la qualité des sols pour le nickel ont été sélectionnées parmi les voies d'exposition écologiques suivantes : recommandations pour la qualité des sols fondées sur le contact avec le sol; recommandations pour la qualité des sols en fonction du cycle des nutriments et de l'énergie; recommandations pour la qualité des sols relative à l'ingestion de sol et de nourriture; et recommandations pour la qualité des sols en fonction de l'environnement relatives au migrations hors site.

Les recommandations pour la qualité des sols visant la protection de la santé humaine établies pour le nickel pour chacune des quatre vocations des terrains sont de : 200 mg/kg pour des terrains à vocation agricole/résidentielle/parc, 310 mg/kg pour les terrains à vocation commerciale et, pour les terrains à vocation industrielle, 1000 mg/kg pour un risque additionnel de cancer à vie de 1×10^{-6} et 2500 mg/kg pour un risque additionnel de cancer à vie de 1×10^{-5}. Les recommandations pour la qualité des sols visant la protection de la santé humaine ont été sélectionnées parmi les voies d'exposition humaines suivantes : recommandations pour la qualité des sols relatives au contact direct pour l'ingestion et le contact dermique, recommandations

pour la qualité des sols relatives au contact direct pour l'inhalation des particules du sol (évaluées pour les effets cancérogènes et non-cancérogènes), et la migration hors site de sol et de poussière provenant des terrains commerciaux ou industriels.

Les recommandations canadiennes pour la qualité des sols visant la protection de l'environnement et de la santé humaine, telles que recommandées par le Conseil canadien des ministres de l'environnement (CCME 2006) sont basées sur les recommandations les plus faibles des recommandations visant la protection de l'environnement ou de la santé humaine. Par conséquent, elles sont: 45 mg/kg pour les terrains à vocation agricole, 45 mg/kg pour les terrains à vocation résidentielle/parc, 89 mg/kg pour les terrains à vocation commerciale et 89 mg/kg pour les terrains à vocation industrielle. Les présentes recommandations pour la qualité des sols pour le nickel remplacent les recommandations pour la qualité des sols, développées en 1999 (EC 1999; CCME 1999), ainsi que les critères provisoires pour l'assainissement du sol pour le nickel (CCME 1991).

1 INTRODUCTION

Canadian Environmental Quality Guidelines are intended to protect, sustain, and enhance the quality of the Canadian environment and its many beneficial uses. They are generic numerical concentrations or narrative statements that specify levels of toxic substances or other parameters in the ambient environment that are recommended to protect and maintain wildlife and/or the specified uses of water, sediment, and soil. These values are developed by the Canadian Council of Ministers of the Environment (CCME) for toxic substances and other parameters (e.g., nutrients, pH) of concern in the ambient environment.

The development of Canadian Soil Quality Guidelines was initiated through the National Contaminated Sites Remediation Program (NCSRP). In response to the urgent need to begin remediation of high priority "orphan" contaminated sites, an interim set of soil remediation criteria was adopted from values that were in use in various jurisdictions across Canada (CCME 1991). Although the NCSRP program ended in March of 1995, soil quality guidelines continue to be developed by CCME because of the continued need for soil quality guidelines for the management of soil quality with a particular focus on remediation of contaminated sites.

Canadian Soil Quality Guidelines are developed according to a protocol developed by CCME (CCME 1996a, later revised as 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. The lowest value generated by the two approaches for each of the four land uses is recommended by CCME as the Canadian Soil Quality Guideline. The original Canadian Soil Quality Guideline for nickel was first published in the *Canadian Environmental Quality Guidelines* (CCME 1999) in 1999. The original nickel soil quality guideline only included guidelines for environmental health (i.e., no human health soil quality guidelines), and its derivation was documented in a supporting scientific document developed by Environment Canada (EC 1999). This revision to the Canadian Soil Quality Guideline for Nickel supersedes the 1999 nickel soil quality guidelines and the 1991 interim remediation criteria for soil (CCME 1991). The 1991 CCME interim remediation criteria for soil (CCME 1991) should be used only when soil quality guidelines based on the CCME protocol (CCME 1996a, or 2006 update) have not yet been developed for a given substance.

This scientific criteria document provides the background information and rationale for the derivation of environmental and human health soil quality guidelines for nickel. This document contains a review of information on the chemical and physical properties of nickel, sources and emissions in Canada, the distribution and behaviour of nickel in the environment, and the toxicological effects of nickel on microbial processes, plants, invertebrates, livestock, wildlife, and the behaviour and effects in humans and mammalian species. This information is used to derive soil quality guidelines for nickel to protect human and ecological receptors in four types of land uses: agricultural, residential/parkland, commercial, and industrial (CCME 2006). The current revision to the environmental soil quality guidelines builds upon toxicity data first reported in the original nickel scientific supporting document (EC 1999), whereas, the derivation of human health soil quality guidelines for nickel represent new work that first appears in this document.

The Canadian Soil Quality Guidelines presented in this document are intended as general guidance. Site-specific conditions should be considered in the application of these values (CCME 1996b) for guidance on developing site-specific soil objectives). The reader is referred

to CCME (2006) for further generic implementation guidance pertaining to the guidelines. Soil quality guidelines are derived 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, and they do not consider socioeconomic, technological, or political factors. These non-scientific factors are to be considered by site managers at the site-specific level as part of the risk management process. Because these guidelines may be used and applied differently across provincial and territorial jurisdictions, the reader should consult the laws and regulations of the jurisdiction they are working within for applicable implementation procedures.

2 BACKGROUND INFORMATION

2.1 Physical and Chemical Properties

Nickel (Ni; CAS #7440-02-0), is a hard but brittle, silvery white metal with high thermal and electrical conductivities. Powdered nickel is reactive and may spontaneously ignite in air (ATSDR 2005). Nickel is a transition element of Group VIIIa of the Periodic Table, with an atomic number of 28, an atomic weight of 58.693, a melting point of 1455°C, a boiling point of 2913°C and a specific density of 8.9 g/cm^3 at 25°C (Haynes 2011). Nickel exhibits magnetism (but is less magnetic than iron) (Cotton & Wilkinson 1988). Some physical and chemical properties of nickel and nickel compounds are presented in Table 1.

Although nickel can exist in oxidation states of -1, 0, +1,+2, +3 and +4, the most common valence state in the environment and biological organisms is Ni(II) (otherwise noted as Ni^{2+}) (ATSDR 2005). Elemental nickel is insoluble in water and commonly forms stable complexes with ligands containing oxygen, sulphur, phosphorus or arsenic as donor atoms (Cotton & Wilkinson 1988; Haynes 2011). In water, Ni^{2+} forms a number of compounds of varying solubilities with sulphate, nitrate, chloride, hydroxide and carbonate: nickel chloride, nickel sulphate and nickel nitrate are the dominant forms in water; Nickel carbonyl, nickel sulphide and nickel oxide are considered insoluble in water (Haynes 2011). Ni^{2+} has an ionic radius close to those of iron, magnesium, copper and zinc, and can replace essential metals in metallo-enzymes thus causing disruptions in metabolic pathways (McGrath 1995).

2.2 Geochemical Occurrence

Nickel occurs particularly in iron and magnesium ores such as olivine and pyroxenes (NRCC 1981). In minerals, it occurs most frequently in combination with sulphur, arsenic or antimony. Millerite (NiS), red nickel ore (e.g., NiAs) and pentlandite $(NiFe)_9S_8$ are the main minerals. Pentlandite and pyrrhotite represent the most important commercial deposits of nickel in Canada (NRCC 1981; Haynes 2011). In the environment, nickel may be present commonly in a divalent state and can be found in a variety of inorganic and organic compounds, depending on such factors as the medium considered and ambient environmental conditions. Nickel ranks as the 24th most abundant element in the earth's crust, with a crustal abundance range of 37 to 72 mg/kg (Nriagu *et al*. 1982). The highest natural concentrations of nickel tend to occur in ultramafic and mafic rocks with typical nickel concentrations of 1400 to 2000 mg/kg and 130 to 160 mg/kg, respectively (Kabata-Pendias & Pendias 1984).

Table 1. Physical and chemical properties of some nickel compounds*

PROPERTY	***COMPOUND***							
	Nickel	**Nickel chloride**	**Nickel sulphate**	**Nickel sulphide**	**Nickel subsulphide**	**Nickel carbonate**	**Nickel oxide**	**Nickel carbonyl**
Chemical Formula	Ni	$NiCl_2$	$NiSO_4$	NiS	Ni_3S_2	$NiCO_3$	NiO	$Ni(CO)_4$
CAS Registry Number	7440-02-0	7718-54-9	7786-81-4	16812-54-7	12035-72-2	3333-67-3	1313-99-1	13463-39-3
Molecular Weight	58.693	129.599	154.756	90.758	240.210	118.702	74.692	170.734
Physical State (@25ºC)	silvery white metal	yellow hexagonal crystals	green-yellow orthorhombic crystals	yellow hexagonal crystals	yellow hexagonal crystals	green rhombic crystals	green cubic crystals	colourless liquid
% Nickel % nickel in hexahydrate	100	45.29 25	37.9 22.3	64.67	73.30	49.45	78.59	34.38
Melting Point (ºC)	1455	1031	840 (decomposes)	976	789	NA	1957	-19.3
Boiling Point (ºC)	2913	Sublimation pt. 985	NA	NA	NA	NA	NA	42.1 (explodes ≈60°C)
Density ($g \cdot cm^3$ @ or near room temperature)	8.9	3.55	4.01	5.5	5.87	4.389	6.72	1.31
Water Solubility (g/100 mL)	insoluble	67.5 @ 25°C	40.4 @ 25°C	insoluble	NA	0.0043 @ 20°C	insoluble	insoluble

* Haynes 2011
NA = Not Available

2.3 Analytical Methods

As with numerous other metals, inadvertent sample contamination has been a source of error in nickel analysis. Partially because of this, much of the older published data, especially concentrations in body tissues and fluids, are considered to be inaccurate (Nielsen 1986; Nieboer 1992). The use of ultra-trace and clean-lab techniques has resulted in more reliable data than data generated in the past.

Inorganic nickel in environmental media is most commonly analysed using voltammetry, inductively coupled plasma atomic emission spectrometry (ICP/AES) or mass spectrometry (ICP/MS), neutron activation analyses (NAA) and X-ray fluorescence (XRF). In a review of various analytical methodologies for sewage sludge and digestion solutions, detection limits of 1 µg/L were achieved using voltammetry, whereas detection limits in the ng/L range (0.66-36 ng/L) were reported for water using electrothermal, flame, and graphite furnace techniques of atomisation (EC 1994).

In soil samples, the amount of nickel available for analysis can vary depending on the extraction treatment of the samples prior to analysis (Lutwick 1994; Pastorek 1995). For example, *aqua regia* ($1HNO_3$:3HCl) digestion releases the "biologically-relevant" forms of nickel, that is, the forms of nickel adsorbed to soil particles, the forms present in soluble salts and organic matter, and the forms contained in some weak silicates. This treatment leaves most silicates and stable mineral matrices intact. The release of all the nickel from soil for total nickel analysis requires digestion with hydrofluoric acid, generally used in combination with perchloric and nitric acids.

U.S. EPA sample preparation methods for extraction of nickel from sample materials include: EPA Method 3050B *Acid Digestion of Sediments, Sludges, and Soils* (hydrochloric acid digestion); EPA Method 3005A *Acid Digestion of Waters for Total Recoverable or Dissolved Metals for Analysis for FLAA or ICP Spectroscopy* (nitric acid digestion) for extraction from surface and groundwater samples, or; EPA Method 3015 *Microwave Assisted Acid Digestion of Aqueous Samples and Extracts* (US EPA 2003).

CCME recommends the following three analytical methods for the determination of nickel in water and wastewater samples: method SM 3111B, *Direct Air-Acetylene Flame Method* for *the Determination of Metals*; method SM 3113B, *Electrothermal Atomic Absorption Spectrometric of Water and Wastewater*; and method SM 3120B *Inductively Coupled Plasma (ICP) Method, for the Determination of Metals* (CCME 1993). In addition, US EPA Method 6010, Revision 0, "Inductively Coupled Plasma-Atomic Emission Spectroscopy" is recommended by CCME (1993) for the analysis of nickel in ground water, soil, sludge, sediment and other solid waste samples. The estimated instrumental detection limit (DL) of the latter method is 15 µg/L (1 g of soil digested in 100 mL water). The US EPA analytical method 6020 *Inductively Coupled Plasma with Mass Spectrometry* is a more sensitive technique, with an estimated instrumental detection limit (DL) of <0.02 µg/L. This method is applicable to groundwater, aqueous samples, industrial wastes, soils, sludges, sediments and other solid wastes. Preliminary treatment by acid digestion is required for all samples (with the exception of water) to determine total nickel content. Water samples must be filtered and acid-preserved prior to analysis to determine dissolved nickel content (US EPA 2003).

Nickel in $PM_{2.5}$ (particulate matter less than 2.5 µm in diameter) in ambient air samples collected across Canada were measured for the National Air Pollution Surveillance (NAPS) network using

x-ray fluorescence or ICP-MS (EC 2003a). Data quality of the most recent data (2003 to 2009) from the NAPS database has improved with the better method detection limits achieved with ICP-MS analyses (Dann 2007).

2.4 Production and Uses in Canada

Nickel is a commercially viable natural resource in Canada, with industrial activities focussed in nickel mining, smelting and refining. Canada is one of the top five producers of nickel in the world, responsible for approximately 10% of global nickel production (USGS 2011). Canadian nickel production is estimated at 155 000 tonnes in 2010 (USGS 2011). In 2009, 136 594 tonnes of nickel was produced in Canada with the largest amounts produced in Ontario (33.6%), Manitoba (23.7%), Newfoundland and Labrador (21.3%) and Québec (21.3%) (NRCan 2009). Canada exports nickel and nickel products to over 70 countries worldwide (NRCan 2009) and is one of the top five producers of nickel in the world, responsible for approximately 10% of global nickel production (USGS 2011).

The commercial sector accounts for about two-thirds of the nickel market in Canada and nickel-containing stainless steel continues to be the major growth market for nickel (MAC 1991). Approximately 7195 tonnes of nickel were estimated to have been used in Canada in 2007. Nickel from stainless steel scrap is recycled at a rate of 45 to 48% in the production of stainless steel (NRCan 2009). Metallic nickel, sold in the form of cathodes, pellets, powders, briquettes, rondelles and coinage, is used in approximately 3000 alloys that have more than 250 000 applications (MAC 1991). For example, nickel-containing stainless steel is used by chemical and food processing industries and in the medical profession. Iron-nickel alloys are also important materials for the electric industry while nickel-copper alloys are used in shipbuilding.

Nickel compounds are also useful in various industries. Nickel carbonate hydroxide is employed in plating and catalysis; nickel carbonate used in electric components; anhydrous nickel chloride is used as an adsorbent in certain gas masks and in nickel plating; nickel hydroxide is an electrode material; nickel oxide is an important raw material in metallurgical operations for smelting and alloy-producing processes; nickel sulphate can be a catalyser or employed in electrolyte solution and jewellery; and nickel nitrate is employed by nickel-plating and nickel-containing battery industries (WHO 1991).

2.5 Sources and Concentrations in the Canadian Environment

The background concentrations and environmental fate of metals strongly depend on geological and biological characteristics and therefore, any assessment of potential risks associated with metals should take into consideration regional differences in metal content in the natural environment (Chapman & Wang 2000). High concentrations of metals can occur naturally in Canadian soils, stream sediments, and water, blurring the distinction between anthropogenic pollution versus naturally occurring bodies of ore (EC 1996). Soils and sediments reflect the composition of parent material, resulting in higher metal concentrations in mineralised areas (Wilson *et al.* 1998) and lake or stream sediments can act as sinks, accumulating elements derived from surrounding watersheds (i.e., nickel within bedrock, glacial sediments and soils). Mining districts are characterised by naturally occurring metals in soil, sediment, rock and water at concentrations that could result in their classification as "contaminated sites". In the determination

of anthropogenic metal contamination of soils, no single guideline concentration can adequately represent the variance in background concentrations across Canada (Painter *et al*. 1994).

Nickel is naturally released into Canadian surface waters, sediments, and soils by weathering and erosion of geological materials (i.e., bedrock) (Painter *et al*. 1994). In addition, nickel enters the aquatic environment in effluent and leachates as well as through atmospheric deposition from anthropogenic releases (EC 1994). Natural sources of airborne nickel include soil dust, sea salt, volcanoes, forest fires and particulate exudates from vegetation (NRCC 1981; Richardson *et al*. 2001; Schmidt & Andren 1980; Warren & Delavaut 1954). In Canada, the estimated contribution of natural sources to airborne nickel is approximately 170 to 2700 t/y, with wind-blown dust being the dominant source (Richardson *et al*. 2001). Sea spray may be a major contributor to atmospheric nickel in coastal areas. Although forest fires can be short-term sources, they are intense sources (Havas & Hutchinson 1983).

There is very little quantitative information available on the speciation of nickel in various environmental media. Concentrations of nickel are generally reported as total nickel, and unless otherwise specified, are assumed to be reported as such. Concentrations are given on a wet weight basis for food, biota and human tissues and on a dry weight basis for other media, unless otherwise indicated.

Reviews on the emission of nickel from major anthropogenic sources have been presented for Canada (e.g., Jacques 1987; NRCC 1981). Primary base metal production represents an important anthropogenic source in Canada. The contribution of smelting and refining of base metals was estimated to be 1100 tonnes of nickel as air emission and 64 tonnes as effluents in the 1988 mining year (MacLatchy 1992). Based on data from Environment Canada's National Pollutant Release Inventory (NPRI), 412 tonnes of nickel were released to the environment by major emitters in 2006, of which 356 tonnes were released to air, 49 tonnes were released to water and 1.9 tonnes to land; over half of this amount was released from the Vale Inco facility in Thompson, MB. Other major emitters were facilities in the mining, smelting, petroleum refining and manufacturing industries (EC 2007). Some minor atmospheric releases have been attributed to the alloy production and the scrap reprocessing industries, the incineration of municipal garbage and sewage sludge, the manufacture of cement, coke oven and cooling tower operations and the mining/milling of asbestos (EC and HC 1994; Jacques 1987; WHO 1991). Globally, the largest anthropogenic releases are from fossil fuel (predominantly coal and oil) combustion and nickel mining and smelting (McGrath 1995). Virtually every industry (e.g., electric power stations and heating and industrial plants, gasoline combustion, non-ferrous metal smelters, kiln operations in cement plants, and refuse incineration) will emit heavy metals *via* high temperature processes into the atmospheric, aquatic, and terrestrial ecosystems (Wilson *et al*. 1998).

The natural oxidation of sulphide minerals in ore and acid mine drainage contributes a significant portion of the nickel in mine effluents (MacLatchy 1992). Effluents from gold mines can contain significant amounts of nickel (Boyd 1991-92). The cyanidation process that leaches gold from ore also extracts nickel and other metals. Uranium and stainless steel industries contribute additional emissions into the Canadian aquatic environment (Boyd 1991-92; MacLatchy 1992). Although not as significant as the metal production processes, fossil fuel combustion also represents an important part (20%) of the national emission inventory for nickel (Jacques 1987).

Industrial effluents containing significant amounts of nickel come from nickel mining, smelting

and refining, metal plating, gold mining and uranium extraction and iron and steel processing. Nickel from nickel mining and refining operations is disposed of onto land as waste rock, in the form of slags and sludges and as tailings released into ponds (EC 1994; Jacques 1987).

Anthropogenic nickel is found in a variety of compounds from a high-temperature green variety to low-temperature black products. High-temperature green nickel oxide is relatively inert and is the predominant form in nickel refineries, whereas black nickel oxides are more chemically active. More complex and reactive nickel oxides, such as copper-nickel oxides, are often formed as by-products of industrial processes. Nickel subsulfide (Ni_3S_2) and nickel sulfide (NiS) occur as intermediates in the processing of sulfidic ores. Nickel subsulfide is found in two forms: the low-temperature green form, α-Ni_3S_2 (heazlewoodite), and the high-temperature bronze-yellow form (β-Ni_3S_2). Nickel sulfide forms dark green to black crystals or a powder (α-NiS, β-NiS, or amorphous NiS, respectively) (cited in Goodman 2011). Sections 2.5.1 to 2.5.12 form the basis for selection of typical environmental concentrations (background) of nickel in environmental media that are not associated with contamination for use in the derivation of Canadian Soil Quality Guidelines (chapters 7 and 8 and Appendix 10).

2.5.1 Ambient Air

Little information is available on speciation of nickel in ambient air. Most data in the literature refer to total concentrations in particles; however, Ontario has implemented species-specific measurements of nickel in their ambient air monitoring program in 2003. The results from urban areas and areas influenced by a nickel source showed that nickel sulphate was the dominant species (57-85%), followed by nickel oxide and nickel hydroxide, which made up less than 20%. Limited sampling of air filters and house dust in Sudbury, ON, indicated a small amount of nickel subsulphide (<10%) may be emitted from the Copper Cliff smelter (OMOE 2011a). Available data are summarised in Appendix 1.

Data on Canadian nickel concentrations in air in Canada, reported as $PM_{2.5}$ (particulate matter less than 2.5 μm in aerodynamic diameter) were provided by Environment Canada from the National Air Pollution Surveillance (NAPS), a Canada-wide network of monitoring stations operated by federal, provincial, territorial and municipal governments and agencies. Based on the 2003 to 2009 NAPS dataset, the overall mean concentration of nickel in $PM_{2.5}$ from urban and rural stations was 0.94 ng/m^3 (n=3054 samples) (HC 2011). The mean concentration of $PM_{2.5}$ calculated from the 2003 to 2009 NAPS dataset was used to estimate typical nickel concentrations in ambient air in Canada for the purposes of this document.

Nickel $PM_{2.5}$ concentrations measured in ambient air in Canada were found to be similar between urban and rural areas (Appendix 1). A median rural $PM_{2.5}$ concentration of 1.0 ng/m^3 and a median urban $PM_{2.5}$ concentration of 0.6 ng/m^3 were reported in the vicinity of Ottawa-area homes (Rasmussen *et al*. 2006). Similarly, an analysis of a subset of the NAPS dataset from 2007 to 2009 showed a mean $PM_{2.5}$ concentration of 0.5 ng/m^3 in rural areas compared to 0.8 ng/m^3 in urban areas (Dann 2010). Similar outdoor air concentration ranges were reported in other studies (Niu *et al*. 2010a; Bell *et al*. 1994). Niu *et al.* (2010a) reported median outdoor air concentrations of 1.0 ng/m^3 and 1.3 ng/m^3 (ED-XRF and ICP-MS respectively), and a mean concentration of 1.4 ng/m^3 (based on ICP-MS results). When size-selective particle sampling was used to separate two urban PM samples collected in Ottawa, ON (without nearby industrial sources) into nano (57-100 nm), fine (100-1000 nm) and coarse (1000-10 000 nm) fractions, a general trend of increasing nickel

concentration with decreasing aerodynamic diameter was evident, but there were significant differences between the concentrations of nickel in the smaller diameter fractions in the two samples. The median concentration among ten fractions (10 000, 5600, 3200, 1800, 1000, 560, 320, 180, 97 and 57 nm diameter) of the two samples were 251±195 (range 46-853) µg/g and 269±200 (range 58-37 041) µg/g. Particle size distribution and element correlation analysis suggest that the elements concentrated in the nano- and fine-size fractions originated mainly from vehicular combustion and emission. Long-range airborne transport and soil or road dust resuspension may also contribute (Niu *et al*. 2010).

The annual mean concentration of nickel was reported to be less than 0.5 ng/m^3 in remote areas such as the Canadian Arctic (Hoff & Barrie 1986; Chan & Lusis 1988). Higher levels reported in older data for remote or rural sites may be due in part to higher detection limits at the time of analyses (i.e. prior to the use of ICP/MS), rather than actual observed levels (Dann 2010).

A time-dependent decrease in annual average concentrations of nickel was observed between 1994 (0.34 ng/m^3) and 2001 (0.13 ng/m^3), along with more frequent occurrence of non-detectable (nd) concentrations (i.e., 4 nd in 1994 and 32 nd in 2001) in Alert, NWT (INAC 2003). Annual averages for nickel from 1994 to 2001 (n=374) were derived based on ICP-MS analysis of PM_{10} (Gong 2004).

Higher concentrations of nickel in total suspended particulates (TSP) have been reported in the vicinity of industrial sources. For example, maximum concentrations of nickel in air samples taken near Copper Cliff, ON in 1980, 1986 and 1988 were 4400, 2300 and 6100 ng/m^3, respectively (Brecher *et al*. 1989; Dobrin 1992; OMOE 1992) and average nickel concentrations in air samples from the Copper Cliff-Sudbury area ranged from 100 to 250 ng/m^3 between 1978 and 1988 (Dobrin 1992; Chan & Lusis 1988).

Vegetation biomonitoring has been conducted to evaluate metal content in air and airborne deposition. Tree foliage sampling data were available for background locations in Ontario and Manitoba. In Ontario, nickel was detected in the foliage of silver maple trees (n=63) at rural locations in Essex and Kent counties in trace amounts (0.8 to 2.1 µg/g dry weight) (Gizyn 2002). By comparison, nickel concentrations in coniferous trees (n=3) were below detection (i.e., <0.1 µg/g, dry weight) in rural northern Manitoba (Yee 2004).

2.5.2 Indoor Air

The available data on nickel concentrations in indoor air are summarised in Appendix 1. Limited data from Canadian sources on indoor air are available. As such, data from non-Canadian sources (Van Winkle & Scheff 2001; USEPA 2009; Stranger *et al*. 2009; Molnár *et al*. 2006; Li *et al*. 1993; Balasubramanian & Lee 2007; Adgate *et al*. 1998; Graney *et al*. 2004) were considered, in addition to selected Canadian sources of indoor air data (AB Health 1998; Bell *et al*. 1994; Rasmussen *et al*. 2006). Using this expanded data set, a mean indoor air concentration of 7.21±10.4 ng/m^3 (mean ± SD) for the $PM_{2.5}$ fraction was estimated as representative of indoor air concentrations in Canada (HC 2011).

In Ottawa, ON, Rasmussen *et al.* (2006) measured particulate matter (PM) simultaneously in indoor air (in two size ranges: $PM_{2.5}$ and PM_{10}) and outdoor air (PM_{10}) in ten rural homes and ten urban homes. The median nickel $PM_{2.5}$ and PM_{10} levels in rural homes were found to be slightly higher (0.7 ng/m^3 and 1.5 ng/m^3, respectively) in comparison to urban homes (0.6 ng/m^3 and 1.0

ng/m^3). Nickel concentrations in ambient $PM_{2.5}$ were slightly higher (1.0 ng/m^3) than concentrations measured in rural homes (0.7 ng/m^3), but there was no difference between median nickel concentrations in ambient $PM_{2.5}$ and those found air in urban homes (0.6 ng/m^3).

Indoor air quality studies in Windsor, ON reported an average nickel concentration of 1.5 ng/m^3, which was in the same range as levels in corresponding outdoor air samples (daily averages ranged from 1.3 to 1.9 ng/m^3). In a statistical analysis of all three phases of the Windsor Air Quality study, the indoor mean concentration of nickel (n=37) was reported to be 1.3 ng/m^3 (range: 0.3-9.2 ng/m^3) with airborne nickel concentrations found to be slightly lower in smoke-free homes (n=22; mean 1.1 ng/m^3 and range 0.4-2.3 ng/m^3) than in the homes of smokers (n=15; mean 1.6 ng/m^3 and range 0.3-9.2 ng/m^3) (Bell *et al*. 1994). In a U.S. indoor air quality study conducted in 1986, week-long samples of fine ($PM_{2.5}$) air particles collected from 394 homes in two counties in New York State reported mean nickel concentrations in the 2 to 3 ng/m^3 range (Koutrakis *et al*. 1992).

2.5.3 Indoor Dust

Similar to indoor air, there is a lack of data on indoor settled dust concentrations. As such, indoor dust concentrations based on studies from Canada (Rasmussen *et al*. 2001; 2008), the United States (USEPA 2009; Adgate *et al*. 1998) and data from other developed countries (Chattopadhyay *et al*. 2003; Davis & Gulson 2005; Lisiewicz *et al*. 2000; Madany *et al*. 1994; Turkoglu *et al*. 2004; Turner & Simmonds 2006) were used to estimate typical Canadian concentrations of nickel in indoor dust, and are summarised in Appendix 1. A mean nickel concentration of 48.14±40.97 µg/g in indoor settled dust was derived based on these studies (HC 2011). A slightly lower median nickel concentration in house dust (40 µg/g) was derived from a review of several studies from various cities around the world (Fergusson & Kim 1991). Similarly, Rasmussen *et al.* (2008) reported a median total nickel concentration of 41 µg/g in house dust based on dust samples collected from 22 residential homes in Ottawa, ON. In an earlier study, total nickel concentrations in house dust ranged from 16.0 to 243.3 µg/g with an arithmetic mean of 62.9 µg/g, a geometric mean of 53.6 µg/g and a median of 51.5 µg/g (Rasmussen *et al*. 2001).

In the Ottawa house dust studies, Rasmussen *et al.* (2001 and 2008) reported that metals in house dust may be found at higher concentrations compared to concentrations in residential garden soil. Therefore house dust may contribute significantly to exposure to metals in residential urban environments. Rasmussen *et al.* (2008) noted that the elevated indoor/outdoor (I/O) ratios in this study were comparable to reported I/O ratios in other urban residential settings in the United Kingdom and New Zealand (Kim & Fergusson 1993; Culbard *et al*. 1988).

2.5.4 Soil

Nickel is naturally present in soil as a result of chemical and mechanical weathering of parent rock material. Nickel is present in granites, sandstones and limestones in concentrations ranging from 5 to 20 mg/kg, but it can also occur in high concentrations in ultramafic and mafic bedrock and soils overlying these types of bedrock, where nickel is naturally enriched. Nickel concentrations in Canadian soils and world averages are summarised in Appendix 1.

For the purpose of this soil quality guideline, a mean total nickel concentration of 26.8 mg/kg calculated from background till data (excluding areas of nickel enriched rocks and nickel bearing mineral occurrences) compiled by the Geological Survey of Canada (Grunsky 2010; Rencz *et al*. 2006) is considered to be representative of typical nickel concentration in background soils in

Canada. Similar mean concentrations of total nickel in Canadian background soils have been reported by other researchers (Sheppard *et al*. 2007; Sanei *et al.* 2007; SENES 2002; McKeague & Wolynetz 1980).

Background nickel concentrations can range up to four orders of magnitude and can differ widely due to local geological conditions (Rencz *et al*. 2006). High concentrations of nickel in soils and tills are often associated with mafic and ultramafic rock types in Canada (Rencz 1980; Roberts 1980; Klassen & Thompson 1990; Kaszycki 1986). Areas of naturally nickel-enriched soils exist in most regions, with the possible exception of the St. Lawrence River lowlands and the southern plain regions of Alberta and Saskatchewan (Doyle 1991). Rencz and Shilts (1980) reported total nickel concentrations of up to about 1200 µg/g in the silt- and clay-size fraction (<64 µm) of till, near an outcrop of ultramafic rock in the Thetford Mines, QC area, and from 80 to 560 mg/kg total nickel in acidic soils associated with sulphide ore bodies near Ferguson Lake, NWT. Roberts (1980) reported naturally high concentrations (mean of 3460 mg/kg total nickel) in neutral (pH 6.8-7.3) nickel-enriched soils developed on ultramafic (serpentine) bedrock in western Newfoundland. In areas which may be naturally enriched with nickel, additional information on a regional or local background levels of nickel is required to support the development of regional or site specific soil quality objectives for sites in Canada.

Atmospheric deposition of nickel from anthropogenic sources can increase concentrations of nickel in topsoil near major sources of emissions such as nickel mining, smelting and refinery operations. Depth-specific sampling at several sites in the Sudbury, ON, area indicated that nickel concentrations were much higher in samples collected from depths of 0-5 cm than in samples from depths of 6-10 cm or 11-15 cm (Gratton *et al*. 2000). Another study near Sudbury in 2001 reported nickel concentrations in soils ranging from 14 mg/kg to 435 mg/kg (Feisthauer *et al*. 2006). Similarly, nickel levels in surface soils from the Rodney Street Community in Port Colborne, ON, which is influenced by industrial emissions, were found to average approximately 2500 mg/kg (OMOE 2002). Nickel concentrations in undisturbed soil in rural woodlots, downwind of the INCO nickel refinery were found to be much higher than in adjacent residential and agricultural properties in the Port Colborne area due to emissions from the nickel refinery. The observed differences were reported to be due to atmospheric deposition of particulates from the refinery emissions and absorption of nickel in air by tree foliage, resulting in the accumulation of nickel in leaf litter and other organic matter in the upper surface layer of the forest soil over time (Leece & Rifat 1997). Nickel concentrations of up to 17 000 mg/kg were reported in soil adjacent to a nickel refinery in southern Ontario (Birmingham & McLaughlin 2006).

Although it is unlikely that there will be a large build-up of nickel in soils as a result of application of most fertilisers and agricultural wastes (McGrath 1995), sewage sludge applications may increase nickel levels in soils (Webber *et al*. 1983; Adamo *et al*. 1996).

2.5.5 Surface Water

Nickel concentrations in surface waters in Canada are typically below 2 µg/L. The reported range of concentrations for uncontaminated fresh waters in Canada is 1 to 10 µg/L (Leger 1991; Moore & Ramamoorthy 1984; NRCC 1981). A summary of concentrations is provided in Appendix 1.

Higher concentrations of nickel can be found in waters near point source discharges. Historically, concentrations in surface water samples in the Sudbury area have been elevated. Nickel

concentrations in water ranged from 7.0 to 9.7 µg/L in reference lakes and 52.0 to 338.2 µg/L in five Sudbury, ON area lakes located downstream from a metal point source and three other lakes independent of the downstream gradient (Pyle *et al*. 2005). Nickel concentrations in surface water collected between 1993 and 1994 in the Sudbury region ranged from 14 to 130 µg/L (Graham 1995). Mean concentrations of nickel ranging from 50 to 1400 µg/L were reported in lakes near Sudbury (Hutchinson & Havas 1986; Keller *et al*. 1992; Dixit *et al*. 1991) suggested that a significant fraction of this nickel originates from deposition following releases from local smelters.

Elevated concentrations of nickel in surface waters have also been reported as a result of natural inputs. For example, mean concentrations of up to 6300 µg/L were determined in water samples taken from naturally acidic ponds associated with spontaneous burning of bituminous shales near Smoking Hills, NWT (Havas & Hutchinson 1983).

2.5.6 Groundwater

Groundwater data are summarised in Appendix 1. Groundwater that is used as drinking water is discussed in section 2.5.7.

In British Columbia, total nickel in groundwater ranged from 5.6 to 2910 µg/L, with an overall average of 47 µg/L (n=97) and dissolved nickel concentrations ranged from 5.6 to 920, with an overall average of 26 µg/L (n=94) (Evans 2004).

In Alberta, groundwater monitoring data for nickel were provided for deep (n=101) and shallow (n=111) wells. Nickel concentrations in deep wells ranged from <2 to 272 µg/L (with over 64% of samples below 2 µg/L) and ranged from <1 to 62 µg/L in shallow (with less than 10% of samples below the detection limit of 1 µg/L). An overall average of 6 µg/L was calculated for nickel in shallow groundwater wells (Holt-Oduro 2004).

2.5.7 Drinking Water

Based on nickel concentrations in drinking water from Newfoundland and Labrador, Ontario, and Saskatchewan, an average concentration of 2.9 µg/L (n=12 251) was calculated. The data are based on 1998 to 2007 nickel concentrations in treated water from the Ontario Drinking Water Surveillance Program (DWSP), Saskatchewan drinking water from 2000 to 2009 and tap water concentrations from public water supplies in Newfoundland and Labrador sampled from January 2000 to June 2009 (HC 2011). This value was used as the average nickel concentration for Canada and it is slightly higher than the overall average nickel concentration reported in the 2000 to 2003 TDS, but it is within the range of mean concentrations reported in the TDS. A summary of available nickel concentrations in drinking water is included in Appendix 1.

A nickel concentration of 1.1 µg/L was reported for drinking water from a treatment plant (n=1) in rural northern Manitoba (Yee 2004) An average nickel concentration of 1.2 µg/L was reported for treated water from three locations in Saskatchewan from 1994 to 2006. Concentrations were primarily below the analytical detection limit of 1.0 µg/L and the detection limit was used to calculate the average (Hase 2004).

Drinking water data from the Ontario Drinking Water Surveillance Program for total nickel were provided for 6096 distribution water samples from groundwater (n=996), lake (n=2878), and river (n=2222) drinking water sources from 1990 to 2002 (Cheung 2004) concentrations were reported to be 1.12 µg/L in groundwater, 3.33 µg/L in lake water, and 1.02 µg/L in surface water.

In the Yukon, drinking water concentrations measured from 1999 to 2003 were typically found to be at, or below analytical detection limits (<0.5 to 2 µg/L) (Bergsam 2004). Similarly, total nickel concentrations reported in samples collected from 1995 to 2001 (n=32) were found to be at or below analytical detection limits (<2 µg/L) in over 95% of the samples (Beckerton 2004).

In groundwater sampling in central New Brunswick (Fredericton) from 1993 to 1995, total metals were assessed in 465 water samples obtained from residential kitchen taps. Nickel concentrations were found to range from <7 to 97 µg/L with concentrations below the detection limit of 13 µg/L in 254 samples. A mean nickel concentration of 16.4 µg/L and median of 6.5 µg/L were reported (Boyle *et al*. 1996). In a similar 1991-93 groundwater survey in the Moncton, NB area, nickel concentrations ranged from <13 to 289 µg/L with a mean value of 18.4 µg/L and median of 6.0 µg/L, with nickel concentrations in approximately half the water samples below the detection limit of 13 µg/L (Boyle *et al*. 1994).

As part of the Canada Total Diet Study (TDS), a survey of tap water was conducted from 2000 to 2003 in four Canadian cities. Kitchen tap water was collected from Ottawa, St. John's, Vancouver and Montréal. Mean concentrations ranged from 1.43 µg/L to 3.10 µg/L, with an overall average of 2.37 µg/L. Mean area tap water collected in St. John's and Vancouver were <0.07 µg/L while mean area tap water from Montréal was found to be 0.80 µg/L (Dabeka 2009). These values are within the same range as earlier studies from Ontario, the Atlantic provinces and Alberta (EC 1989a; Jones-White 1992; Moon *et al*. 1988). Some bottled water data is available for Canada (Dabeka *et al*. 2002) and is reported in Appendix 1 (commercial foods section). This data was not considered in estimating exposure via drinking water.

2.5.8 Sediment

A summary of available background concentrations in sediment is provided in Appendix 1.

Concentrations of nickel in sediments from Canadian lakes varied from <10 to >4000 mg/kg dry weight (dw) (Bradley & Morris 1986; Bodo 1989). The highest concentrations were generally reported in contaminated surface or subsurface sediments while the lowest were measured in deeper or uncontaminated sediments. Background concentrations in Canadian freshwater sediments range from 2 to 50 mg/kg dw (Bodo 1989; Arafat & Nriagu 1986; Jackson 1988; Moore & Ramamoorthy 1984).

Nickel in stream sediments collected in 2004 from 20 ecoregions in the Yukon were analysed using a Leforte (reverse *aqua regia*) hot digest and instrumental neutron activation. Mean concentrations of total nickel ranged from 16.31 to 111.1 mg/kg and median concentrations ranged from 8 to 38 mg/kg (Garrett 2004).

2.5.9 Biota

Nickel concentrations in biota are reported as total nickel on a wet weight (ww) or fresh weight basis, unless otherwise indicated. A summary table is provided in Appendix 1.

Concentrations of nickel were measured in produce (lettuce, beet tops, carrots and potatoes) collected from 9 urban gardens in east Saint John, NB, 2 urban gardens in west Saint John, NB and 1 rural garden (with the exception of beet tops) in Fredericton, NB (Pilgrim & Schroeder 1997). Concentrations were reported to be consistently higher in produce collected from the city gardens. Mean nickel concentration from urban gardens ranged from 0.17 µg/g to 0.22 µg/g (potatoes), 0.9

µg/g to 2.4 µg/g (lettuce) and 1.2 µg/g to 3.1 µg/g (beet tops), while rural mean concentrations for nickel ranged from 0.5 µg/g (carrots) to 1.5 µg/g (lettuce).

Nickel was detected in radishes (0.5 and 0.7 µg/g, wet weight), but was below detection (i.e., <0.1 µg/g) in potatoes, carrots, turnips, strawberries, blueberries and mossberries sampled in rural northern Manitoba (Yee 2004).

Higher nickel concentrations in fruits and vegetables may occur as a result of regional sources of contamination. For example, the concentration of nickel in washed lettuce grown within a 40 km radius of Sudbury, ON, was reported to be as high as 166 µg Ni/g dry weight (dw) (Hutchinson *et al.* 1981). However, the Sudbury Soil Study (SARA 2008) showed lettuce levels more similar to those from NB. The Sudbury study analysed root, leafy and above-ground vegetables from residential (n=64), commercial (n=15) and wildland sites (n=10) at locations selected to represent a variety of soil nickel concentrations. In residential soils the following ranges of concentrations (µg/g w.w.) were observed: <dl-1.169 (beets); 0.061-2.512 (carrots); 0.035-2.705 (cucumbers); 0.088-2.960 (lettuce); 0.116-2.364 (onions); <dl-2.030 (potatoes); <dl-1.843 (tomatoes); and 0.047-1.888 (zucchini). For commercial sites concentrations (µg/g w.w.) ranges were: <dl-0.930 (cucumbers); <dl-1.580 (potatoes); and <dl-0.432 (strawberries). For wildlands blueberry nickel concentrations ranged from 0.264-1.034 and 0.103-0.255 µg/g w.w. for mushrooms.

Arctic surfclam and male crabs (Atlantic snowcrab, queen crab and spider crab) were collected in 1996 from various locations off the coast of Newfoundland as part of the National Contaminants Information System (NCIS) (Fancey 2004). Tissue analyses were conducted by ICP-MS with a method detection limit of 0.01 µg/g. Nickel concentrations of clams and crabs are summarised in Appendix 1 and reported in µg/g as total nickel (dw). In arctic surfclam collected south of Newfoundland (Banquereau Bank), nickel concentrations ranged from 0.73 to 5.57 µg/g (whole organism, n=19). Nickel levels in tissue (gills, testes, viscera, cheliped muscle, coxal muscle and leg muscle) from male crabs sampled from eight locations in Newfoundland were found to range from 0.13 µg/g to 51.4 µg/g (Fancey 2004). The maximum detected nickel concentration consistently occurred in the gills of the crabs. In the data provided for both crab and clams there was a greater frequency of occurrence of lower range concentrations compared to high concentrations.

Nickel concentrations in muscle or combined livers/hepatopancreas tissues from marine fish and crabs (n=5/species) collected from two sites in Boundary Bay (inshore and offshore) and from Roberts Bank, BC (Swain & Walton 1994) were conducted using ICP-MS. Nickel concentrations in muscle tissue from Dungeness crab (*Cancer magister*) and starry flounder (*Platichthys stellatus*) were below the analytical detection limit of 1.0 µg/g in all samples. Both median and mean nickel concentrations in muscle tissue of butter sole were <1.0 µg/g and a maximum concentration of 3.1 µg/g. In composite samples of hepatopancreas, median nickel concentrations (dw) of 1.4 µg/g (0.20 µg/g ww), 2.3 µg/g (0.31 µg/g ww) and 2.1 µg/g (0.38 µg/g ww) were reported for crabs collected from the in-shore Boundary Bay, off-shore Boundary Bay and Roberts Bank sites, respectively. The mean nickel concentration in whole staghorn sculpins collected from the in-shore Boundary Bay site was 2.2 µg/g dw (0.44 µg/g ww).

Total nickel concentrations in walleye fish collected from two sites in Lake Erie (n=15), were below the analytical detection limit of 0.02 µg/g in 80% of the samples. In Lake Huron, a mean nickel concentration of 0.052 µg/g was determined assuming a value of ½ the detection limit for

samples (10%) below analytical detection. In Lake Ontario, nickel concentrations were below detection (<0.02 µg/g) in 55% of the samples collected in 1995-1997 and below detection (<0.05 µg/g) in 95% of samples collected in 2002 (Trivedi 2004). Whole animal analyses were conducted using graphite furnace atomic absorption spectrophotometry (AAS); a detection limit of 0.02 µg/g (dw) was reported for 1995-1997 samples and 0.05 µg/g (dw) for 2002 samples (Trivedi 2004).

As part of a contaminant monitoring program in the Northwest Territories, the livers and kidneys of 20 barren ground caribou (Beverly herd) were analysed for metals and nickel concentrations were generally below analytical detection limits, although the detection limits were not reported in this study (Elkin 2001). Nickel concentrations ranging from <0.01 to 1.33 µg/g were reported in caribou tissue from the Northwest Territories. Nickel was also measured in the kidney tissue of Banks Island Peary caribou (n=22) and barren-ground caribou (Bluenose herd, n=52) of the western NWT. All samples were below analytical detection (<0.1 µg/g, or, in the case one sample, <0.8 µg/g) (Larter & Nagy 2000).

It should be noted that in the case of all biota monitoring, the age and size of the species collected and analysed are variables that can affect metal uptake and resulting metal concentrations in tissues.

2.5.10 Commercial Foods

Nickel concentrations in foods are reported as total nickel on a wet weight or fresh weight basis, unless otherwise indicated.

Since 1969, Health Canada has conducted Total Diet Studies (TDS) to estimate the dietary intakes of chemicals by Canadians in different age-sex groups. For the most recent Total Diet Studies (as cited in HC 2011), food samples were analysed using inductively coupled plasma-mass spectrometry (ICP-MS) and concentrations were reported in ng/g (fresh weight). The detection limits of the analyses varied depending on the type of food and the reagent blanks. The 1995 Canadian Total Diet Study indicated the major contributors of nickel to the typical Canadian diet included meat and poultry (37%), bakery goods and cereals (19%), soups (15%) and vegetables (11%) (Dabeka & McKenzie 1995); however, beans (including cocoa), grains, nuts and seeds may contribute more to intake in vegetarians and other groups with higher than average intakes of these foods (Anke *et al*. 2000). Nickel concentrations were determined in 143 food composites in 2000. The highest levels of nickel in foods purchased in Ottawa in 2000 as part of the 2000-2004 Total Diet Study were found in shelled seeds (3.173 µg/g), white sugar (2.600 µg/g), herbs and spices (2.122 µg/g) and nuts (1.960 µg/g). Data from the Canadian Total Diet Studies from 2000 to 2007 were used in the determination of the estimated daily intake of nickel from food sources, with the exception of infant formula, which is based on Dabeka (1989) and explained further in Section 2.5.11. Foods data is discussed further in section 8.2 and found in Appendices 1 and 9.

Data from the 2000-2007 Canadian Total Diet Studies were provided directly by Health Canada's Food Directorate and then normalised to correspond to the age groups used in this document. Depending on the body weight used, mean daily intakes of 280 µg Ni/day from food for Canadian adult consumers based on a 70.7 kg adult and 240 µg Ni/day based on a 60 kg adult were calculated. These intakes are similar to the intake of 282 µg Ni/day previously reported for Canada for 1986-1988 (Dabeka & McKenzie 1995). The nickel intake rates calculated from the 2000-2007 studies are within the range of 200 to 300 µg/day reported by the World Health

Organization (WHO 1991), but are above those reported in Total Diet Studies conducted in the United Kingdom (i.e., 120 µg/day) (Ysart *et al*. 2000), France (i.e., 74 µg/day) (Noel *et al*. 2003) and Australia (i.e., 150 µg/day for men and 115 µg/day for women) (Food Standards Australia New Zealand FSANZ 2008). While the total daily nickel intake from an average Danish diet was estimated to be 150 (Nielsen & Flyvholm 1984) to 167 (Larsen *et al*. 2002) µg/day, daily intake in Danes could reach over 900 µg/day due to consumption of certain high-nickel foods (oatmeal, legumes [including soybeans], nuts, cocoa and chocolate) (Nielsen & Flyvholm 1984). Analysis of the 1984 U.S. Food and Drug Administration Total Diet Study found the mean nickel intakes for infants and young children ranged 69 to 90 µg/day, 71 to 97 µg/day for adolescents and 74 to 100 µg/day for adults and the elderly (Pennington & Jones 1987).

A significant issue regarding nickel determination in foods analysed in the 2000-2004 Canadian Total Diet Study involves potential nickel contamination of foods from cooking sources (utensils and cookware) and from the nickel analyses itself (see Section 2.3). It is well known that leaching of nickel from stainless steel cookware may significantly increase the nickel content of foods prepared in contact with this alloy (WHO 1991; Grandjean *et al*. 1989; Dabeka & McKenzie 1995). Nickel was detected in the leachates from seven different stainless steel utensils, subjected to corrosion tests, at concentrations ranging from 0.01 to 0.21µg/g (Kuligowski & Halperin 1992). A study conducted on electric kettles in the Netherlands found that 10 of 26 kettles tested released more than 50 µg/L of nickel into water (Berg *et al*. 2000). An investigation of the impact of using stainless steel utensils in cooking found that their contribution to total nickel intake was negligible, but that new frying pans could contribute anywhere from 5% to 50% of the total dietary nickel intake during the first use (Flint & Packirisamy 1995; 1997). Nickel release during cooking with stainless steel utensils may be enhanced if the foods cooked are acidic (Christensen & Moller 1978). In addition to adventitious nickel from cookware, some food processing methods such as milling of flour and the catalytic hydrogenation of fats and oils using nickel catalysts may result in higher than average nickel concentrations in some foods (WHO 1991).

There was some concern that nickel-based samplers and skimming cones used in the ICP-MS analyses in the 2000, 2001 and 2002 Canadian Total Diet Studies, could have resulted in nickel contamination during analysis (Dabeka 2009). In order to resolve this, the results of the 2000, 2001 and 2002 Total Diet Study were compared to the results of the 1986 Total Diet Study. The food samples in the 1986 Total Diet Study were analysed using a different analytical analysis (graphic furnace atomic absorption spectroscopy) from the current analytical method (ICP-MS) where nickel contamination from skimmers and cones could potentially be introduced. The results of the 1986 study were slightly lower than the results of the 2000-2002 estimated daily intake values when appropriate age groups were compared but show the same trend of decreasing intake of nickel as the age groups increased. Considering that the results of the 1986 and 2000 to 2002 studies are very similar and show the same trend across all age groups, any nickel contamination that may have been introduced during the analyses of the food samples does not appear to have made a significant contribution of nickel to the food samples, therefore, the data from the 2000 to 2002 study are considered valid.

2.5.11 Infant Formula and Human Breast Milk

Nickel concentrations in infant formulas measured in the 2000-2002 Canadian Total Diet Study were typically below the method detection limits. For milk-based formula, nickel concentrations

were below detection limits that ranged from <18 ng/g to <67 ng/g while the average nickel concentrations in soy based formula were 306 ng/g in 2000, <67 ng/g in 2001 and 86 ng/g in 2002 (Dabeka 2004). The reported detection limits for nickel in infant formulas analysed in the 2000-2002 Canadian Total Diet Study do not appear to be adequately sensitive to obtain meaningful values to estimate daily dietary intake. However, nickel concentrations of 2.7 ng/g to 171 ng/g were detected in ready-to-use infant formulas available in Canada. Milk-based formula with added iron (n=27) and without added iron (n=6) contained mean (and median) nickel concentrations of 7.5 (7.4) ng/g and 5.7 (5.5) ng/g, respectively. Soy-based formula (n=16) contained higher concentrations of nickel with reported mean and median of 63.7 ng/g and 31.2 ng/g, respectively. The overall mean and median concentrations for ready-to-use formula were 24.9 ng/g and 7.6 ng/g, respectively (Dabeka 1989). Metals and other elements are generally found at higher concentrations in soy-based infant formulas in comparison to milk-based formulas (Ikem *et al*. 2002).

In a U.S. study of 13 healthy, well-nourished women, nickel concentrations in breast milk (n=46) ranged from 0.52 to 2.04 µg/L with an average concentration of 1.16±0.41 µg/L (Casey & Neville 1987). A median nickel concentration of 13.3 µg/L (range 11-16 µg/L) was reported in a study of human whole milk samples collected from six countries and analysed at three months post-partum (Parr *et al.* 1991), and mean and median nickel concentrations of 5.8 µg/L and 5.3 µg/L respectively, (range 3.7-10.7 µg/L) were detected in milk from Portuguese mothers (Almeida *et al.* 2008). In a Canadian study, breast milk was collected once a week for 8 weeks with a final sample collected at 3 months, from mothers living in Newfoundland. The milk samples were analysed for a range of elements using inductively coupled plasma-mass spectrometry. In 19 mothers with full-term infants, median nickel concentrations increased from 3µg/L, one week after birth to 28 µg/L after 12 weeks. Median concentrations in milk from 24 mothers with pre-term infants ranged from undetectable to 18 µg/L with no clear temporal trend (Friel *et al*. 1999). For the purpose of calculating an EDI (Appendix 10), a mean nickel concentration of 19.3µg/L for exclusively breast-fed infants was derived based on Friel *et al.* (1999 in HC 2011).

2.5.12 Consumer Products

Nickel is found in a variety of medical devices such as joint implants, intrauterine devices, and acupuncture needles. It is also found in products used in dentistry such as fixation devices and fixed and removable prostheses. Research indicates that nickel release from dental casting alloys into acidic salivary solutions can occur (Covington *et al.* 1985; Wolfaardt & Peters 1992) and that localised, high concentrations in air (25.9 µg/m^3) can result from the grinding of such alloys (Rom *et al*. 1984). Various household products contain nickel, which was detected in 33 of 34 samples of different types of cleaning agents with a mean concentration range of 0.08 µg/g in bleaching agents to 19.17 µg/g in scouring powders (Nava *et al*. 1987); pigmented makeup products (Cha *et al*. 2010), including "play" makeup for children (Corazza *et al*. 2009), may contain nickel, as may lotions (Bocca *et al*. 2007) and other personal consumer products (although generally at concentrations below those thought to trigger allergic reactions) (Basketter *et al*. 1993). Mobile phones (Jensen *et al*. 2011), hand tools (Thyssen *et al*. 2011), children's toys (Thyssen 2010), hair accessories (Thyssen *et al*. 2009) and other common household products (Thyssen *et al*. 2010) may also release nickel.

Mainstream smoke produced by five samples each of five brands of Canadian cigarettes (n=300) sampled from 1968 to 1988 contained from 0.21 to 0.74 µg of nickel per cigarette with a mean

concentration of 0.42 µg per cigarette. Levels of nickel present in side stream smoke were similar, ranging from 0.2 to 0.64 µg per cigarette with a mean of 0.35 µg per cigarette (Rickert 1991). Domestic cigarettes analysed in 2004, were found to contain a mean nickel concentration of 0.2504 µg/cigarette, while imported brands contained 0.8233 µg/cigarette (Hammond & O'Connor 2008). The imported cigarette brands were found to contain significantly higher nickel levels than those found in domestic brands, but no corresponding emissions data were available.

2.6 Existing Criteria and Guidelines

Guidelines, criteria and standards for nickel in soil, surface water and groundwater from various jurisdictions in Canada and around the world are listed in Table 2 below.

Table 2. Existing environmental criteria and guidelines for nickel in various jurisdictions

Jurisdiction	Category	Criterion/Guideline	Reference
Canada	Soil Quality Guideline (all land uses)	50 mg/kg	(CCME 1999)
Canada	Water Quality Guideline (Aquatic Life)	0.025-0.15 mg/L	(CCME 1999)
	Water Quality Guideline (Irrigation)	0.2 mg/L	(CCME 1999)
	Water Quality Guideline (Livestock)	1.0 mg/L	(CCME 1999)
Québec	Generic Soil Quality Criteria		
	A (background concentrations and quantification limits for organics)	50 mg/kg	
	B (maximum acceptable limit for residential, recreational, institutional and commercial (in residential area) land uses)	100 mg/kg	
	C (Maximum acceptable limit for commercial (in non-residential areas) and industrial land uses)	500 mg/kg	
	Groundwater - drinking water	20 µg/L	
	Groundwater - seepage into surface water	260 µg/L	(MEF 1998)
Alberta	Alberta Tier 1 Soil Remediation Guidelines (fine and coarse soils)		
	Natural Area	50 mg/kg	
	Agricultural	50 mg/kg	
	Residential/Parkland	50 mg/kg	
	Commercial	50 mg/kg	
	Industrial	50 mg/kg	(AENV 2010)
British Columbia	Soil remediation standards		
	Agricultural	150 mg/kg	
	Residential/Urban park	100 mg/kg	
	Industrial/Commercial	500 mg/kg	(BCMOE 2011)
Yukon	Generic Numerical Soil Standard		
	Agricultural	150 mg/kg	
	Park	100 mg/kg	
	Residential	100 mg/kg	
	Commercial	500 mg/kg	
	Industrial	500 mg/kg	(YTDOE 2002)
Ontario	Full Depth Background Site Condition Standards		
	Agricultural	37 mg/kg	(OMOE 2011b) Background values typical of uncontaminated soils, groundwater and sediments
	Residential/Parkland/Commercial/Industrial/Institutional	82 mg/kg	
	Groundwater (all uses)	14 µg/L	
	Sediment	16 mg/kg	

Jurisdiction	Category	Criterion/Guideline	Reference
Ontario (continued)	Full Depth Generic Site Condition Standards in a Potable Ground Water Condition		(OMOE 2011b) *Standard in brackets applies to medium and fine textured soils
	Agricultural	(130 mg/kg)* 100 mg/kg	
	Residential/Parkland/Institutional Use	(130 mg/kg)* 100 mg/kg	
	Industrial/Commercial/Community Property	(340 mg/kg)* 270 mg/kg	
	Groundwater (all uses)	100 µg/L	
	Full Depth Generic Site Condition Standards in a Non-Potable Ground Water Condition		
	Residential/Parkland/Institutional Use	(130 mg/kg)* 100 mg/kg	
	Industrial/Commercial/Community Property	(340 mg/kg)* 270 mg/kg	
	Groundwater (all uses)	490 µg/L	
	Stratified Site Condition Standards in a Potable Ground Water Condition		
	Residential/Parkland/Institutional Property (subsurface soil)	510 mg/kg	
	Commercial/Industrial/Community Property (subsurface soil)	510 mg/kg	
	Stratified Site Condition Standards in a Non-Potable Ground Water Condition		
	Residential/Parkland/Institutional Use (subsurface soil)	510 mg/kg	
	Commercial/Industrial/Community Property (subsurface soil)	510 mg/kg	
Denmark	Soil Quality Guideline	10.0 mg/kg	(DEPA 1995)
Netherlands	Environmental Quality Objectives		(MHSPE 1994)
	Standard Soil		
	Target Value	35 mg/kg	
	Intervention Value	210 mg/kg	

3 ENVIRONMENTAL FATE AND BEHAVIOUR

Due to its use and release into the environment, nickel is distributed in the atmosphere, water, sediment, soils and biota worldwide. As an element, nickel cannot be degraded in the environment. As such, the fate of nickel is dependent on the many physicochemical and biological factors that influence cycling among biotic and abiotic components of the environment. The most important of these factors are pH and the presence and abundance of organic materials, hydroxides, clay minerals, cations and complexing ligands (NRCC 1981). Nickel has a high affinity for negatively charged surfaces associated with clay minerals, hydroxides, organic compounds and carbonates. Consequently, it tends to be removed rapidly from solution. Although surface soils and aquatic sediments may act as temporary sinks for nickel, changes in environmental conditions have the potential to remobilise and transport it to other compartments of the ecosystem. The following discussion is intended to provide an overview of the fate and persistence of nickel in the environment.

3.1 Atmosphere

Nickel has a boiling point of 2913°C (Haynes 2011) and therefore, is not likely to volatilise. In Canada, most nickel entering the atmosphere is in particulate form and originates from from metal production activities (Jacques 1987). In Ontario, sampling in urban areas and areas influenced by a nickel source indicated nickel sulphate was the dominant species (57-85%), followed by nickel oxide and nickel hydroxide, which made up less than 20% of the nickel detected (OMOE 2011a). Atmospheric nickel originating from smelting operations and fossil fuel combustion is predominantly in the form of nickel sulphate, subsulphide and oxide (Henry & Knapp 1980; Gilman & Ruckerbauer 1962). Limited sampling of air filters and house dust in Sudbury, ON, indicated a small amount of nickel subsulphide (<10%) may be emitted from the Copper Cliff smelter (OMOE 2011a). Speciation of nickel compounds in Florida ambient air (PM10), using X-ray absorption fine structure (XAFS) spectroscopy and sequential extraction, showed $NiSO4•xH_2O$was much more abundant (78%) than oxidic nickel, possibly in the form of $NiFe_2O_4$ (22%) but lacked NiS (<5%) (Galbreath *et al*. 2003). Fuchjohann *et al*. (2001) speciated total suspended particulate samples from both urban and industrial sites in Dortmund, Germany using sequential extraction. Soluble and oxidic forms predominated (>84% of extractable nickel) followed by metallic and sulfidic fractions. Metallic nickel is believed to comprise only a small proportion of the total nickel present in ambient air in Canada (MacLatchy 1992). Nickel carbonyl is formed during metallurgical operations involving nickel and released in gaseous form (NRCC 1981); however, this volatile compound is of little concern in the environment since its half-life in air is less than 0.1 second (Stedman & Hikade 1980).

The transport and distribution of nickel particulates is strongly influenced by particle diameter and meteorological conditions (Schmidt & Andren 1980). Anthropogenic nickel has been reported to enter the atmosphere in particulate matter in the 0.1-2 µm size range; naturally emitted nickel is typically found in larger particles, ranging from 2 to 10 µm (OMOE 2011a.; Beijer & Jernelov 1986). The residence time of nickel particles in the atmosphere was estimated to be 5 to 8 days for most nickel-containing particles of natural and anthropogenic origin (Schmidt & Andren 1980); however, the atmospheric half-life of small airborne nickel particulates (0.3-0.5 µm) can be as long as 30 days.

Nickel associated with fine particulate matter (<10 µm) is transported over long distances (Beijer & Jernelov 1986). The potential for long-range transport of nickel particles was demonstrated in the Norwegian Arctic where high atmospheric nickel concentrations were traced to emission sources in North America, Greenland and Europe (ATSDR 2005). Similar studies in the Canadian Arctic have demonstrated that 86% of the atmospheric nickel in Alert, NWT results from anthropogenic sources in Eurasia (INAC 2003).

Coagulation and condensation may occur as aerosols age and particles may be recaptured by micro- and mesoscale convection and become incorporated into the microstructure of clouds. Precipitation (including both wet and dry deposition) is expected to represent the most important environmental fate process for nickel released into the atmosphere (Schmidt & Andren 1980). Larger particles (>5µm) are removed by gravitational settling, while smaller particles are removed by wet and dry deposition processes with the importance of wet deposition (versus dry) increasing as particle size decreases (Schmidt & Andren 1980; ATSDR 2005). Nickel deposition rates measured in 1982 for southern, central and northern Ontario were 0.25, 0.28 and 0.18 mg/m^2/year (dry deposition) and 0.5, 0.5 and 0.4 mg/m^2/year (wet deposition). The atmospheric input of nickel into the Great Lakes was estimated (1993) to range from 160-590 ng Ni/m^2/year; this pathway accounted for 60-80% of the total anthropogenic nickel input to Lake Superior, and 20-70% of nickel input in Lakes Erie and Ontario (ATSDR 2005). Rates of nickel deposition to sediments were found to be highest in spring and fall, and lower in summer and winter in studies conducted in the Lake Hertel area of Québec (Gelinas *et al*. 2000).

3.2 Water

Nickel is naturally present in waters as a result of natural atmospheric and hydrological processes, but its distribution is largely influenced by anthropogenic sources (Brecher *et al*. 1989; WHO 1991). Nickel is known to enter the aquatic environment through atmospheric deposition (dry and wet), soil erosion, as well as in effluents and leachates. Nickel is relatively mobile and is transported in natural waters in both particulate and dissolved forms. Nickel adsorbs strongly to mineral surfaces (e.g., oxides and hydrous oxides of iron, manganese, and aluminum) which affects concentrations of nickel in water (ATSDR 2005). It has been reported that 95% of the nickel transported in the Yukon River was in suspended particulate form (Gibbs 1977); however, other reports suggest that relatively little nickel is present in suspended solids in most Canadian lake waters (Nriagu *et al*. 1982; Rossman & Barnes 1988). The nickel which is present in sediments and suspended solids is distributed among organic materials, precipitated and co-precipitated particle coatings, and crystalline particles. In natural waters, the divalent ion is generally the dominant form while nickel sulphate is the predominant soluble form if sulphate concentrations are high. Nickel sulphate can also be increased by disturbance of sediments through dredging or other activities (Richter 1980; Degtiareva & Elektorowica 2001).

The factors affecting the transport, fate and biological availability of nickel in fresh and salt water are the pH, oxidation-reduction potential, ionic strength, type and concentration of organic and inorganic ligands (in particular humic and fulvic acids) and the presence of solid surfaces for adsorption (in particular, hydrous iron and manganese oxides) (Callahan *et al*. 1979; Semkin 1975; Snodgrass 1980). Decreasing pH or increasing concentrations of organic ligands, may result in desorption of nickel from suspended particulate material or sediment into the water column in the divalent cation form (Callahan *et al*. 1979). The presence of reducing conditions, along with

sulphur in some sediments results in the formation of the relatively insoluble nickel sulphide (Ankley *et al*. 1991). Notably, under reducing conditions, microbial activity can play a role in nickel sulphide formation via the conversion of sulphate to sulphide (Babich & Stotzky 1983a; 1983b). When aerobic conditions exist and the pH is less than 9, soluble nickel compounds are formed with hydroxide carbonate, sulphate, and naturally occurring organic ligands, resulting in the presence of nickel in the water phase (Callahan *et al*. 1979).

3.3 Sediment

Nickel in sediments and suspended solids can be distributed between various phases such as organic material, precipitated/coprecipitated particle coatings and crystalline particles. As an example, nickel distribution in the Yukon River has been documented to be 48% in particle coatings, 30% in crystalline particles and 15% associated with the organically-bound particulate material (Gibbs 1977).

The distribution is strongly affected by physical and chemical parameters such as pH, ionic strength, and the type and concentration of organic and inorganic compounds that can act as ligands or adsorbents for nickel (Callahan *et al.* 1979; Snodgrass 1980). Humic and fulvic acids as well as hydrous iron and manganese play an important role in adsorption processes. Changes in some physical and chemical parameters may result in desorption of nickel from particulate matter into the water column (DiToro *et al.* 1986). Microbial activity can alter the oxidation-reduction conditions of sediment and, under reducing conditions, insoluble nickel sulphide is formed in the presence of sulphur (Ankley *et al*. 1991).

3.4 Indoor Dust

Rasmussen *et al.* (2008) reported that indoor dust and soil are geochemically distinct. Indoor dust has approximately five times the organic matter of soil samples. In studies of house dust, street dust and residential garden soils in Ottawa, ON, Rasmussen *et al.* (2001; 2008) showed that metals in house dust may accumulate at higher concentrations than in residential garden soil and can contribute significantly to exposure to metals in residential urban environments. Organic carbon is a key factor controlling metal partitioning and bioavailability. The higher metal concentrations in indoor dust compared to soils may be explained by the affinity some metals have for organic matter, in addition to the smaller particle size of dust (Rasmussen 2004).

3.5 Soil

Natural nickel concentrations have been found to be correlated to aluminum and iron concentrations, as well as clay content, and negatively correlated with soil particles >20 µm (Echevarria *et al.* 2006). Nickel can be substituted for iron or magnesium in ferromagnesian and sulphide minerals (Massoura *et al.* 2006) and the binding of nickel to soil may result in the displacement of calcium, magnesium and sodium into soil solution (Ponizovsky *et al*. 2008).

Based on sequential extraction methods, the predominant forms of nickel in dust arising from soil are likely to be silicates and oxides (NRCC 1981). Generally, over 50% of the nickel in soils may be associated with the residual fraction (HF and $HClO_4$ soluble), around 20% may be associated with the iron and manganese oxide fraction and most of the rest is bound up with the carbonate fraction (Hickey & Kittrick 1984) with only minimal amounts associated with the exchangeable and organic fractions (McGrath 1995). Nickel in contaminated soils has been found to occur

primarily in the precipitated and adsorbed or complexed forms as particulates, with very small amounts present in water-soluble form (Ma 1997; Cottenie *et al*. 1979). Nickel is generally strongly sorbed and chelated to soil surfaces (with Fe and Mn oxides, clays and organic matter) and may be occluded in oxides. In soil solution, nickel occurs mainly as organic or inorganic complexes, particularly $NiCO_3$ at high pH (Ge *et al*. 2000). The organic fraction has been reported to assume more importance in sewage sludge amended soils, where sandy loam soil treated for seven years with composted sludge was reported to contain 23% nickel in the organic form, 41% in the sulphide/residual form and 34% in the carbonate form (Chang *et al*. 1984)..

The distribution of nickel in soil profiles can vary depending on the origin of the soil and pedogenic processes (McGrath 1995). The adsorption of nickel to soil is site-specific and is affected by pH, soil texture, bulk density, organic matter, clay minerals, hydroxides and groundwater flow (ATSDR 2005). The origin of the nickel may also have a role; naturally occurring nickel may be less bioavailable than nickel associated with anthropogenic sources (Echevarria *et al.* 2006). Nickel concentrations in surface and subsurface soils may be similar. However, numerous studies (Griffith *et al*. 1984; McKeague & Wolynetz 1980; Soon & Abboud 1990; Wall & Marsh. 1988) have indicated that surface A horizons, subjected to leaching by rain, can be nickel-depleted leading to lower concentrations in the A soil horizons than in relatively unweathered C horizons. The leached nickel accumulates in subsurface B horizon soils where it tends to sorb onto iron and manganese oxide and where it can substitute for magnesium in the lattice of soil clay minerals (NRCC 1981). Such processes tend to decrease the solubility and mobility of nickel resulting in less nickel reaching the ground water. These factors, however, only play a secondary role in nickel distribution between the solid and solution phases of soil (Anderson & Christensen 1988). The primary factor determining the distribution of nickel between the two phases is pH. Decreases in pH, specifically below 6.5, result in increased solubility and mobilisation of nickel and higher concentrations in the aqueous phase (Sunderman Jr. & Oskarsson 1988; Weng *et al*. 2003; ATSDR 2005). Notably, plant (and soil organisms) bioavailability is strongly favoured under such conditions of low pH (Bisessar 1989; Echevarria *et al*. 2006; Halstead *et al*. 1969). This pH effect is very pronounced in acid soils from the nickel-contaminated soils from the Sudbury region (McGrath 1995). Nickel mobility may also be affected by clay mineralogy, soil organic matter content, infiltration, and soil drainage (Hesterberg 1998).

On the basis of nickel concentrations in soils and estimates of the loss of nickel from continents, the residence time of nickel in soils was estimated to be about 3500 years (Nriagu 1980). Nickel rapidly adsorbs to soils and is desorbed very slowly; bioavailable nickel may be reduced more quickly than total nickel by processes such as uptake by plants and leaching, resulting in a lower proportion of bioavailable nickel in aged soils (Lee *et al*. 2001; Echevarria *et al*. 2006).

4 ESSENTIALITY

4.1 Microorganisms

Microbes generally concentrate nickel from their growth medium, possibly *via* Mg^{2+} uptake pathways (Webb 1970). Nickel may also facilitate iron absorption or metabolism. Microorganisms which possess nickel-containing proteins appear to have evolved nickel homeostatic mechanisms (cited in Macomber & Hausinger 2011). Nickel is a cofactor or structural component of several microbial metalloenzymes including urease, [NiFe] hydrogenase, Ni-superoxide dismutase, acireductone dioxygenase, acetyl CoA synthase/decarbonylase, carbon monoxide dehydrogenase and methyl coenzyme M reductase (the latter three also critical in methanogenic archea) (Konhauser *et al*. 2009), as well as some forms of glyoxalase and glycerol-1-phosphate (cited in IOM 2001; Macomber & Hausinger 2011; Denkhaus & Salnikow 2002).

4.2 Terrestrial Plants

Nickel is an essential element, or micronutrient in plants (Brown *et al*. 1987a; 1987c; Aller *et al*. 1990; Dixon *et al*. 1975; EU 2008; Salt *et al*. 2002; Eskew *et al.* 1983). Nickel is a known cofactor of urease in many plants and is essential for nitrogen metabolism, as well as proper germination in cereal grains: nickel deficiency may produce chlorosis and necrotic spots, reduce crop yields, disrupt iron metabolism and reduce urease activity (cited in Phipps *et al*. 2002). Foliar urea treatment of low-Ni soybean plants suffered leaf damage, which was alleviated with higher seed nickel and external nickel supply and resulted in significantly higher yields (Kutman *et al.* 2013). Nickel deficiency may be observed in urea-fed plants.

4.3 Terrestrial Invertebrates

Nickel is considered potentially essential in invertebrates (as an enzyme cofactor and in nitrogen metabolism) (Hopkin 1989), but has been proven essential in only a few species (e.g., ground beetles) (Bednarska & Laskowski 2008). There are no data regarding the required nickel intake for invertebrates (cited in Phipps *et al*. 2002 and EU 2008).

4.4 Mammals and Birds

Nickel is thought to be an ultratrace essential element in several animal species (Phipps *et al*. 2002; Nielsen & Sandstead 1974; Mertz 1979; Arpasova *et al*. 2007; Apostoli *et al*. 2006; Anke *et al*. 1984; Adriano 2001). The dietary requirements to prevent nickel deficiency appear to be quite variable, but have been estimated for some species, including rats and chicks (50 µg/kg diet), monogastric mammals (over 50 µg/kg diet; minipigs 100 µg/kg diet), and ruminants (over 110 µg/kg diet) (cited in Phipps *et al.* 2002). Nickel deficiency generally does not occur naturally in mammals and birds.

Nickel is thought to act as an enzyme cofactor/activator in animals. In animals fed nickel-depleted diets, adverse effects include depressed growth, reproductive performance and plasma glucose, altered distribution and function of other divalent cations, such as iron, copper, calcium and zinc (Spears 1984; Annora *et al*. 2009), changes in pigmentation, reduced hematocrit and liver abnormalities (Stangl & Kirchgessner 1996) (and cited in Phipps *et al.* 2002 and ATSDR 2005). Nickel is suspected to interact with folate or vitamin B_{12} in the metabolism of methionine

(Uthus 1997). Nickel depletion also impaired glucose metabolism and reduced specific activities of many enzymes involved in carbohydrate and amino acid metabolism (cited in Nielsen 1991).

However, depletion of dietary nickel may also have expended or impaired intestinal absorption of iron and other metals, as evidenced by reduced hepatic iron, copper and zinc concentrations in the nickel-depleted animals. The alterations in serum and hepatic lipid profiles in nickel-depleted animals (Stangl & Kirchgessner 1996) were similar to those occurring in animals fed a moderately iron-deficient diet. Some of the hematological effects of nickel may also have been pharmacologic, rather than physiological (Nielsen *et al.* 1984). It is also possible nickel may not be strictly essential in animals (or humans), but may instead be required for normal development of the gastrointestinal microflora (Denkhaus & Salnikow 2002).

4.5 Humans

There is considerable debate as to the essentiality of nickel as a dietary trace mineral in humans. Extrapolation from animal data led some researchers to conclude nickel likewise serves an essential function in humans (Anke *et al.* 1984; Nielsen & Sandstead 1974). However, there have been no studies assessing the essentiality of nickel in humans and no deficiency symptoms have been described (Anke *et al*. 1995), nor has a biochemical function been clearly demonstrated in higher animals or humans (Uthus & Seaborn 1996). The Institute of Medicine (IOM) concluded there is no clear biological function in humans and provides no daily recommended intakes for nickel (IOM 2001).

5 BEHAVIOUR AND EFFECTS IN BIOTA

The available information on the toxicological effects of nickel on soil microbial processes, terrestrial plants and invertebrates, as well as mammals and birds has been reviewed and summarised in this chapter in support of the derivation of environmental soil quality guidelines. This information has been tabulated in Appendices 2 to 6.

One way to assess the potential hazards of nickel-contaminated soils to terrestrial organisms is to examine effects-based toxicity studies. The LOEC endpoints reported in the toxicity tables represent the lowest-observed-effects concentration at which there was a statistically significant difference from controls, as reported by the author(s) (biological significance was determined during guideline derivation before inclusion to the data-set used to derive the guideline). If the author(s) reported no such statistical tests, the percentage of adverse effects, as compared to the controls, resulting from nickel concentrations within the soil will be calculated by CCME from the data presented by the author(s). This percentage of adverse effect is represented by an EC (effects concentration) endpoint in the toxicity appendices. Actual EC_x endpoints reported by the author(s), such as EC_{50} or EC_{25}, will be presented as such without any calculation of a percentage of adverse effect. Measured concentrations and metal extraction methods are reported in the toxicity tables only if they involve a strong acid, such as HCl or HNO_3; otherwise, the nominal concentrations are reported.

Plants and animals may accumulate contaminants over time if the amount to which they are directly exposed is greater than the amount they can eliminate through excretion and metabolic activity (Noble 1990). The transfer of contaminants directly from a medium to an organism is termed bioconcentration. The process by which contaminants are taken up by terrestrial and aquatic organisms directly from the medium and through consuming contaminated food is referred to as bioaccumulation (CCME 2006). The bioconcentration factor (BCF) is the ratio of a substance's concentration in an organism to its concentration in ambient water, soil, sediment, or air (Connell 1990). Most studies in the scientific literature do not directly state BCFs, but report concentrations in organisms and in soil separately.

5.1 Soil microbial processes

Microorganisms are a critical part of most terrestrial ecosystems. Heavy metals affect microbial growth and survival if they are present in relatively high concentrations (Bååth 1989). Changes to the structure and function of microorganism populations may have adverse effects on the functioning of the ecosystem. The toxicity of nickel to microorganisms in soil varies among a variety of soil types. The addition of clay minerals (montmorillonite, kaolinite) in soil can reduce the toxicity to fungi (Babich & Stotzky 1982). Enhancement of clay content in soil increases its cation exchange capacity (CEC), and then protects against nickel toxicity. In a study investigating nickel toxicity in five Dutch soil types, inhibition of respiration rate was greatest in the sandy soil and least in the clay soil (Doelman & Haanstra 1984). Similarly, toxicity thresholds for soil microbial processes including nitrification, glucose-induced respiration and carbon mineralisation were found to be increased in soils with higher CEC and clay content (Oorts *et al*. 2006). Increasing soil pH was also reported to decrease the toxicity of nickel to several microorganisms such as eurobacteria, actinomycetes, yeasts and fungi (Babich and Stotzky 1982). The toxicity of nickel to carbon mineralisation and nitrification in soil is also lower in alkaline than acidic soil (Giashuddin & Cornfield 1979). Doelman and Haanstra (1984)

have reported that pH is the main abiotic factor controlling the effects of nickel on soil microbial respiration. Aging of soils and leaching have both been found to reduce the toxicity of nickel to microbial processes, and toxicity tests conducted using freshly spiked soils may therefore overestimate toxicity when compared to typical contaminated sites (Oorts *et al*. 2007).

A summary of the available toxicological information of the effects of nickel to microorganisms and microbial toxicity studies consulted or selected for use in soil quality guidelines derivation are presented in Appendix 2. The toxic level of nickel for microorganisms and microbial processes is highly variable. In at least some cases the toxicity may be a function of the free Ni^{2+} concentration rather than the total nickel concentration (Hu *et al*. 2002), although other studies have found that toxicity could not be predicted by nickel speciation (Van Nostrand *et al*. 2005). Effect concentrations for soil microbial processes ranged from 10 to more than 2000 mg/kg (Appendix 2).

The addition of nickel to soil (as $NiCl_2$) of 294 mg Ni/kg reduced nitrification and nitrogen mineralisation by 17% (Liang & Tabatabai 1978; 1977). A nickel concentration of 1000 mg/kg reduced nitrogen mineralisation by 36% and nitrification by 68% (Giashuddin & Cornfield 1978).

In a study of various fungi, the growth and survival of *Aspergillus flavus* and *Gliocladium sp*. were reduced after a three-day exposure to 250 mg/kg of $NiCl_2$ in an acidic (pH 4.7) soil (Babich & Stotzky 1982). The most sensitive species in this study was *Aspergillus clavatus* which showed reduced growth when exposed to a nickel concentration of 50 mg/kg.

In studies assessing the effects of nickel on phosphatase and urease activities in various types of soil, nickel was much less toxic in sand, with EC_{50} values of 1109 and 100 mg/kg, respectively, for phosphatase and urease activities; higher EC_{50} values after 18 months than after 6 weeks (Doelman & Haanstra 1989; 1986). This reduction in toxicity with time may be due to an ability of some microorganisms to adapt (Cornfield 1977). An additional explanation may be a slow binding of nickel to certain types of soil.

Sensitivity of other enzymatic activities, such as arylsulphate and pyrophosphatase to nickel has been demonstrated. Addition of 1468 mg Ni/kg decreased arylsulphate and pyrophosphatase activities by 26% and 5%, respectively (Al-Khafaji & Tabatabai 1979; Scott *et al*. 1985).

Carbon mineralisation was also affected by addition of nickel to soils. Carbon mineralisation decreased after a 2 to 6 week exposure to 10 mg Ni/kg of $NiSO_4$ (the lowest exposure concentration tested) in sandy soil (Cornfield 1977). Carbon mineralisation was reduced 55% at nickel concentration as low as 6.6 mg/kg in a sandy loam with unreported pH (Brookes & McGrath 1984). In contrast, only a 24% reduction in carbon mineralisation was reported at soil nickel concentrations as high as 1000 mg/kg (Bhuiya 1972). In a study on effects of several metals (such as Ni) from a Cu-Zn smelter in Québec, soil respiration was suggested to be a better indicator than phosphatase activity in assessing metal stresses to soil microbial populations (Dumonet *et al*. 1992).

5.2 Terrestrial Plants

5.2.1 Metabolic fate and behaviour

Nickel is an essential trace element in plants, used in various coenzymes and regulatory functions (Salt *et al*. 2002). Good correlations were reported between concentrations of nickel in terrestrial plants and those in numerous Canadian soils (Rencz 1980; Elmosly & Abdel-Sabour 1997; Cataldo *et al*. 1978; Aschmann & Zasoski 1987). Availability of nickel to plants is largely controlled by various soil factors such as pH, organic matter content, clay and hydrous iron and manganese oxide content, and cation exchange capacity (Haq *et al*. 1980; Richter 1980) with soil pH being of particular importance. Low soil pH (≤6.0) strongly favours the bioavailability of nickel (Halstead *et al*. 1969; Bisessar 1989). At low pH, acid-soluble nickel compounds are unstable and the capacity of soil to remove nickel from pore water through adsorption is low. The chemical species of nickel does not appear to be a major factor in predicting plant uptake. Nickel uptake was higher in freshly added salt solutions, compared to field studies, at lower concentrations and lower uptake at higher nickel concentrations, possibly due to toxicity; however, nickel plant concentrations from salt solutions were within the 95% prediction interval of field data regressions (Efroymson *et al*. 2004).

A number of methods have been proposed for the evaluation of nickel availability from soil to plants. Correlations between metal content in plants and extractable nickel in soils using different extractants showed that 0.1 M HCl is the best selective extraction method to estimate the plant-availability of nickel (Qian *et al*. 1996). Other studies have suggested that extraction with diethylenetriaminepentaacetic acid (DTPA) and 0.01 M $Sr(NO_3)_2$ can be used to estimate the available nickel concentration (Kukier & Chaney 2001). Menzies *et al.* (2007) analyzed results from the literature for the effectiveness of various extractants in predicting availability of metals to plants and concluded that neutral salt extractants (e.g., $CaCl_2$) provided the most reliable estimate of phytoavailability (compared to total concentration, acid extractant, and complexing reagents) for a variety of metals; however, for nickel only results for DTPA and $CaCl_2$ extraction were presented. A study of soils from inactive railway yards in Montréal found that plant uptake could not be predicted by any of the free, total dissolved or total soil concentrations (Ge *et al*. 2000).

Accumulation of nickel in plants is not only influenced by soil properties, accumulation is also dependent on the plant species (Appendix 7). The amount of nickel accumulation appears to be affected by xylem transport rates and the accumulation of organic acids in plants (Yang *et al*. 1997). Some plant species, termed hyperaccumulators, may contain more than 1000 mg Ni/kg (Greger 1999; Brooks 1980; Adriano 2001). Nickel hyperaccumulators with foliar nickel concentrations above 10000 mg/kg, and annual removal rates of 100-400 kg Ni/ha, may provide significant remediation over time. Environment Canada's PHYTOREM database identifies plants which have demonstrated the ability to tolerate, accumulate, or hyperaccumulate for a range of metals (EC 2003b). Nickel accumulation can also be affected by the life stage of the plant and varies between different parts of the plant; a study conducted using oats found that nickel concentrations increased during initial growth stages then subsequently decreased and that concentrations were higher in the grain than the straw (Poulik 1997).

Although some plant species can bioconcentrate nickel to higher levels than in the soil, most plants have bioconcentration factors of less than 1 (Torres & Johnson 2001a; 2001b; Gratton *et al*. 2000; Efroymson *et al*. 2004) (see Appendix 7 for soil-to-plant bioconcentration factors).

5.2.2 Toxicity

Although nickel is essential for plant growth (Aller *et al*. 1990; Brown *et al*. 1987a; 1987b; Salt *et al*. 2002; Dixon *et al*. 1975), relatively high concentrations of nickel can have adverse effects on plants. Appendix 3 summarises the toxicological effects of nickel on plants, listing studies that were used for guideline derivation and those consulted but not used in guideline derivation.

Several authors have reported that nickel can affect the iron status of plants (Adriano 2001; Khalid & Tinsley 1980). Toxicity may also be caused by nickel accumulating in cell cytoplasm and binding to cell components; nickel-tolerant plants are capable of flushing nickel from the cytoplasm to vacuoles (Salt *et al*. 2002). But most nickel tolerant plants actually exclude nickel by not absorbing nickel into the roots, or not translocating it to the shoots. Only a small fraction of nickel tolerant plants are accumulators or hyperaccumulators of nickel. General signs of nickel phytotoxicity are reduced growth of roots and shoots, poor branching, deformation of various plant parts, decreased yield, leaf spotting, abnormal flower shape, mitotic root tip disturbance, germination inhibition and chlorosis (McIlveen & Negusanti 1993; Rauser 1978). Effect levels are normally below 80 mg/kg dw of plant, but effects have been reported in tolerant plants containing up to 1000 mg/kg dw tissues (Kabata-Pendias & Pendias 1984; Cox & Hutchinson 1981; Brooks 1980). Symptoms of injury were observed for a variety of vegetables containing as little as 15 to 95 mg Ni/kg in plant tops (Frank *et al*. 1982). Generally, the degree of toxic effect on plants is a function of nickel concentrations in their tissues. For example, inhibition of photosynthesis and transpiration in sunflowers depends on the nickel concentration in leaves and the exposure period (Bazzaz *et al*. 1974).

Nickel toxicity to plants can be significantly affected by soil pH, with lower pH resulting in higher toxicity (Weng *et al*. 2004). This is believed to be primarily due to the higher bioavailability at lower pH. The use of limestone to raise the soil pH has been found to reduce nickel toxicity; the addition of hydrous ferric oxide has been found to be less effective and crop-specific (Kukier & Chaney 2001; Everhart *et al*. 2006). The opposite effect has been observed in toxicity tests using nutrient solutions instead of soils, with higher toxicity observed with increasing pH; this is believed to be because high pH increases binding to the soil (decreases toxicity), but also increases bioaccumulation (Weng *et al*. 2003); therefore, studies conducted using nutrient solutions, which lack soil binding processes, may not be representative of toxicity in soil. In studies investigating the relationship between soil properties (in 16-17 different soils) and nickel toxicity, soil pH has been observed to be the single best predictor of toxicity (Li *et al.* 2011), as well as cation exchange capacity (Rooney *et al.* 2007).

Some studies have shown that soil texture also affects nickel phytotoxicity; for example, clover was found to be more nickel-tolerant in fine soils than coarse soils (Elmosly & Abdel-Sabour 1997). Toxicity may also be affected by soil nutrients; for example, one study found that nickel was less toxic to sunflowers if both nitrate and ammonium were supplied than if only nitrate was supplied (Zornoza *et al*. 1999).

Studies on the effects of dissolved nickel on plants grown in nutrient or sand cultures indicated that effect levels are typically in the range of 2 to 15 mg Ni/L in solution (Whitby & Hutchinson

1974; Vesper & Weidensaul 1978; Vergnano & Hunter 1952; Davis *et al*. 1978). These concentrations in solution can correspond to critical levels of 4 to 26 mg Ni/kg dw in barley tissues (Davis *et al*. 1978). Nickel toxicity in terrestrial plants depends on the plant species: the radicle lengths of various plants grown in hydroponic solutions showed the following order of sensitivity to nickel: turnip > lettuce > cabbage > wheat = radish > millet (Carlson *et al*. 1991). A concentration of 2 mg/L reduced lettuce radicle lengths by 59%. A study of the effects of nickel on four different tree species resulted in similar effect levels. The authors reported retarded growth and development of trees grown in solution containing 2 mg/L (Heale & Ormrod 1982). However, results from plants grown on filter paper may not be relevant to properly assess the phytotoxicity of nickel in soil. Nickel-mediated effects of on radicle growth of selected woody species germinated on paper filters occur at concentrations ranging from 1 to 5 mg/L, 100 times lower than those in organic soils producing similar effects (Patterson & Olson 1982).

Tolerance to nickel in soils has been documented for a variety of plants that grow in ultramafic (serpentine) soils and mine waste (Verkleij 1990). Many of these species are tolerant by reduced nickel uptake. However, other plant species hyperaccumulate nickel (Baker & Brooks 1989) and avoid toxicity by sequestration of nickel ions as the citrate complex (Shier 1994). In some cases, the presence of these hyperaccumulating plants is a result of adaptation mechanisms allowing them to grow on highly contaminated soils.

As indicated above, various soil properties have shown an influence on nickel toxicity and in some cases these relationships have been described using statistical models where soil parameter(s) have demonstrated to be reliable predictors of toxicity. However, currently the soil protocol (CCME 2006) does not provide a method for incorporating known factors that influence toxicity in the derivation process for generic soil quality guidelines. Assessing the influence of soil properties on the risk of adverse effects to organisms should be evaluated using a ecological risk assessment. For guidance on developing site-specific remediation objectives incorporating toxicity-modifying environmental factors, please consult *A Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life 2007* (CCME 2007), and the Canadian water quality guideline for the protection of aquatic life for cadmium.

5.3 Terrestrial Invertebrates

5.3.1 Metabolic fate and behaviour

Many studies have indicated that uptake and accumulation of nickel by earthworms occurs in contaminated soils, but only to a limited extent (Gish & Christensen 1973; Ma 1982; Neuhauser *et al*. 1985). Generally, concentrations in the animal increase with increasing ambient soil concentration, but concentration factors were often found to be much lower than 1. A study of earthworms in 20 Dutch field soils found bioconcentration factors ranging from 0.07 to 1.2, with the nickel concentration in earthworms correlated with both the total soil concentration and the total pore water concentration (Janssen *et al*. 1997). Arthropods from a wetland with elevated nickel were found to have nickel concentrations approximately two orders of magnitude lower than the soil concentrations (Torres & Johnson 2001a). In a field study, Ma (1982) demonstrated that soil pH and CEC both affected nickel uptake in earthworms. Significant negative correlations were found between the concentration factor of heavy metals and these two soil properties. Reduction of pH and CEC led to increased desorption of metal cations and higher nickel concentrations in pore water. After a literature review of concentrations in earthworm,

isopod, and beetle species, and concentrations in soil, a soil-to-invertebrate BCF of 0.30 (range=0.06-2.4) has been estimated (Appendix 7).

Bioaccumulation in earthworms may be a considerable threat to those organisms feeding on earthworms (e.g., robins). Studies have shown that earthworms accumulate nickel from soil or litter (Pietz *et al*. 1984; Neuhauser *et al*. 1985; Ma 1982; Gish & Christensen 1973), but no studies have shown that birds have been poisoned by feeding on contaminated earthworms.

5.3.2 Toxicity

Nickel is considered to be essential to terrestrial invertebrates (Hopkin 1989), but the level of nickel required to maintain normal function is not known. However, relatively high concentrations in soils may result in toxicity symptoms for invertebrates. Appendix 4 summarises the collected toxicological studies available for terrestrial invertebrates, listing studies that were used for guideline derivation, and those consulted but not used in guideline derivation. The principal terrestrial invertebrate used to investigate nickel toxicity has been the earthworm since it is one of the largest and most easily obtained organisms of the soil biota. Effect levels ranged from 20 to 40 000 mg/kg for two earthworm species (*Eisenia foetida* and *Lumbricus rubellus*). An LC_{50} value of 243 mg Ni/kg soil was estimated for *Eisenia foetida* in an artificial soil (Neuhauser *et al.* 1985).

Using the same test (growth rate) and the same organism (*Eisenia foetida*), effects of nickel acetate, nickel carbonate, nickel chloride, nickel nitrate and nickel sulphate were reported to occur at concentrations ranging between 200 and 500 mg/kg while an effect level for nickel oxide, the least soluble, was as high as 40 000 mg/kg (Malecki *et al*. 1982). Using a contact test (filter paper), Neuhauser *et al*. (1985) found similar results indicating that each of the soluble nickel salts tested (acetate, chloride, nitrate and sulphate) was not significantly different from any of the others. This contrasts with nematodes, for which nickel chloride has been observed to be more toxic than nickel nitrate (Peredney & Williams 2000a).

The toxicity of soil nickel to earthworms also depends on the influence of soil factors determining the bioavailability of that metal to earthworms. Factors influencing bioaccumulation of nickel in the terrestrial biota are discussed in Section 4.4 below. Ma (1982) documented that concentration factors of heavy metals in earthworms were negatively correlated with the soil pH and cation exchange capacity (CEC).

5.4 Vertebrates, Birds and Other Wildlife

5.4.1 Toxicokinetics

Mammals and birds are capable of accumulating nickel, and dietary exposure is probably the most important route under most circumstances. Upon ingestion, the absorption of nickel is influenced by many factors including solubility of the nickel compound, dose, age and diet. Absorption often results in relatively low bioaccumulation factors (BAF = [nickel] in bird or mammal tissues/[nickel] in diet). Studies in rats, dogs and mice indicate that only 1 to 10% of orally-administered nickel (Ni, $NiCl_2$ and $NiSO_4$) is absorbed by the gastrointestinal tract from diet or drinking water (Ho & Furst 1973; Schroeder *et al*. 1974; Ambrose *et al*. 1976). The low potential for bioaccumulation of nickel by avian species has been confirmed by results of monitoring programs conducted in the field. For example, a field study showed reduced

accumulation of nickel in terrestrial wild birds and noted concentrations in body tissues of ruffed grouse (*Bonasa umbellus*) living near Sudbury, ON were 10 times lower than those in dietary items of grouse collected in contaminated areas (Rose & Parker 1983).

Numerous studies on rats (Whanger 1973), ducks (Cain & Pafford 1981), livestock (O'Dell *et al.* 1971; Spears *et al.* 1986), and wild mammals and birds (Rose & Parker 1983; Outridge & Scheuhammer 1993) have indicated that after nickel is absorbed and distributed in the body, it accumulates to a high extent in the kidney of animals and birds. However, no accumulation of nickel in any tissues was observed in rats exposed to 5 mg/L in drinking water (Schroeder *et al*. 1974).

Animals have a high capability to eliminate absorbed nickel. The majority of nickel that is absorbed by animals is eliminated in urine (Angerer & Lehnert 1990; Elias *et al.*1989; Ghezzi *et al.* 1989; Hassler *et al.* 1983; Torjussen & Andersen 1979). Faeces appear to be the most important routes of elimination for unabsorbed nickel, such as nickel oxide and nickel subsulphide (ATSDR 2005). Tedeschi and Sunderman (1957) noted that dogs excreted 90% of ingested nickel in faeces and 10% in urine.

Biomagnification of bioaccumulated chemicals occurs when the concentration of the chemical increases as the chemical passes up through two or more trophic levels, resulting in an efficient transfer of chemicals from food to consumer (CCREM 1987). No avian or mammalian species are known to biomagnify nickel in the environment. Studies comparing nickel concentrations in wildlife and their food reported that concentrations were either similar in different trophic levels or even declined with increasing trophic level (Beyer & Miller 1990; Scanlon 1987). Similarly, nickel concentrations measured in mouse carcasses from a wetland were less than the detection limit of 0.6 mg/kg, despite higher nickel concentrations being measured in food sources (Torres & Johnson 2001a); concentrations were also much lower than those predicted using published bioaccumulation models (Torres & Johnson 2001b).

Further information on the biomagnification of nickel, as well as exposure of biota to nickel and nickel toxicokinetics, aas elimination rates, ingestion and exposure of nickel to biota are required to more accurately model the behaviour of nickel through food webs. However, the low concentration factors strongly indicate that biomagnification does not present a problem for nickel in the lower food chain.

5.4.2 Toxicity

Avian toxicity studies selected for use in soil quality guidelines derivation are presented in Appendix 6. Only a few studies on the toxicity of nickel to livestock and no studies with wildlife, except rats, mice and mallards, were available. The results of controlled acute toxicity studies have demonstrated that nickel is moderately toxic to mammals and birds. The toxic level of nickel for these terrestrial vertebrates is highly variable. Doses associated with harmful effects in laboratory animals, livestock and mallards ranged from 500 to 2500 mg/kg (administered in food) (see Appendices 5 and 6).

According to studies of Ambrose *et al.* (1976) and Weber and Reid (1969), female mammals appeared to be less sensitive to nickel than males. Doses with observed effects on growth of rats (Wistar) were 125 and 50 mg Ni/kg bw per day for females and males, respectively (Ambrose *et*

al. 1976). Similarly, Weber and Reid (1969) who studied growth and feed uptake in mice (Webster) reported higher effect levels for females than those for males.

Several authors have investigated the effects of nickel on reproduction and development in terrestrial mammals (Appendix 5). Changes to sperm quality in laboratory animals have been reported (ATSDR 2005). Generally, the reproduction performance is only slightly affected by oral nickel exposure. Ambrose *et al.* (1976) studied three generations of rats and did not observe any adverse effects on fertility, gestation, viability and lactation in rats exposed to diets containing 1000 mg Ni/kg. Studies on the effects of nickel on growth of several mammals indicated highly toxic levels. For example, effects on growth were observed in mice exposed to a daily dose of 1600 mg Ni/kg body weight (Weber and Reid 1969). Growth rate of rats and dogs significantly decreased at similar nickel concentrations (1000 to 2500 mg/kg) in the diet (Ambrose *et al.* 1976).

According to the available toxicity data, terrestrial birds appear to be less sensitive to nickel than terrestrial mammals. Adult mallards (*Anas platyrhynchos*) ingesting diets containing 800 mg Ni/kg bw for 90 days exhibited no observable effects on the following endpoints: body weight, histological changes in liver and kidney and changes in blood chemistry (Eastin Jr. & O'Shea 1981). Even reproductive endpoints (egg laying, hatchability and hatchling survival) were unaffected at such nickel levels in the diet. However, newly-hatched mallard ducklings were more sensitive to nickel and presented symptoms when exposed to diet levels of 1200 mg Ni/kg (Cain & Pafford 1981). Newly hatched chickens (*Gallinus domesticus*) had significantly slower growth rates when maintained on diets containing 300 mg Ni/kg (Ling & Leach 1979). The form of ingested nickel was reported to be independent of effect levels. Decreased growth rates in chicks fed diets containing nickel have been reported, but no significant difference between the two forms (sulphate and acetate) of ingested nickel were noted (Weber & Reid 1968). Nickel and its inorganic compounds do not appear to be carcinogenic to animals when orally administered, but the data are still uncertain because of the limited number of studies. In chronic oral studies (e.g., Schroeder & Mitchener 1975), absorption of nickel acetate dissolved in drinking water at 5 mg/L did not result in increased tumour incidences throughout the lifetime of mice. Similar results were observed with rats fed nickel sulphate at 2500 mg Ni/kg diet for 2 years (Ambrose *et al.* 1976). On the other hand, many studies have tested nickel for carcinogenicity in animals by injection (Sunderman & Horak 1981). For example, Sunderman (1984) reported nickel carcinogenic activity and found metastases in rats receiving a single injection of 14 mg Ni per rat.

Limited information exists on the effects of nickel on mammalian immune systems. Dieter *et al.* (1988) studied immunologic responses in mice exposed to nickel sulphate in drinking water. The authors noted several immune function responses such as changes in spleen cellularity and natural killer cell (NK) activity. However, nickel concentrations in the drinking water were very high (1 to 10 g/L) and probably not comparable to assess standard contaminated environments.

6 BEHAVIOUR AND EFFECTS IN HUMANS AND EXPERIMENTAL ANIMALS

The toxicological review of nickel is focused on $NiSO_4$, $NiCl_2$, NiO and Ni_3S_2, which are the predominant forms of nickel in the environment and in contaminated soils. Nickel carbonyl ($Ni(CO)_4$), for which exposure is primarily occupational, will be addressed only briefly.

6.1 Overview

The mammalian toxicology of nickel has been recently reviewed by various health agencies that include the Agency for Toxic Substances and Disease Registry (ATSDR 2005), the US Environmental Protection Agency (US EPA 1996), the Institute of Medicine (IOM 2001), the Office of Environmental Health Hazard Assessment (OEHHA 2012), the Texas Commission on Environmental Quality (TCEQ 2011), the International Agency for Research on Cancer (IARC 2011), and the World Health Organization (2007). In addition, Health Canada (1996) completed a human health based toxicological review of the various species of nickel.

It is not the role or the intent of this document to comprehensively re-evaluate the mammalian toxicology of nickel. Such reviews have been carried out by agencies responsible for protecting human health in Canada and other jurisdictions, as noted above. Accordingly, the sections below briefly describe the key studies that have been completed on nickel and that have been used for the development of toxicological reference values (TRVs) for nickel, and present recommendations for the TRVs that are most appropriate for the development of SQGs.

6.2 Classification

Both cancer and non-cancer endpoints are significant in the toxicological evaluation of nickel. Health Canada (1996) classifies oxidic, sulphidic and soluble nickel as Group I carcinogens (carcinogenic to humans) via inhalation. This classification is specific to these forms of nickel via the inhalation route. US EPA (1996) classifies nickel refinery dust (most of which is considered to be nickel subsulphide) as a Class A carcinogen (carcinogenic to humans) based on human data where lung and nasal tumours were elevated in workers exposed to nickel refinery dust and on animal data in which carcinomas were produced in rats by inhalation and injection (e.g., Sunderman 1984; Sunderman & Horak 1981).

Considering the relevant environmental exposure pathways, the relative toxicities of different salts, and the toxicological data available, it was determined that the toxicological reference values (TRVs) for nickel should be based on nickel sulphate (for oral exposures) and nickel sulphate/oxide (for inhalation exposures). In development of TRVs for the inhalation route, it was found that the non-cancer endpoint for inhalation of nickel sulphate/oxide was not necessarily protective of cancer risks. Consequently, the SQG have been developed for protection of both non-cancer and cancer endpoints (section 6.9).

6.3 Bioaccessibility of nickel

The selection of an appropriate estimate of nickel bioaccessibility in soil and dust is complicated by the variety of *in vitro* methods used (Saikat *et al*. 2007), none of which are able to fully mimic *in vivo* processes. Particle size fractionation and nickel speciation may also affect results.

The choice of the solvent phase used to assess nickel bioaccessibility may influence the results significantly. In physiologically based extraction test (PBET) assays using soils from Torino,

Italy, more nickel was extracted in the second phase, likely due to the high affinity of nickel for the glycine in the extraction solution, and suggesting the intestine may play a significant role in nickel solubilisation (Poggio *et al*. 2009). However this effect does not appear to be consistent for all PBET assays. When testing pure nickel compounds, Ni^{2+} release in synthetic gastric juice was much greater than in synthetic intestinal fluid, even for water-soluble substances (Henderson *et al*. 2012). In dust samples from seven English homes, the mean (±SD) nickel bioaccessibility in the gastric phase of the PBET was ≈18±15%, and ≈15±10% in the intestinal phase (Turner & Ip 2007). More nickel was dissolved in simulated lung fluid soil in 1 hr than in two weak leach (salt) solutions in 3 hr. The authors speculated that the organic components (amino acids in the simulated lung fluid) act as weak chelating agents, dissolving compounds otherwise insoluble in aqueous solutions (Drysdale *et al*. 2011). However, studies assessing dissolution of commercially available powdered nickel compounds in various solutions concluded deionised water produces more representative results than synthetic lung fluids (containing citrate and acetate, but no amino acids) (Oller *et al*. 2009).

The dominant nickel species present in the soil may also modify bioaccessibility. In studies using pure nickel compounds, water-soluble forms of nickel ($NiSO_4$, $NiCl_2$, $Ni(CH_3COO)_2$, $Ni(SO_3N_2)_2$ and NiF_2) and nickel hydroxycarbonate were all nearly completely dissolved in simulated gastric fluid (0.07 N HCl) within 2 hr. In contrast, Ni^{2+} released from the water soluble substances in intestinal fluid (neutral pH, without glycine or amino acids) ranged from 29-78% after 72 hr, and nickel hydroxycarbonate released only 1.35% of available nickel. The gastric bioaccessibility of sparingly- or insoluble (green or black) oxidic and sulfidic nickel compounds did not exceed 30% of available nickel within the first few hours and. The most refractory of these materials, green NiO, released essentially no available nickel. No appreciable nickel release was measured in neutral intestinal fluid (all <1%) (Henderson *et al*. 2012).

Soil particle size fractionation may also affect bioaccessibility. Several studies indicate that bioaccessibility is higher in the smaller soil size fractions (<2µm) than the larger size fractions (15-53% *vs*. 8-14% (Drysdale *et al*. 2011); 58% *vs*. 43% (Rasmussen 2004; 2008)). In a Spanish study of urban soils from Torino and Sevilla, nickel bioaccessibility (Simple Bioacessibility Extraction Test; SBET) for whole soils ranged from 8 to 14%, but was highest (15-53%) in the <2 µm fraction. Sevilla soils, in contrast, had lower bioaccessibility (18-58%) in the <2 µm fraction than in whole soil (34-86%), and the 2-10 µm fraction had the highest values (46-83%) (Madrid *et al*. 2008).

The US Geological Survey and the Geological Survey of Canada sampled soils at approximately 40 km intervals along north-south and east-west transects across the two countries to examine variations in bioaccessibility of various metals in unpolluted soils. Two size fractions (<2 mm and <250 mm) were extracted and analysed using a low pH *in vitro* PBET test to simulate the gastric phase of digestion. No difference was observed in bioaccessibility values for nickel between the two size fractions. The observed range for the <2 mm fraction is 3-30.6% (median 15%) and that of the <250 mm size fraction is 3.6-34.1% (median 14%) (Moman *et al*. 2009).

Organic matter content of the soil/dust, might have played a role in some bioaccessibility studies, but testing has proved inconclusive, appearing to explain approximately 65% of variability in nickel bioaccessibility in Canadian house dust (Rasmussen 2004; Rasmussen *et al*. 2008), while a similar study of house dust from UK homes found no clear correlations between organic carbon content of the dust samples and nickel bioaccessibility (Turner & Simmonds 2006). In an

Italian study assessing nickel bioaccessibilty of soils in the Torino region, significant differences were noted for soils from agricultural *vs.* residential sites in the PBET assay (phase 1 mean ± SD: 4 ± 0.2 *vs.* 16 ± 2, and phase 2; 8 ± 0.4 *vs.* 27 ± 6.7, respectively) (Poggio *et al*. 2009). In urban samples from the Torino area, a higher proportion of the soil metal content was found in bioaccessible forms at roadsides than in parks (Sialelli *et al*. 2011).

The duration and route of exposure of bioaccessibility assays must also be considered. Many studies assess bioaccessibility over a 24-48 hr period; however, retention of nickel particles in the nose and lung may be much longer (Torjussen & Andersen 1979). One hour to seven day incubation of soil samples initially subjected to a water/salt extraction (weak leach) in simulated lung fluid resulted in 0.5-1% nickel bioaccessibility after 1 hr, rising to 1-2% after 1 day and 1.5-3% after 1 week, with no peak (Drysdale *et al*. 2011).

In vivo relative oral bioavailability of nickel from three soil types from Port Colborne, ON was determined through oral administration to Sprague-Dawley rats (Ollson *et al*. 2003; Koch *et al*. 2005). *In vitro* bioaccessibility ranged from 4.8-18%. The relative bioavailability of nickel from soils was 3.9% for Welland clay, 3.2% for organic soil and 2.1% for fill. A bioaccessibility study (*in vitro* simulated gastric or gastrointestinal digestion) using two naturally weathered surface soils from nickel-impacted areas indicated that average bioaccessibility was 3.59% in the <70 µm size fraction of sandy soil from Sudbury, ON *vs*. 18.7% in the 150-250 µm fraction (soil concentration≈200 mg/kg) (Vasiluk *et al*. 2011). There was little difference in bioaccessibility in the two size fractions analysed from heavy clay soil Port Colborne, ON (11%; soil concentration≈2000 mg/kg). The bioaccessiblity results for the larger size fraction from Sudbury were comparable to OMOE (mean 16.5%; range 11.8-23.3%) and external laboratory (means 14 and 18%; ranges 7.6-28%) (Birmingham & McLaughlin 2006) measurements; however another study reported 44% bioaccessibility (SARA 2008). Co-incubation of the PBET-solubilised soil with Caco-2 cells resulted in ≈7-fold lower estimates of oral bioaccessibility than the PBET alone for <70 µm Sudbury soil and almost negligible bioaccessiblity for both Port Colborne soil fractions. Comparison of absolute and relative absorption after gavage-administration of soils *vs.* $NiSO_4 \cdot 6H_2O$ in rats indicated 0% nickel absorption from the <70 µm fractions, ≈12% (31% RBA) and 22% (56% RBA) from the 150-250 µm fractions and approximately 39% of $NiSO_4 \cdot 6H_2O$ were absorbed within 24 hr, as estimated by fecal excretion (Vasiluk *et al*. 2011). See section 8.3: Nickel Speciation in the Environment.

6.4 Toxicokinetics

6.4.1 Cellular uptake at primary sites of absorption

According to the "Nickel-Ion (Bioavailability) Hypothesis" (Costa *et al*. 1981; Goodman *et al*. 2011b; Hansen & Stern 1983), the Ni^{2+} ion is the active agent in nickel toxicity, mutagenesis and carcinogenesis, and the intracellular nickel concentration is a major determinant of toxicity, regardless of the nickel compound or the cell uptake mechanism.

Lipid-soluble $Ni(CO)_4$ likely enters cells rapidly due to simple diffusion, and thus has pronounced cytotoxic and carcinogenic effects.

Soluble nickel may be dissolved in extracellular fluids, fluids lining the gastrointestinal (GI) and respiratory tracts and in sweat. Some extracellular Ni^{2+} may be transferred to the cytosol via ion channels, but uptake is thought to occur more readily after binding to small, diffusible proteins

and low-molecular-weight ligands (histidine, albumin and other cation carriers) to form lipophilic complexes (Menon & Nieboer 1986; Nieboer *et al*. 1984; Weinzierl & Webb 1972). Alveolar macrophages, alveolar Type I cells and renal cells may take up dissolved Ni^{2+} via fluid pinocytosis and exocytosis which maintains stable cell volume and osmolarity (Steinman *et al*. 1983; Grant & Donaldson 2009). Exocytosis possibly explains the rapid loss of soluble nickel taken into the cell (Edwards *et al*. 1998; Ke *et al*. 2007). Alternately, at high concentrations, dissolved metals may precipitate in the lysosomal compartment, due to acid phosphatase-mediated reactions. Precipitation may serve as a protective mechanism for the organism: if formed within airway macrophages, they may be removed by mucuciliary activity; when trapped within airway epithelial cells, they may be unable to cross into the circulation; when formed in renal cells, they may be excreted in urine (Galle *et al*. 1992; Berry *et al*. 1993; 1988; 1997).

Particles containing moderately-soluble nickel (e.g., Ni_3S_2) may also release some Ni^{2+} into solution prior to uptake, (the mechanisms of dissolution of poorly soluble nickel are not completely understood) (cited in Costa *et al*. 1981 and Fletcher *et al.* 1994). In primary cultures of guinea pig alveolar macrophages, two different pathways for Ni_3S_2 uptake were observed: (i) phagocytosis of α-Ni_3S_2 crystals and subsequent degradation to minute particles, which were recovered bound to the membranes of phagocytic vacuoles and lysosomal membranes, and (ii) extracellular degradation to regular round particles (0.1-0.2 μm diam) and irregular minute particles (10-30 nm diam). The round particles entered the cell by pinocytosis, while the minute particles were bound preferentially to cell membranes and cytoplasmic organelles, liposomes and the euchromatinic part of nuclei (Shirali *et al*. 1991).

Inhaled particles of poorly-soluble nickel (e.g., NiO) may be taken up by active phagocytosis or non-specific pinocytosis. They are then thought to undergo dissolution (likely after fusion with acidic secondary lysosomes) to release high concentrations of Ni^{2+} ions into the cytosol or other cellular compartments (Steinman *et al*. 1983; Grant & Donaldson 2009), which may include the nucleus. Some Ni^{2+} from poorly soluble nickel particles may be released extracellularly, depending on the composition of biological fluids: Ni^{2+} released by both green and black NiO particles in an aqueous solution containing amino acids was much greater than for NiO particles in water. The solubility of poorly soluble nickel particles also increases as particle size is reduced: ultrafine NiO (20-100 nm) particles showed up to150-fold higher solubility than fine NiO (1-2 μm) particles (Horie *et al*. 2009).

Pino-/phagocytosis is therefore greatly influenced by aqueous solubility as a function of the form of nickel, particle size and the physical properties of the nickel-containing particles. Crystalline particles are taken up much more readily than amorphous forms. Negative surface charge appears to favour greater uptake. Particles >5 um diam are generally not endocytosed, especially by epithelial cells. The general trend for endo-/phagocytosis of nickel particles of similar size therefore appears to be: water-soluble Ni < metallic Ni < amorphous NiS < [NiO < nickel-copper oxides] < crystalline NiS < crystalline Ni_3S_2 (Goodman *et al*. 2011).

6.4.2 Absorption and bioavailability of nickel

6.4.2.1 Absorption and bioavailability of ingested nickel:

The rate of absorption of ingested nickel is generally dependent upon its aqueous solubility (Ishimatsu *et al*. 1995). The reported bioavailability of soluble nickel in human oral challenge studies has ranged from 1 to 40%, with significant inter-individual differences noted. In fasted

subjects, bioavailability ranged from 28.7-40.1% (mean=33.1%) for physiologically-relevant doses of ^{62}NiO or ^{62}Ni metal (Patriarca *et al*. 1997) and from 12 to 32% for large doses of soluble $NiSO_4$ or $NiCl_2$ (Cronin *et al*. 1980; Nielsen *et al*. 1999; Sunderman Jr *et al*. 1989) and from 0.7 to 5.7% when administered with food (Sunderman Jr *et al*. 1989; Nielsen *et al*. 1999; Menne *et al*. 1978; Gawkrodger *et al*. 1986; Christensen & Lagesson 1981).

While co-administration of food appears to limit the uptake of nickel (Sunderman Jr *et al*. 1989; Solomons *et al*. 1982), ≈1% of nickel in food is absorbed (Horak & Sunderman Jr 1973). There is currently no quantitative information regarding the absorption of insoluble nickel compounds after ingestion or the human bioavailability of nickel in soil.

The estimated absorbed fraction of various nickel compounds to rats increased with solubility: 0.01-0.09% for insoluble Ni metal and NiOs; 0.5-2.1% for slightly soluble Ni_3S_2 and NiS and 9.8, 11.1 and 33.8% for soluble $NiCl_2$, $NiSO_4$ and $Ni(NO_3)_2$, respectively (Ishimatsu *et al*. 1995). Other studies found slightly lower values for $NiCl_2$ (1.7-10%) (Nielsen *et al*. 1993) or 3-6% for ^{63}Ni (Ho & Furst 1973). The relative oral bioavailability of $NiCl_2$ in an aqueous slurry with sandy loam soil was 63.1%, but was only 33.5% for a clay loam soil slurry (Griffin *et al*. 1990). Hack *et al*., (2002) compared the *in vitro* bioaccessiblity of contaminants from German soils with the *in vivo* bioavailability of these contamniants in young minipigs. The in vivo bioavailability of nickel in seven contaminated soils following oral dosing to young minipigs was low (0.14-2.2%). The bioaccesssibility of soil nickel from 22 conatminated soils added to milk powder was 8-54%. The relative oral bioavailability of soil nickel ranged from 2-36%. See section 8.4 for more on relative absorption factors.

6.4.2.2 Absorption and bioavailability of inhaled nickel

The fate of inhaled nickel particles depends upon their size and solubility (cited in Goodman *et al*. 2011; Hack *et al*. 2007; Hsieh 1999; Oller 2002). Following inhalation exposure of rats to green ^{63}NiO or $^{63}Ni_3S_2$ aerosols, the fractional deposition patterns showed ≈60-65% deposition in the upper respiratory tract and 35-40% in the lower respiratory tract (Benson *et al*. 1994).

Poorly-soluble nickel (e.g., NiO) particles have limited systemic absorption, and are largely cleared from the lung by mucociliary activity and airway/alveolar macrophage phagocytosis, and then swallowed and excreted, unabsorbed, in feces (Benson *et al.* 1994; English *et al.* 1981). Pinocytosis of nickel particles may also occur in nasal and pulmonary epithelial cells with retention within the interstitium or transport to lymph nodes. Finer particles may be more readily absorbed than larger particles. Urinary elimination data from one subject working with finer NiO particles had much greater systemic absorption than 19 co-workers exposed to larger particles (Roels *et al*. 1993).

Inhaled moderately-soluble nickel particles (e.g., Ni_3S_2) are partially cleared by mucociliary activity and phagocytosis, and may be taken up into the epithelium. Moderately-soluble particles may also be dissolved in the respiratory tract lining with epithelial uptake of the resulting Ni^{2+} ions by pinocytosis or ion channels. Systemic absorption of some of this nickel is indicated by both urinary and fecal elimination in laboratory animals *in vivo* (Valentine & Fisher 1984).

Particles containing soluble nickel are likely fully or partially dissolved in the fluid lining the respiratory tract. Some of the resulting ionic or complexed nickel may be removed by mucociliary clearance, but urinary elimination of the bulk of inhaled soluble nickel in laboratory

animals indicates that most is absorbed systemically (Benson *et al*. 1995). See section 8.4 for information on relative absorption factors for nickel.

6.4.2.3 Dermal absorption and bioavailability of nickel

The interpretation of dermal permeation or absorption estimates for nickel is complicated by the variety of approaches taken by individual investigators, e.g., with respect to diffusion cell design, vehicle, nickel species, skin thickness, age of the donor or subject, anatomical site, open application or occlusion, human *vs* animal, or data acquired *in vivo vs. in vitro*.

6.4.2.3.1 Nickel uptake *in vitro*

In formalin-fixed sections of human skin soaked in $NiSO_4$, Ni^{2+} binding was most evident in the stratum corneum (SC), especially within the deeper layers, sweat ducts and hair follicles; with a particular affinity for keratin (Wells 1956). Nickel was also preferentially taken up from the cell culture medium by mouse (Lacy *et al*. 1996) and human keratinocyte (Ermolli *et al*. 2001) cell lines.

In studies of $NiSO_4 \cdot 6H_2O$ or $NiCl_2 \cdot 6H_2O$, full-thickness human skin samples were mounted in diffusion cells for 144-239 hr. Permeation was slow, with a lag time of ≈50 hr (Fullerton *et al*. 1986) or 70-98 hr (cited in Hostýnek 2003) before nickel appeared in the recipient chamber.

After 144 hr without occlusion, Fullerton *et al*. (1986) observed only 0.23% recovery of the applied dose of $NiCl_2$ and ≈3.5% with occlusion in breast skin samples. Follow-up tape stripping experiments showed 50% of the unoccluded dose was found in the SC after 96 hr, 10.6% in the viable epidermis, 1.6% in the dermis and only 0.4% found in the recipient chamber. Application of higher nickel concentrations increased the rate of transfer to the recipient solution (Fullerton *et al*. 1988). When the permeation of $NiCl_2$ and $NiSO_4$ were compared in two additional breast skin samples and a leg skin sample under occluded conditions, Ni^{2+} from $NiCl_2$ permeated the skin ≈4- to 50-fold more rapidly (≈4.5-15% after ≈150 hr, with the lower value obtained for the leg skin sample) than $NiSO_4$ (<0.5% of the applied dose) (Fullerton *et al*. 1986).

There is limited information regarding dermal permeation of nickel in soil *in vitro*. In pig skin samples, total permeation of $^{63}NiCl_2$ (in ethanol) alone was 57.9% after 16 hr, with 57.6% retained in the skin and 0.4% in the receptor solution. The effects of a soil matrix were assessed using two different soils (one with a three-fold greater organic matter content than the other; pHs of 4.2 and 5), as was the influence of weathering (3 months) of the soil-nickel mixtures (Abdel-Rahman *et al*. 2010, Abdel-Rahman & Turkall 2011). Permeation was reduced to a similar extent for freshly $^{63}NiCl_2$-spiked samples of either soil type (to 11.5 or 12.4% of the available dose), and was further reduced after aging of the soil-nickel mixtures (to 2.8 or 1.8% of the available dose) (Turkall *et al*. 2008).

In a 24-hr dermal permeation study of $^{63}NiCl_2$ with and without a soil matrix in viable human breast skin $^{63}NiCl_2$ (in acetone) or an aqueous slurry of soil and nickel (soil load of 5 mg/cm^2; soil pH 4.5) were added to occluded diffusion cells, and the recipient chamber solution was collected at 6-hr intervals for 24 hr. Dermal permeation was 22.8% (20.9% in the skin depot and 1.8% in the recipient chamber) in the absence of soil and only 1.0% with soil (Moody *et al*. 2009). In this study, the authors estimated that hand exposure to nickel-contaminated soil (assuming 840 cm^2 surface area, total adhesion of the 5 mg/cm^2 of the soil load and equivalent skin retention and permeation) would result in an uptake rate of 0.4 ng Ni/cm^2/hr or 0.3 µg Ni/hr

x 8 hr work day, yielding a total systemic exposure of 2.4 µg/day. Barring saturation, absorption was predicted to increase linearly with soil nickel concentration and surface area exposed.

Both Moody *et al.* (2009) and Turkall *et al.* (2008) obtained greater permeation of $^{63}NiCl_2$ without soil. Disruption of the skin barrier by acetone or ethanol vehicles may also have increased permeation without soil, giving the appearance of a much greater retarding effect of soil. Dermal permeation of soluble nickel is increased by solvents (Sharata & Burnette 1988; Turkall *et al*. 2003), which induce ultrastructural changes in the skin as early as 5 min after application, possibly creating a more porous intracellular structure and alteration of diffusion pathways (Sharata & Burnette 1988).

While the above *in vitro* data indicate slow dermal permeation, nickel contact allergy is frequent, indicating facile skin penetration and/or nickel accumulation on repeated exposure. A significant limitation of *in vitro* assays is lack of blood flow, which can remove absorbed nickel and maintain the diffusion gradient (Hostýnek 2003); dissolution of soil nickel in sweat and other skin exudates may also increase nickel dermal uptake through "shunt" pathways (transappendageal diffusion *via* hair follicles, sweat and sebaceous glands) *in vivo* (Hostýnek *et al*. 2002; Emmett *et al*. 1988). See section 8.4 for relative absorption factors.

6.4.2.3.2 Dermal absorption of nickel *in vivo*

After application of $^{57}NiSO_4$ to forearm or leg sites (occluded), detectable radioactivity declined by 61% after 41 hr, indicating penetration and/or systemic uptake. The most rapid reductions occurred in the early hours of the experiment (Norgaard 1955).

Analysis of sequential tape strippings after the application of $NiCl_2$, $NiSO_4$, $Ni(NO_3)_2$ or $Ni(CH_3COO)_2$ solutions (in methanol) to arm and back skin of human volunteers showed the arm SC was ≈2-fold more permeable to nickel than back SC. During the first 24 hr, most of the nickel salts remained at the skin surface or in the outer layers. Similar to *in vivo* studies, the ratio of nickel concentrations in the outer SC to those in the inner SC was directly proportional to the size of the counter ion (i.e., $Ni(CH_3COO)_2$ > $Ni(NO_3)_2$ > $NiSO_4$ > $NiCl_2$) (Fullerton *et al*. 1986). Only $Ni(NO_3)_2$ penetrated the SC to a significant degree. These findings are suggestive of ion pairing in the diffusion of Ni^{2+} through the SC, which likely involves transcellular pathways for most nickel compounds. More lipophilic forms, such as $Ni(NO_3)_2$, may also penetrate skin *via* intercellular and "shunt" transport (Hostýnek *et al*. 2001a).

When metallic nickel dust was applied to the forearm of three volunteers under an occlusive dressing, nickel was present in the outer SC after 5 min, and in the epidermis after ≤96 hr exposures. The authors concluded the nickel metal was oxidised to soluble compounds able to penetrate the SC (Hostýnek 2003), presumably by the intercellular route (Hostýnek *et al*. 2001b).

When allergic subjects immersed a finger for 10 min daily into 10 mg Ni/L (as $NiCl_2$) solutions in water for one week, and into 100 mg Ni/L solutions for a second week, local uptake occurred, as indicated by increased local vesicle formation and blood flow (Nielsen *et al*. 1999).

Systemic absorption of nickel ($NiSO_4$ or $NiCl_2$) has been demonstrated in laboratory animals within 24 hr of application (Norgaard 1957; Lloyd 1980; Lacy *et al*. 1996); however chemical depilatories and/or alcohol-based vehicles may have enhanced nickel absorption. Significant amounts of nickel remained at the site of application 48 hr after application (Lacy *et al*. 1996).

6.4.3 Distribution

Once solubilised, nickel is readily distributed throughout the body (Li *et al*. 2008), but the resulting tissue concentrations may be influenced by the chemical form, route of exposure and the time since exposure. While renal nickel concentrations may initially be greater than other tissues, nickel clearance from the kidney is more rapid than for lung, liver or adrenal glands (Oskarsson & Tjalve 1979a; Wase *et al*. 1954; Nielsen *et al*. 1993; Clary 1975).

Most blood nickel is found in red blood cells (Barashkov *et al.* 2003; Templeton *et al*. 1994). Plasma nickel is bound to histidine, albumin and an α2-macroglobulin (Sunderman Jr *et al.* 1972; Nomoto *et al*. 1971; 1973; Lucassen & Sarkar 1979). The target of nickel binding in tissues is not known: it is a weak metallothionein (MT) inducer (Kurowska & Bal 2010; Fleet *et al*. 1990).

Mean nickel concentrations in autopsy tissue samples were greatest in the lung, followed by the thyroid, adrenal tissues, kidney, heart, liver, brain, spleen and pancreas; hilar lymph nodes, spinal cord/pituitary, testes and ovary (Rezuke *et al.* 1987). Elevated ovarian nickel was also noted in a Norwegian study (Rahil-Khazen *et al.* 2002). Pulmonary and renal accumulation was also noted in the general public (data from Zober *et al*. (1984); Sunderman *et al*. (1971); Seemann *et al*. (1985); Chen *et al.* (1977) as compiled by Rezuke *et a*l. (1987)). Bone had higher nickel concentrations than lungs (Bocio *et al.* 2005). Tissue (especially lung) concentrations increase with increased air or water concentrations and with age (Bocio *et al*. 2005; Kollmeier *et al*. 1990). Lungs from males in the industrialised Ruhr region had two-fold greater nickel concentrations than those from females (Kollmeier et al. 1990).

Selective respiratory tract retention has been demonstrated in occupationally-exposed workers. Pulmonary nickel concentrations were 112- to 5800-fold higher in refinery workers and ≈500-fold higher in stainless steel welders than in controls (Raithel *et al.* 1993; Raithel *et al*. 1988). Pulmonary nickel concentrations averaged 330±380 μg/g (dry weight) in workers exposed to less-soluble nickel compounds, 34±48 μg/g in workers exposed to soluble nickel compounds and 0.76±0.39 μg/g in controls (Andersen & Svenes 1989). Nasal tissues of exposed workers, especially to Ni_3S_2 and NiO dusts, also retain inhaled nickel for long periods ($T_{1/2}$ = 3.5 yr) (Torjussen & Andersen 1979).

Single or repeated inhalation/IT exposures to NiO particles in rats (Kodama *et al*. 1993; English *et al.* 1981), showed minimal extra-respiratory tract distribution and greater pulmonary retention than for Ni_3S_2 (Benson *et al*. 1994) or $NiCl_2$ (Carvalho & Ziemer 1982; Clary 1975), the nickel from which was detected in blood and tissues within hours of exposure (Benson *et al*. 1994).

Dermal nickel accumulation was evident in mice administered $^{63}NiCl_2$ IV (Oskarsson & Tjalve 1979b) and was greater in iron-deficient rats administered $^{63}NiCl_2$ by gavage or IP injection than in iron-sufficient animals (Tallkvist & Tjälve 1997). When female subjects were administered a single 12 μg/kg bw dose of $^{61}NiSO_4$ in drinking water after fasting overnight, dermal intercellular nickel concentrations (collected by the suction-blister technique) (Benfeldt *et al.* 1999) increased ≈8-fold in the first few hours after administration (Benfeldt *et al*. 1999).

Nickel uptake in the olfactory epithelium, with migration to the olfactory bulb and related areas in the brain was noted in rats after intranasal instillation of $^{63}NiCl_2$ (Henriksson *et al*. 1997; Tallkvist *et al.* 1998), and a dog exposed to urban pollution (Calderón-Garcidueñas *et al*. 2003).

Oral administration of $NiCl_2$ in rats resulted in tissue and serum nickel concentrations proportional to intake; with the highest concentrations in the kidney, lung and serum, testes and ovaries (100-1200 mg Ni/L; 3 or 6 mths in drinking water (Cempel & Janicka 2002; Severa *et al*. 1995)); however, no nickel accumulation was evident in liver, heart, lung, kidney or spleen at lower doses (5 mg/L in drinking water; lifetime exposure (Schroeder *et al*. 1974)). After gavage administration of eight nickel compounds, nickel concentrations were higher in rat tissue after exposure to soluble nickel, and were very low after exposure to sparingly-soluble nickel compounds (Ishimatsu *et al*. 1995). After gavage administration of $NiCl_2$, mice stomach, intestines, kidneys, carcass, lungs, testicles, liver and spleen all retained nickel initially, whereas the intestines retained nickel after repeated administration (Nielsen *et al.* 1993) as did additional tissue types (hair, hypothalamus, hypophysis and pancreas) (Li *et al*. 2008).

In pregnant rats administered $NiSO_4$ by gavage, nickel appeared in the fetal blood and amniotic fluid in a dose-dependent fashion, producing nickel concentrations in the fetus similar to those in the dam (Morvai *et al*. 1992; Szakmáry *et al.* 1995).

6.4.4 Metabolism

While Ni^{2+} is subject to ligand transfer processes, nickel cannot be altered by enzymatic processes in the body. Nickel carbonyl ($Ni(CO)_4$) undergoes intracellular decomposition and oxidation to Ni^{2+} and CO (Kasprzak & Sunderman Jr 1969); other nickel compounds appear to undergo only dissolution. After decomposition of Ni_3S_2, the free nickel appears to form an organic Ni-P complex (Hachimi *et al*. 1995; Hildebrand *et al*. 1990; Hildebrand *et al*. 1991). Once inside the cell, Ni^{2+} may participate in the formation of reactive oxygen and/or nitrogen species (likely by Fenton- and Haber-Weiss-type reactions); however, Ni^{2+} redox activity may vary depending on the degree of complex formation with free amino acids or proteins (cited in Beyersmann & Hartwig 2008). The oxidation of Ni^{2+} by reactive oxygen species within the skin, leads to the formation of immunogenic Ni^{3+} and Ni^{4+} (Artik *et al*. 1999), which may react with low-molecular weight ligands to form diffusible lipophilic species (Hostýnek 2003). Biomethylation of nickel occurs in methanogenic bacteria, but has not been reported in higher organisms (cited in Thayer 2002).

6.4.5 Elimination

Absorbed nickel may be eliminated in urine, bile, sweat or breast milk; elimination *via* exhalation occurs only after exposure to $^{63}Ni(CO)_4$ (Sunderman Jr & Selin 1968). In laboratory animals, much systemically-absorbed nickel is eliminated in urine in a dose-dependent fashion (Koizumi *et al*. 2004), regardless of the exposure route (Clary 1975; Li *et al*. 2008; Smith & Hackley 1968). In humans, much absorbed nickel is eliminated in urine (Torjussen & Andersen 1979), although urinary excretion may be quite variable after inhalation exposure (Hassler *et al*. 1983; Ghezzi *et al*. 1989) and especially after ingestion (Christensen *et al*. 1979; Menne *et al*. 1978).

Over 90% of ingested nickel is excreted in the feces in both humans (Horak & Sunderman Jr 1973) and laboratory animals (Ho & Furst 1973; Uthus 1999; Tedeschi & Sunderman 1957). For the first few days after inhalation/IT instillation, fecal elimination of insoluble nickel particles dominates; thereafter, urinary elimination becomes progressively more dominant (Benson *et al*. 1994). In contrast, urinary elimination predominates after inhalation/IT instillation of soluble

nickel (English *et al*. 1981). Inhaled moderately soluble nickel particles are eliminated in both the urine and feces (Valentine & Fisher 1984).

Biliary nickel excretion in laboratory animals is estimated at 0.5-5% of the administered dose (Sunderman Jr & Selin 1968; Smith & Hackley 1968; Marzouk & Sunderman Jr 1985) and may average 2-5 µg/day in non-exposed humans (Rezuke *et al*. 1987). Enterohepatic recirculation is not considered significant (Patriarca *et al*. 1997); however, intestinal cells may secrete nickel into the intestinal lumen (Tallkvist & Tjälve 1998).

Nickel excretion in human sweat may be significant with concentrations of 5-116 ug Ni/L (Tallkvist & Tjälve 1998; Hohnadel *et al*. 1973; Horak & Sunderman Jr 1973; Christensen *et al*. 1979) and production ranging from <1 litre to several litres per day (Weinheimer *et al*. 2008; Stofan *et al*. 2007). Mean nickel concentrations in human milk ranged from 1.16 to 19.3 µg/L (Parr *et al*. 1991; Friel *et al*. 1999; Casey & Neville 1987; Almeida *et al*. 2008).

Laboratory animal data for soluble Ni^{2+} (oral/IV) fit a two-compartment model with bi-phasic elimination ($T_{1/2\alpha}$ and $T_{1/2\beta}$ ranging from 0.79-6 hr and 41-83 hr, respectively) (Li *et al*. 2008; Onkelinx *et al*. 1973). Extending the Onkelinx *et al*. (1973) model to humans, provided a urinary elimination $T_{1/2}$ of 28±9 hr (Sunderman Jr *et al*. 1989). Kinetic modelling predicted urinary elimination $T_{1/2}$s of 17-39 hr in electroplaters (Tossavainen *et al*. 1980), and 30-53 hr for mould makers and welders inhaling insoluble nickel compounds (Zober *et al*. 1984; Raithel *et al*. 1982).

The relatively short $T_{1/2}$ values for animals and humans do not preclude longer-term storage deposits in the body, as suggested by retention of absorbed dietary nickel (14% in women and 26% in men) (Anke *et al*. 1995), and similar retention of 16.73% (Li *et al*. 2008) and 11% (7.2-14.2%) (Patriarca & Fell 1996) of exogenous Ni^{2+} in rats and humans, respectively, and persistently elevated urinary elimination in retired (Torjussen & Andersen 1979) and current nickel workers (Akesson & Skerfving 1985; Morgan & Rouge 1984). Assuming 30% retention of absorbed nickel, half lives of 200 (Bennett 1982) and 1200 days (ICRP 1981) for retained nickel in humans have been estimated.

After ingestion, the gastrointestinal tract may retain significant quantities of nickel (Nielsen *et al*. 1993; Li *et al*. 2008). Retention of inhaled particles in the respiratory tract may represent another storage depot. Particle phagocytosis is largely completed within hours of exposure, but may become delayed at high lung particle burdens (>1 µL/g of lung) or with protracted exposure; Ni-induced cytotoxicity may also limit clearance (Benson *et al*. 1995; Lehnert *et al*. 1989; Menzel *et al*. 1987; Oberdorster *et al*. 1995), as may low solubility. Following acute inhalation or IT instillation in rats, the pulmonary clearance $T_{1/2}$ was 20 hr for NiS (amorphous), 2-3 days for $NiSO_4$, 4-6 days for Ni_3S_2, 32 days for metallic Ni (ultrafine) and >120 days for NiO (Tanaka *et al*. 1988; Serita *et al*. 1999; Hirano *et al*. 1994; Benson *et al*. 1994). Clearance of NiO increased with decreasing particle diameter (Kodama *et al*. 1985), with $T_{1/2}$s of 11.5 and 21 months for 1.2 and 4.0 µm particles, respectively (Tanaka *et al*. 1985). Repeated inhalation of $NiSO_4$, amorphous NiS or Ni_3S_2 did not alter pulmonary clearance or result in pulmonary accumulation in rats or mice (Tanaka *et al*. 1988; Dunnick *et al*. 1989; Benson *et al*. 1995). In contrast, in mice and rats repeat exposure to green NiO, resulted in accumulation in the lungs and impaired clearance of acutely inhaled ^{63}NiO (Benson *et al*. 1995; Dunnick *et al*. 1989; Oberdorster *et al*. 1995b; Tanaka *et al*. 1985; Tanaka *et al*. 1986; Wehner & Craig 1972).

6.5 Acute Toxicity

ATSDR (2005) summarised the acute effects following ingestion in laboratory animals and humans. The LD_{50} for nickel sulphate (the most soluble and acutely toxic of the nickel species) has been reported to from 39-46 mg/kg body weight (bw) in rats. Health Canada (EC and HC 1994) reported that "soluble" nickel salts (e.g., nickel chloride, nickel sulphate, nickel nitrate and nickel ammonium sulphate) are moderately to highly acutely toxic to rats (LD_{50}s = 42.5-112 mg Ni/kg bw) while nickel powder and the insoluble nickel salts (green and black nickel oxides, nickel subsulphide, and amorphous nickel sulphide) are less acutely toxic (LD_{50}s = 3200-9000 mg Ni/kg bw).

Accidental ingestion of water containing nickel sulphate, nickel chloride and chloride hexahydrate (range= 0.5-2.5 g Ni) caused acute gastrointestinal and neurological symptoms including nausea, abdominal pain, diarrhea, vomiting and shortness of breath in 20/38 workers (Sunderman *et al.* 1988). Another subject who ingested approximately 50 μg Ni/kg as nickel sulfate in water was reported to have developed transient hemianopsia coincident with peak serum concentrations (Sunderman Jr *et al*. 1989). A 2 yr old child died (due to cardiac arrest) within hours of accidental ingestion of nickel sulphate crystals (estimated exposure = 570 mg Ni/kg bw) (Daldrup *et al*. 1983).

A worker became ill and died 13 days later after a 90-minute exposure to an estimated concentration of 382 mg Ni/m^3 (estimated total inhaled dose = 1 g), of principally metallic nickel, of which 65% of particles were <1.4 μm, and the majority were 50 nm in diameter. Histological examination of the man's lungs revealed alveolar wall damage and oedema in alveolar spaces and marked tubular necrosis in the kidneys. Nickel particles <25nm in diameter were identified in lung macrophages using transmission electron microscopy. High levels of nickel were also measured in his urine (Phillips *et al*. 2010; Rendall *et al*. 1994).

Acute dermal exposure to nickel seems to be primarily associated with the development of nickel sensitivity (see 6.7, Nickel allergy, below).

6.6 Subchronic and Chronic Systemic Toxicity

6.6.1 Oral Exposure

A number of studies have investigated the effects of longer term oral exposure to nickel in both laboratory animals and humans. Loss in body weight, renal, developmental and reproductive effects have been well documented (Vermeire *et al*. 1991; SLI 2000; Ambrose *et al*. 1976; ABC 1988). Effects in other systems (cardiac, gastrointestinal, hematological, immunological, and neurological) were also summarised in ATSDR (2005) report. The studies with the most relevance to the development of the toxicological reference value for nickel sulphate are discussed below and in Section 6.9.1.

In a 2-year study, Ambrose *et al*. (1976) reported decreased body weights in Wistar rats fed nickel sulphate. In this study, rats (25 per sex per dose) were fed 0, 100, 1000 or 2500 ppm nickel in food (dose rates estimated as 0, 5, 50 and 125 mg Ni/kg bw/day). Various effects were noted in the mid-dose group including significantly higher heart-to-body weight and lower liver-to-body weight ratios than controls (females only). In addition, the high dose male and female rats had decreased overall body weights but males showed effects at lower doses than females

(50 *vs*. 125 mg Ni/kg bw/day respectively). No significant effects were reported at the low dose group. In terms of growth effects, male rats showed effects at lower doses than females. The growth rates of dogs were likewise reduced when similar concentrations of nickel added to their feed (Ambrose *et al*. 1976). In a 4-week study in Webster mice, significant negative effects on growth and feed utilisation occurred at lower doses of nickel acetate for females (estimated doses = 250 and 208 mg/kg bw, respectively) than in males (293 and 293 mg/kg bw, respectively) (Weber and Reid 1969) (see also Appendix 5).

Based on the Ambrose *et al* (1976) study, a Lowest Observed Adverse Effect Level (LOAEL) of 50 mg/kg bw/day was identified while the No Observed Adverse Effect Level (NOAEL) was identified to be 5 mg/kg bw/day. This study has been used as the basis of the oral TRVs published by Health Canada (HC 1996), the US Environmental Protection Agency (US EPA 1996) and the IOM (IOM 2001).

6.6.2 Inhalation Exposure

Numerous studies have investigated the effects of long term inhalation exposure to nickel in both laboratory animals and humans (see also Rhinitis/Asthma, below). Mortality studies have not shown evidence of an increase in the risk of death as a result of non-malignant (non-cancerous) respiratory disease among several cohorts of nickel-exposed workers (from Canada, Norway, Finland and the UK) (IARC 1990).

A cross-sectional study, pulmonary function testing indicated vital capacity and expiratory flows were reduced in shipyard stainless steel welders exposed to elevated concentrations of nickel and chromium (Kilburn *et al.* 1989) No evidence of lung effects associated with lung and nasal cancers were evident in workers exposed to concentrations as high as 100mg/m^3 from Sudbury, ON. When chest radiographs from 745 nickel sinter plant workers from the Copper Cliff, Sudbury plant (where a high incidence of nasal and lung cancers was found among workers employed from 1948 to 1963 (IARC 1990) who had been exposed to nickel at concentrations as high as 100 mg/m^3 were examined, there was no evidence of increased small irregular opacities, which can be indicative of inflammatory or fibrogenic response in the lungs (pneumoconiosis (Muir *et al*. 1993)). Evaluation of nickel refinery workers in Norway showed a dose-response dependant increased risk of pulmonary fibrosis after controlling for age, smoking status and asbestos exposure for both soluble and suphidic nickel, although the dose-response trend was less clear for sulphidic nickel (Berge & Skyberg 2003).

In the case of inhalation exposures, the ATSDR (2005) review concluded that nickel sulphate is more acutely toxic than nickel subsulphide or nickel oxide. In rats exposed to nickel *via* the inhalation route for 6 hours per day for 12 days at 700 µg Ni/m^3, effects included alveolitis, chronic lung inflammation, alveolar macrophage hyperplasia and atrophy of the nasal olfactory epithelium. Non-respiratory effects include loss in body weight, renal, developmental and reproductive effects. Immunological effects have also been noted in mice (Dunnick *et al*. 1989; NTP 1996a; 1996b; 1996c; Spiegelberg *et al*. 1984; Weischer *et al*. 1980; Vyskočil *et al*. 1994). The studies of most relevance to the development of the toxicological reference values (section 6.9.2) for nickel sulphate and nickel oxide are discussed below.

Spiegelberg *et al*. (1984) reported dose-related effects to the respiratory and immune systems in a study exposing rats to nickel oxide at concentrations of 25 and 150 µg Ni/m^3 for 24 hours/day, 7 days/week for 4 months. Increases in lung granulocytes, lymphocytes and multinucleated

macrophage counts were noted in all groups. The LOAEL was reported to be 25 µg Ni/m^3 while a NOAEL was not identified. This study was used by Health Canada (1996) to develop an inhalation TRV for nickel oxide (section 6.9.2).

Dunnick *et al.* (1989) reported dose-related effects on nasal tissue and the respiratory system in mice and rats exposed to nickel sulphate. In this study, groups of male and female mice and rats (7-10 per sex per dose group) were exposed to concentrations of 0, 20, 50, 100, 200 and 400 µg Ni/m^3 for 6 hours/day, 5 days/week for 13 weeks. Inflammation of the lungs, alveolar macrophage hyperplasia and nasal olfactory epithelium atrophy were noted as critical effects. The LOAEL was reported to be 20 µg Ni/m^3 in rats (due to alveolar macrophage hyperplasia in females) while a NOAEL was not identified. This study was used by Health Canada (1996) to develop an inhalation TRV for nickel sulphate. It is noted that no information is provided on whether or not the control group received sulphate aerosols (without nickel), therefore, it is not possible to determine whether the effects may have been at least partially due to inhalation of particulate sulphates.

NTP (1996a) reported respiratory effects in rats exposed to nickel sulphate in air. In this study, groups of rats (63-65 per sex, per dose group) were exposed to nickel sulphate hexahydrate at concentrations of 0, 120, 250 or 500 µg/m^3, (equivalent to 0, 30, 60 or 110 µg Ni/m^3), for 6 hours/day, 5 days/week for 2 years. No significant effects on survival, body weight or clinical signs were observed. Treatment-related effects included lung lesions (chronic active inflammation, alveolar macrophage hyperplasia, alveolar proteinosis and fibrosis) in rats exposed to 60 or 110 µg Ni/m^3. In addition, a significant increase in the incidence of lymphoid hyperplasia and atrophy of the olfactory epithelium were noted in the high concentration group. No alteration on tumour incidence was noted. The LOAEL was reported to be 60 µg Ni/m^3 while the NOAEL was identified at 30 µg/m^3.

In a second study, groups of mice (80 per sex per dose group) were exposed to nickel sulphate hexahydrate at concentrations of 0, 250, 500 or 1000 µg/m^3 (equivalent to 0, 60, 110 or 220 µg Ni/m^3) for 6 hours/day, 5 days/week for 2 years (NTP 1996a). No significant effects on survival, body weight or clinical signs were observed. Treatment-related effects included lung lesions (macrophage and lymphoid hyperplasia) and atrophy of the olfactory epithelium in mice exposed to 110 or 220 µg Ni/m^3. Additionally, significant increases in the incidence of lymphoid hyperplasia and atrophy of the olfactory epithelium were noted in the high concentration group. No change in tumour incidence was noted. NTP (1996a) reported a LOAEL of 110 µg Ni/m^3 and a NOAEL of 60 µg Ni/m^3.

6.6.3 Reproductive Effects and Teratogenicity

There is evidence that oral exposure to nickel may cause reproductive effects in laboratory animals (Appendix 5). Ambrose *et al.* (1976) studied three generations of rats and did not observe any adverse effects on fertility, gestation, viability and lactation in rats exposed to diets containing 1000 mg Ni/kg. However, changes to sperm quality in laboratory animals have been reported (cited in ATSDR 2005). Generally, reproductive performance is only slightly affected by oral nickel exposure. The most relevant studies with regard to derivation of the oral TRV (SLI 2000b; Smith *et al.* 1993) (section 6.9.1) are discussed below.

Post-implantation loss and perinatal mortality were investigated in a two-generation rat study: 1, 2.5, 5.0 and 10 mg/kg bw/day (equivalent to 0.22, 0.55, 1.1 and 2.2 mg Ni/kg bw/day) nickel

sulphate hexahydrate dissolved in water was administered by oral gavage to male and female rats (28 animals/sex). A NOAEL of 2.2 mg Ni/kg bw/day was reported. In addition to the developmental endpoints, the authors reported slight changes to liver weight (<10% of the controls) in the two highest dose groups but they were concluded to be of no toxicological significance (SLI 2000b). Based on a re-evaluation of the SLI (2000b) data, the Danish Environmental Protection Agency (DEPA) considered that there was a mechanistic basis to assume that post-implantation loss and perinatal mortality represented similar endpoints (EU 2004; 2008). WHO (2005) supported the EU (2004) analysis and likewise concluded that effects on the developing fetus resulting in post-implantation loss or death shortly after birth appeared to be due to the same mechanism and that the combination of the endpoints was considered appropriate. Combination of the endpoints resulted in the identification of a LOAEL of 2.2 mg Ni/kg bw/day (EU 2004) and a NOAEL of 1.1 mg/kg bw/day (EU 2004; 2008) using the DEPA approach. A revised statistical analysis of the SLI (2000b) study data also supported a LOAEL of 2.2 mg/kg bw/day and a NOAEL of 1.1 mgkg bw/day for perinatal lethality (Sommer *et al*. 2002). Both WHO (2005) and EU (2008) adopted the DEPA re-analysis of the SLI (2000b) data and the NOAEL of 1.1 mg/kg bw/day was used to develop the human health-based soil quality guideline (SQG_{HH}) in the current document (see Section 6.9).

Smith *et al*. (1993) reported increased perinatal death in rats administered nickel chloride in drinking water (0, 10, 50 or 250 ppm Ni) for 11 weeks prior to mating and then during two successive gestation and lactation periods. Results indicated an increased frequency of perinatal death at all doses, giving a LOAEL of 10 ppm Ni. This concentration was calculated by Smith *et al.* (1993) as equivalent to a dose of 1.3 mg Ni/kg bw/day, based on median intake levels. The more recent study of SLI (2000b) is deemed most suitable for estimation of health effects from soluble nickel.

Effects of soluble nickel compounds on male reproductive organs in rats and mice have been reported. Effects on the testes and epidiymus include motility, morphology, motility, decreased sperm count and alterations in marker testiculary enzyme activity (Pandey *et al*. 1999; Pandey & Srivastava 2000; Käkelä *et al*. 1999; Bábiková *et al*. 2007; Toman *et al*. 2012). Though limited by small numbers of animals and poor dose-response design, effects on male reproductive organs occurred at levels similar to those in developmental toxicity studies, i.e., down to a NOAEL of 1.1. mg Ni/bw (Pandey *et al*. 1999; Pandey & Srivastava 2000) and support the selection of the animal developmental toxicity endpoint (section 6.9.1).

6.7 Nickel allergy

6.7.1 Allergic contact dermatitis

Nickel is one of the major causes of allergic contact dermatitis (ACD) worldwide, with an estimated median incidence of 8.6% (range 0.7-27.8%) among the general population and 17.1% for the female population (Thyssen *et al*. 2007). In the UK, nickel is believed to play a role in up to 18% of cases of occupational contact dermatitis (Meyer *et al*. 2000).

The induction of sensitisation and the elicitation of nickel ACD are dependent upon T lymphocytes, which orchestrate a typical delayed type hypersensitivity reaction. Skin sensitisation occurs as a result of Ni^{2+} hapten formation by binding to proteins or immunogenic peptides (likely *via* histidine residues (Sinigaglia 1994)).

Major determinants of induction and elicitation of nickel ACD include the nature (source composition, anatomic site, vehicle, skin penetration [e.g., piercing] and/or occlusion) and extent (duration, surface area and concentration of nickel per unit area of skin) of exposure. In challenge testing, $NiCl_2$ produces positive reactions more frequently than $NiSO_4$ (Wall 1980; Räsänen *et al*. 1999), likely due to greater dermal permeation and/or greater irritant/cytotoxic properties (Fullerton *et al*. 1989). Both $NiCl_2$ and $NiSO_4$ may penetrate through rubber (but not PVC) gloves to elicit skin reactions; the occlusion provided by the gloves may increase nickel dermal permeation and sweating (Wall 1980). Typically, the response to nickel patch testing is more consistent as the concentration and/or duration increase (Kalimo *et al*. 1985). Elicitation of ACD is generally independent of the skin surface area to which the allergen is applied (cited in Kimber *et al*. 2002); however, for nickel, the size of the exposed area, and therefore the total amount applied, may also influence reaction severity and latency, even though the dose per unit area is the same (Fischer *et al*. 2007a).

In the mouse local lymph node assay (LLNA), the induction threshold for nickel was 140 μg/cm^2 (Ryan *et al*. 2002). Generally LLNA and human thresholds correlate well (Peiser *et al*. 2012).

The amount of absorbed nickel required to elicit dermal reactions appears to be very small: X-ray microanalysis of reactive patch-tested skin detected nickel only with the keratin cell layer, sweat ducts and hair follicles (Kalimo *et al*. 1985). Studies assessing the nickel ACD elicitation threshold, obtained positive dermal challenge responses after single or repeated exposures using open occluded, penetrating or oral (see 6.7.2) protocols.

Most dose-response studies have employed a single occluded Finn chamber exposure to $NiSO_4 \cdot H_2O$ in ethanol or water (Allenby & Goodwin 1983; Emmett *et al*. 1988; Fischer, Johansen, *et al*. 2007; Hindsén & Bruze 1998; Hindsén *et al*. 1997; 1999; 2005; Nielsen *et al*. 1999; Rystedt & Fischer 1983; Wahlberg & Skog 1971). The lowest dose per unit area at which 10% of allergic individuals will react within two days of application (ED_{10}) was calculated to be 0.78 μg Ni/cm^2 (95% CI 0.13-2.2), while the ED_1 was 0.048 μg/cm^2 (95% CI 0.0018-0.24) (Fischer *et al*. 2007b). Meta-analysis of pre-2005 studies concluded that 5% of sensitised subjects react to 0.44 μg Ni/cm^2 and 10% react to 1.04 μg Ni/cm^2 (Fischer *et al*. 2005).

In one study employing single open application, 4 of 51 (7.8%) of sensitised persons responded with redness/vesicles to 15 μg Ni/cm^2 (as $NiCl_2$ in ethanol), while 20 more had papular follicular reactions, which may have been local reactions in areas of high nickel uptake (sweat ducts and hair follicles - see 6.4.2.3); follicular reactions were also seen at 0.015-1.5 μg Ni/cm^2 (Menne & Calvin 1993). In a similar open testing study, 7 of 15 (46%) Ni-sensitive subjects reacted at 37.5 μg Ni/cm^2, and 10 (66%) reacted at 75 μg Ni/cm^2; papules were also seen in some subjects at 37.5 and 75 μg Ni/cm^2 (Christensen & Wall 1987). In contrast, 20% $NiCl_2$ produced no response in normal subjects (Christensen & Wall 1987). In single open application of $NiSO_4$, 0/2 subjects reacted at 0.05 or 0.5 μg Ni/cm^2, and 0/3 subjects reacted to 2.5 μg Ni/cm^2, but increasing numbers reacted at the higher concentrations as follows: 6/21 (28%) at 5.0 μg Ni/cm^2, 6/19 (31%) at 15 μg Ni/cm^2, 7/19 (37%) at 30 μg Ni/cm^2 and 11/18 (61%) at 45 μg Ni/cm^2 (Gawkrodger *et al*. 2012).

In repeated open application testing (ROAT) for up to 21 days, 22% of Ni-allergic subjects reacted at 0.035 μg Ni/cm^2 (as $NiSO_4 \cdot 6H_2O$). The cumulative ROAT dose at 1, 2 and 3 weeks

was equivalent to the ED_{10} for patch tests (0.78 µg Ni/cm^2) (Fischer *et al*. 2007), likely reflecting cumulative absorption of nickel (ED_{xx}(ROAT) = 0.0330 ED_{xx}(patch test)) (Fischer *et al*. 2009).

Another key determinant of ACD is the susceptibility of the exposed individual (Kimber *et al*. 2002), which may vary significantly over time (Hindsén *et al*. 1999). In humans, nickel-induced allergic contact dermatitis develops much more readily in irritated skin (cited in Hostýnek 2003) and at sites of previous allergic contact dermatitis and varies directly with the intensity of, and inversely with the time since the previous episode (Hindsén *et al*. 1997; 2001). The potential to induce or elicit allergic reactions to nickel in areas of thinner skin and/or abraded skin may be of greater concern (Dickel *et al*. 2010); the irritant potency may also be greater in young children (Jøhnke *et al*. 2004). Conversely, tanned skinned may be thicker and therefore more resistant to nickel or produce delayed reactions (Christensen & Wall 1987). Co-exposure to skin lotions (Zachariae *et al*. 2003) or irritants (Shah *et al*. 1998; Fischer *et al*. 2005; Agner *et al*. 2002) may increase the severity of response. Once sensitised, allergic response on re-exposure appears to be a long-term phenomenon (Nielsen *et al*. 2001).

6.7.2 Systemic contact dermatitis

Systemic Nickel Allergy Syndrome (SNAS) is characterised by new-onset urticaria and eczema or exacerbation of previous positive patch tests/eczema triggered by dietary nickel intake. Abdominal pain, diarrhea or constipation, respiratory and other minor symptoms may also be noted (Nielsen *et al*. 1999; Picarelli *et al*. 2011; Turi *et al*. 2008; Veien 2011). SNAS appears to be induced after oral provocation tests using soluble forms of nickel (generally $NiSO_4$) (Kaaber *et al*. 1978; 1979; Hindsén *et al*. 2001; Gawkrodger *et al*. 1986; Cronin *et al*. 1980; Christensen & Moller 1975); symptoms were reduced in some subjects following a nickel-reduced diet (Gawkrodger *et al*. 1988; Picarelli *et al*. 2011; Silvestri & Barmettler 2011; Tennstedt 2011; Veien *et al*. 1983; 1993) and hand eczema was aggravated in women fed a high-nickel diet (Nielsen *et al*. 1990). The response to nickel ingestion is antigen-specific: only the nickel patch-test site was reactivated after oral challenge in subjects who had a previous positive nickel patch test and an irritant reaction to a benzalkonium chloride patch test (Christensen *et al*. 1981). Some controversy remains as to the veracity of systemic symptons due to dietary nickel, in part owing to the difficulty in measuring or controlling intake from food (Pizzutelli 2011).

Some studies have established LOAELs of 0.6 mg (9.7 µg Ni/kg bw) (Cronin *et al.* 1980) and 12 µg Ni/kg bw (Nielsen *et al.* 1999) in females for exacerbation of hand eczema. The lowest LOAEL was obtained in a double-blind, placebo-controlled study in which 4 of 10 subjects in each dose group reacted to challenge after administration of 1 and 0.3 mg (the latter corresponding to 4.8 µg/kg for a 62 kg female and 4.3 µg/kg for a 70 kg man) (Jensen *et al*. 2003). Subjects were generally fasted overnight (see 6.4.2.1), although no other measures to control nickel intake were instituted.

In a modified meta-analysis of oral nickel challenge studies with similar designs and protocols (9 studies and 171 subjects) (Bedello *et al*. 1985; Christensen & Moller 1975; Gawkrodger *et al*. 1986; Kaaber *et al*. 1979; 1978; Hindsén *et al*. 2001; Roduner *et al*. 1987; Sertoli *et al*. 1985; Veien & Kaaber 1979), the authors concluded that reaction rates tended to increase with challenge dose. Model results predicted dermal reactions in 1% of nickel-sensitive patients after ingestion of 0.22, 0.35 or 0.53 mg nickel (depending on which of three dose-response curves was

used). Similarly, 10% of these patients would react after ingestion of 0.55, 0.87 or 1.33 mg nickel (Jensen *et al*. 2006).

The oral elicitation threshold for dermatitis (Nielsen *et al*. 1999) has been used to develop guidelines for drinking water (WHO 2005), soil guidelines for Ni (Environment Agency, 2009; Australia 2010), EU Risk Assessment of nickel for the indirect exposure of man via the environment (for REACH) (EU 2008b; DeBrouwere *et al*. 2012) and supports the selection of the animal developmental toxicity endpoint (section 6.9.1). Migration limits for Ni ($\mu g/cm^2$/week) have been used by the European Union to develop limits for dermal contact with Ni-based products (EU 2004a; Manchananda 2011).

6.7.3 Rhinitis/Asthma

The allergic/immune manifestations of nickel exposure may also include nasal inflammation (rhinitis, rhinorrea, sneezing and nasal obstruction) and bronchial asthma/bronchitis, with or without nickel-induced ACD/hand eczema.

Sporadic cases of nickel-induced rhinitis and/or asthma, often work-related, have been reported in the literature, generally among patients who tested positive on skin allergy testing (Block & Yeung 1982; Davies 1986; De Hauteclocque *et al.* 2002; Dolovich *et al*. 1984; Fisher *et al*. 1982; Hong *et al*. 1986; Malo *et al*. 1982; 1985; Maciariello *et al*. 2010; McConnell *et al*. 1973; Novey *et al*. 1983; Spinelli *et al*. 2005; Stelting & Platzek 2005). Analyses of data from Canada and the UK place $NiSO_4$ among the 10 most frequent causes of occupational allergic contact dermatitis (OACD) and occupational asthma (OA) (Arrandale *et al*. 2012). Seven out of eight asthmatic patients with hard metal asthma due to cobalt, showed reduced FEV_1 (-20% or more) after inhaling $NiSO_4$. Eight control subjects with no history of hard metal exposure, including six asthmatics, had no bronchoconstrictive response to $NiSO_4$ (Shirakawa *et al*. 1990).

Temporal associations among ambient $PM_{2.5}$, individual metal constituents of $PM_{2.5}$ (nickel, vanadium, zinc and elemental carbon) and longitudinal reports of respiratory symptoms through 24 months of age were assessed in a New York City cohort study involving 653 children. An increase in interquartile range (IQR) concentration of ambient nickel (0.014 mg/m^3) was associated significantly with a 28% increased probability of wheeze (P=0.0006); larger effect estimates were obtained in models containing observations from only the cold/flu season (Patel *et al*. 2009).

There are limited experimental data regarding the effects of nickel on the mammalian immune systems. Several immune function responses such as changes in spleen cellularity and natural killer cell (NK) activity were noted in mice exposed to nickel sulphate in drinking water; however, concentrations were very high (1-10 g/L) (Dieter *et al.* 1988).

6.8 Genotoxicity, carcinogenicity and carcinogenic mode of action

6.8.1 Genotoxicity

6.8.1.1 Direct DNA reactivity

The induction of DNA damage has been linked to nickel's ability to bind to DNA and nuclear proteins; however, nickel compounds are not mutagenic in bacterial test systems and only weakly mutagenic in cultured mammalian cells. In addition, no increase of ouabain-resistant or

6-thioguanine-resistant colonies has been found in human diploid fibroblasts, even at concentrations of Ni_3S_2 that caused a 200-fold increase in the frequency of anchorage-independence (cited in Cameron *et al*. 2011; Costa *et al*. 2005; IARC 2011; Salnikow & Zhitkovich 2008; Sivulka 2005; Zhao *et al*. 2009).

6.8.1.2 Indirect DNA reactivity (via Ni-induced reaction oxygen species)

Nickel may bind to histone proteins within heterochromatin and generate reactive oxygen species (ROS) through Ni^{3+}/Ni^{2+}. These radicals could interact with DNA to damage bases, induce DNA strand breaks, sister chromatid exchange and/or cross-links between DNA and protein. However, such effects are generally noted only at cytotoxic concentrations and such damage may be predominantly confined to local heterochromatic regions of DNA that lack active genes. As noted above, all *in vitro* mutation assays with nickel have been negative for the induction of point mutations. Damage to heterochromatin may nonetheless lead to chromosomal aberrations (breaks, gaps, exchanges) involving nearby coding regions, which could affect critical tumour suppressor or cell senescence genes. Nickel-mediated cytotoxicity may also lead to secondary ROS generation, which may damage DNA if able to access the nucleus (cited in IARC 2011; Oller *et al*. 1997).

6.8.1.3 Indirect genotoxicity through epigenetic, cytotoxic, immunosuppressive, inflammatory or proliferative effects

Epigenetic changes, including DNA methylation alterations, changes in histone acetylation, methylation or ubiquitylation levels, structural changes and/or activation or suppression of a number of transcription factors, may be primary events in nickel carcinogenesis.

In human lung cells exposed to soluble nickel compounds, histone modifications included loss of acetylation, increased dimethylation and increased ubiquitylation. The mechanisms by which nickel induces DNA hypermethylation and consequent gene silencing are presently unknown. A major action of nickel is its ability to silence the expression of genes located near heterochromatin by inducing a loss of histone H4 and H3 acetylation and DNA hypermethylation. It can also bind to and selectively damage histones within (non-coding) heterochromatin. Nickel has also been shown to suppress histone H4 acetylation *in vitro* in yeast and mammalian cells. Loss of histone acetylation may reduce the access of transcription-associated proteins to DNA, while histone methylation results in more compacted chromatin and gene silencing. When nickel silences critical genes, such as tumour suppressor genes, the cell is altered to a greater state of neoplastic transformation. It has been postulated that Ni^{2+} may substitute for magnesium (Mg^{2+}) to increase chromatin condensation and trigger *de novo* DNA methylation.

Given Ni^{2+} is similar to Fe^{2+}, Ni^{2+} may either replace Fe^{2+} or interfere with Fe^{2+} uptake, leading to cellular iron. Nickel may also inhibit cellular ascorbate uptake and/or deplete ascorbate due to nickel-induced ROS. Ascorbate is the only anti-oxidant able to maintain the reduced state of enzyme-bound iron of prolyl hydroxylases, which is vital for maintaining enzyme activity. Depletion of intracellular iron and/or ascorbate may therefore inactivate prolyl hydroxylases, including the hypoxia inducible factor (HIF) prolyl- and asparaginyl-hydroxylases. Inhibition of the HIF proline hydroxylases stabilises the HIF protein and activates hypoxic signaling, and produces an alteration of cellular metabolism to a state that mimics permanent hypoxia, including the induction of HIF-1 and activation expression of hypoxia-inducible genes.

Nickel-induced cytotoxicity and inflammation (including upregulation of ROS generation and chronic activation and inflammation of airway/alveolar macrophages leading to general inhibition of phagocytic clearance) within the respiratory tract may promote cellular proliferation and mutation and may reduce respiratory tract defences. Nickel may also suppress natural killer cell activity and interferon production.

Nickel-induced carcinogenesis is known to be tissue-, strain- and species-dependent, indicating genetic predispositions (e.g., variations in the expression of genes involved in the metabolism of antioxidants) may play a role.

Overall, nickel may change gene expression motifs, contributing to stimulated cell proliferation, either by activation of proto-oncogenes or interfering with tumour suppressor genes. Together, the activation of HIF-1 transcription factor, hypermethylation and modification of histones may represent a molecular basis for cellular adaptation in growing tumours. Specifically, a nickel-induced state of activated hypoxic signaling under normal oxygen tension may promote the selection of cells that have altered energy metabolism, changed growth control and/or have become resistant to apoptosis. However, it is possible additional mutagenic events (DNA damage) are required for successful cell transformation (cited in Oller *et al*. 1997; Salnikow & Zhitkovich 2008; Zhao *et al*. 2009; Costa *et al*. 2005; Cameron *et al*. 2011).

6.8.1.4 Nickel(II) as a co-carcinogen

Most metallic compounds, including soluble and insoluble nickel compounds, are able to enhance the cytotoxicity, genotoxicity and carcinogenicity of directly-acting genotoxic agents as a result of inhibition of DNA repair. In particular, nickel may interfere with iron-dependent DNA-repair enzymes (including alkyl DNA dioxygenases and O^6-methylguanine-DNA methyltransferase (MGMT); Ni^{2+} may specifically inhibit nucleotide excision and base excision repair. Inhibition of DNA repair may therefore underly the phenomenon of delayed mutagenicity and chromosomal instability evident long after treatment of cells with nickel (cited in IARC 2011; Salnikow & Zhitkovich 2008).

6.8.2 Carcinogenicity

Orally-administered nickel and its inorganic compounds do not appear to be carcinogenic in laboratory animals (Heim *et al*. 2007, Ambrose *et al*. 1976; Schroeder & Mitchener 1975), but carcinogenic activity has been reported when administered by any other route (inhalation, intramuscular (i.m.), intrarenal (i.r.), intraperitoneal (i.p.), intraocular (i.o.), subcutaneous (s.c.) and intra-articular space (i.a.)) and at all sites of application. Carcinogenic activity depends strongly on the solubility of nickel compounds in water and tissue fluids. As a rule, insoluble compounds, such as NiS, NiO and Ni_3S_2, are better experimental carcinogens than soluble compounds, Ni^{2+} acetate, chloride, or sulfate. However, experiments with Ni^{2+} acetate as the initiating agent (i.p. injection) have shown strong positive results in rodents (cited in Kasprzak *et al*. 2003) (see section 6.9.3 for Unit Risk selection).

In a comprehensive epidemiological analysis of 10 occupational cohorts (>60 000 subjects) exposed to nickel, including workers employed at mining, smelting and refinery operations in Ontario, in which measured total nickel was used to estimate four nickel compounds (metallic nickel, oxidic nickel, sulphidic nickel and soluble nickel salts) Doll *et al*. (1990) concluded that "respiratory cancer risks are primarily related to exposure to 'soluble' nickel at concentrations in

excess of 1 mg Ni/m^3 and to exposure to less 'soluble' forms at concentrations greater than 10 mg Ni/m^3.", the 1990 *International Report of the International Committee on Nickel Carcinogenesis in Man* concluded

> "…although much of the respiratory cancer risk seen among nickel refinery workers could be attributed to exposure to a mixture of oxidic and sulfidic nickel at very high concentrations, exposure to large concentrations of oxidic nickel in the absence of sulfidic nickel was also associated with increased lung and nasal cancer risks. There was also evidence that soluble nickel exposure increased the risk of these cancers and that it may enhance risks associated with exposure to less soluble forms of nickel.
>
> There was no evidence that metallic nickel was associated with increased lung and nasal cancer risks, and no substantial evidence was obtained to suggest that occupational exposure to nickel or any of its compounds was likely to produce cancers elsewhere than in the lung or nose. No excess of any type of cancer was observed in the cohorts that did not show an excess of cancer of the lung and nose…
>
> …Although the investigation did not provide dose-specific estimates of risks for individual nickel species, it is possible to comment on the cancer risks associated with the level of airborne nickel to which the general population is exposed. The evidence…suggests that respiratory cancer risks are primarily related to exposure to soluble nickel at concentrations in excess of 1 mg Ni/m^3 and to exposure to less soluble forms at concentrations greater than 10 mg Ni/m^3. With excess risks being confined to these high levels of exposure and the absence of any evidence of hazard from metallic nickel, it can be concluded that the risk to the general population from exposure to the extremely small concentrations (less than 1 ug Ni/m^3 to which it is exposed in the ambient air is minute, if indeed there is any risk at all." (IARC 1990)

Additional reviews of the respiratory cancer risks in Welsh, Finnish and Norwegian nickel refiners support these findings, indicating that water-soluble nickel compounds were central in the development of cancer (even after adjustment for confounders such as smoking, exposure to arsenic, asbestos, sulphuric acid mists, cobalt and occupational lung carcinogens) (Grimsrud & Andersen 2010; Grimsrud *et al*. 2005; 2002; 2003; 2000; Grimsrud & Peto 2006). These studies also indicated oxidic nickel may be a stronger hazard for nasal cancer than soluble nickel and a multiplicative effect of smoking and total nickel exposure to the risk of lung cancer (Andersen *et al*. 1996). Other reviews have also concluded that oxidic and sulphidic nickel are carcinogenic via inhalation, but found the carcinogenicity of soluble nickel cannot be determined (TERA 1999).

Cohort studies from Canada, Norway, Finland and the UK analysed in the 1990 IARC evaluation of nickel and nickel compounds, indicated elevated risks of lung and nasal cancers among workers involved in nickel sulfide ore smelting and nickel refining processes (high-temperature processing of nickel matte, nickel-copper matte, electrolytic refining and Mond process refining) and exposed to various forms of nickel (metallic nickel, nickel oxides, nickel subsulfide, soluble nickel compounds and nickel carbonyl). Additional support was provided by *in vivo* and *in vitro* carcinogenicity studies. In their 2011 evaluation, IARC again concluded that there is an elevated risk of lung and nasal sinus cancer among nickel refinery workers (Grimsrud & Peto 2006; IARC 1990; Anttila *et al*. 1998; Andersen *et al*. 1996), and of lung cancer risk among nickel smelter workers (Anttila *et al*. 1998; IARC 1990). IARC also concluded there is currently no consistent

epidemiological evidence to suggest nickel compounds cause cancer at sites other than the lung and nasal cavity (IARC 2011).

IARC (2011) found evidence of elevated risk of lung cancer in humans exposed to nickel chloride (Grimsrud *et al*. 2003), nickel sulfate, water-soluble nickel compounds in general (Grimsrud *et al.* 2003; 2002; 2005; Andersen *et al*. 1996), insoluble nickel compounds, nickel oxides (Andersen *et al*. 1996; Anttila *et al*. 1998; Grimsrud *et al*. 2003), nickel sulfides (Grimsrud *et al*. 2002) and mostly insoluble nickel compounds (Andersen *et al*. 1996). An additional study, in which various nickel compounds and lung cancer risk were modelled, identified risk from water-soluble nickel and metallic nickel (Easton *et al*. 1992). The largest study addressing worker exposure to metallic nickel (in combination with nickel oxide) showed a small but significant elevation in lung cancer risk (Arena *et al*. 1998). However, IARC (2011) found the available epidemiological data was insufficient to produce entirely separate dose-response analyses for specific nickel compounds.

Data obtained in experimental animals supported the IARC (2011) analysis of the epidemiological study findings, indicating increased lung tumours (regardless of the exposure route). In rats, chronic inhalation of nickel oxide (NTP 1996a), nickel subsulfide (NTP 1996b; Dunnick *et al*. 1995; Ottolenghi *et al*. 1975) and nickel carbonyl (Sunderman *et al*. 1959; 1957) increased the incidence of lung tumours; however, inhalation of metallic nickel did not (Oller *et al*. 2008). Chronic intratracheal instillation of nickel oxide, nickel subsulfide or metallic nickel increased lung tumours in rats (Pott *et al*. 1987). In mice, chronic intraperitoneal injection of nickel acetate (Poirier *et al*. 1984; Stoner *et al*. 1976) or intramuscular injection of nickel subsulfide (Waalkes *et al*. 2004) also produced lung tumours. Chronic inhalation of nickel oxide, nickel subsulfide (NTP 1996b; Dunnick *et al*. 1995) and metallic nickel (Oller *et al*. 2008) was also associated with increased adrenal medulla pheochomocytoma in rats. Lung tumour formation did not increase after chronic inhalation of nickel sulfate in rats (NTP 1996c; Dunnick *et al*. 1995), gavage exposure of rats to nickel sulfate (Heim *et al*. 2007) or inhalation of nickel subsulfide in mice (Dunnick *et al*. 1995). Transplacental nickel acetate exposure induced malignant pituitary tumours in rat pups (Diwan *et al*. 1992). In addition, various nickel compounds (nickel oxides, nickel sulfides, including nickel subsulfide, nickel sulfate, nickel chloride, nickel acetate, nickel sulfarsenide, nickel arsenide, nickel antimonide, nickel telluride, nickel selenide, nickelocene and metallic nickel) administered by repository injection caused local sarcomas in multiple studies and models (cited in IARC 2011).

6.8.3 Carcinogenic mode of action

According to the "Nickel-Ion (Bioavailability) Hypothesis" (Hansen & Stern 1983; Goodman *et al*. 2011; Costa *et al*. 1981), the carcinogenic potential of the various nickel compounds appear to be a function of the capacity to raise the intracellular concentration of nickel ions and the duration of the increase. The intracellular nickel concentration is a function of the exposure concentration, nickel species, particle size and duration of exposure.

Fluorescent labeling studies have been used to compare the cellular uptake of soluble and insoluble nickel compounds. Both soluble and insoluble nickel compounds were able to elevate Ni^{2+} concentrations in the cytoplasmic and nuclear compartments of the human bronchial epithelial adenocarcinoma A549 cell line after 8 hr incubation; however, when the nickel source was removed, intracellular Ni^{2+} derived from $NiCl_2$ was lost from the cells significantly faster

than that derived from Ni_3S_2 (Ke *et al.* 2007). In the human THP-1 monocyte-macrophage cell line, the time of initial exposure appeared to be a critical factor in the reversibility of soluble Ni uptake: as the initial exposure period increased, the loss of soluble nickel slowed and a greater percentage of cellular nickel was found in the nucleus. Increased nickel retention appeared to be a function of the distribution (i.e., to the nucleus, and nucleoli, which increased from 25% after a 8 hr incubation to 60% after 48 hr) and/or binding, and was not merely the result of increased uptake with prolonged incubation (Edwards *et al.* 1998). Similar reductions in the rate of release of cellular Ni^{2+} as the initial exposure period increased were reported in mouse fibroblast cell lines cultured with $^{63}NiCl_2$, although intracellular nickel concentrations were higher than those reported for human macrophages in Edwards *et al.* (1998): only 36% of the $^{63}Ni^{2+}$ was found in fibroblast nuclei after 48hr (Webb & Weinzierl 1972; Wataha *et al*. 1992). In HaCaT human keratinocytes cultured with 0.1 and 1 mM $^{63}NiCl_2$ for 24 hr, the HaCaT cells were able to take up nickel at concentrations 1.8- to 4-fold greater than those present in the media, suggesting specific intracellular binding sites (which may, in part explain the greater propensity of soluble nickel to remain within the cell after more prolonged incubation); however, the proportion of nickel in the cell pellets (nuclei plus cellular membranes) after lysis never exceeded 4.4% of total cellular nickel (Ermolli *et al*. 2001).

These results indicate that nuclear nickel may be elevated in the continuous presence of any form of nickel. For insoluble nickel particles, intracellular levels are expected to be high as particles are phagocytosed and nickel ions gradually released inside cells, as opposed to the more rapid clearance of soluble nickel (due to maintenance of fluid balance by fluid pinocytosis or other mechanisms; see Cellular Uptake). The greater carcinogenic activity of crystalline nickel sulfides may therefore be a function of greater and more persistent Ni^{2+} accumulation in the cell and/or nucleus than can occur after exposure to soluble nickel salts. Such differences may be particularly important for single or intermittent (e.g., occupational) exposure, but may be less distinct with more prolonged exposure. After 1-3 day exposures to crystalline nickel particles, genes placed near heterochromatin are epigenetic silenced, an effect not seen after similar short-term exposure to soluble nickel compounds; however, a 3-week exposure to soluble $NiCl_2$ is also able to induce gene silencing (Costa *et al*. 2005). Alternately, solubilisation of crystalline nickel may form a more carcinogenic intermediate (as yet unidentified). Soluble nickel may nonetheless have extranuclear effects (e.g., at the cell membrane to alter signal transduction) in target cells; although not sufficient to induce tumours by themselves, may enhance tumour induction by co-exposures to other carcinogenic substances (e.g., $N_{i3}S_2$, cigarette smoke) (cited in Costa *et al*. 1981; Fletcher *et al*. 1994; Goodman *et al*. 2011; Ke *et al*. 2007). Cigarette smoking has been postulated to cause the transformation of respiratory epithelium to squamous epithelium, which may promote and enhance the carcinogenic effects of inhaled nickel from the occupational atmosphere of nickel industry workers (Torjussen *et al*. 2003).

A recent weight of evidence review of the carcinogenicity of water-soluble nickel compounds concluded there was no evidence that soluble nickel compounds act as complete carcinogens (Goodman *et al*. 2009); however, soluble species are suspected to enhance the carcinogenicity of insoluble nickel species (ATSDR 2005; OMOE 2004).

Available data indicate nickel has a limited capacity to interact directly with DNA to produce mutagenic effects (cited in IARC 2011). However, nickel produces significant alterations in cellular metabolism, including stimulation of glycolytic activity, alteration of iron homeostasis,

depletion of ascorbate and hypoxic stress, which lead to the modulation of gene expression through epigenetic changes. Co-exposure to genotoxic carcinogens may exacerbate the genotoxic effects of nickel (cited in Salnikow *et al*. 1999).

6.8.4 Classification

Health Canada (1996) and several other agencies classify nickel as a human carcinogen *via* inhalation. Health Canada (1996) includes oxidic, sulphidic and soluble nickel in Group I (carcinogenic to humans) via the inhalation route. This is supported by both human epidemiological studies and laboratory animal carcinogenicity studies. Health Canada (1996), the US EPA (1996), WHO (2002) and the European Commission (Eur Comm 2007; 2001) have calculated unit risk values for various species of nickel *via* inhalation. Both cancer and non-cancer endpoints are significant in the toxicological evaluation of nickel. Nickel refinery dust (most of which is believed to be nickel subsulphide) and Ni_3S_2 are classified as a Class A carcinogens (carcinogenic to humans) by the US EPA (1996) based on human data where lung and nasal tumours were elevated in exposed workers and on rat data in which carcinomas were produced by inhalation and injection (e.g., Sunderman 1984; Sunderman & Horak 1981). The US EPA also classifies nickel carbonyl as a probable human carcinogen (Group B2) based on the incidences of pulmonary carcinomas and malignant tumours in rats after inhalation and intravenous injection.

The International Agency for Research on Cancer (IARC 1990) evaluation recognised all Ni^{2+} compounds as human carcinogens (Group 1), and metallic nickel was classified as possibly carcinogenic to humans (Group 2B) (IARC 1990).

In view of the overall findings in animals, IARC (2011) concluded there was sufficient evidence for the carcinogenicity of nickel compounds and nickel metal in experimental animals. IARC (2011) also concluded there was sufficient evidence in humans for nasal and/or pulmonary carcinogenicity of mixtures that include nickel compounds and nickel metal. Based on the Norwegian refinery worker studies, the strongest evidence of association was between exposure to water-soluble nickel compounds and the risk of lung cancer; there was also independent evidence for the carcinogenicity of oxidic and sulfidic nickel compounds.

IARC (2011) acknowledged that nickel metal dust can become solubilised and bioavailable after inhalation. In recognition of the underlying concept that all nickel compounds can generate nickel ions at critical sites in their target cells, provision of separate classifications for nickel and nickel compounds was no longer considered warranted and all nickel compounds were considered carcinogenic to humans (Group 1) (IARC 2011)

6.9 Toxicological Reference Values

The potency of nickel appears to be dependent upon its form/speciation in the environment and the route of exposure. For nickel in soils, the most toxic form *via* oral exposure was considered to be total nickel as soluble salts (predominantly nickel sulphate and nickel chloride). For the inhalation pathway, combined soluble, oxidic and sulphidic nickel species were considered to be of greatest toxicological concern. The toxicity reference values (TRVs) selected for combined oral and dermal exposure and for inhalation exposure are discussed below and summarised as follows:

- Combined Oral + Dermal TDI 11µg Ni/kg bw/d
- Inhalation Tolerable Concentration (TC) (non-cancer effects) 0.02 µg/m^3
- Inhalation Unit Risk Value (non-threshold effects) $1.3x10^{-3}$ (µg $Ni/m^3)^{-1}$

6.9.1 Oral Exposure

For evaluation of oral exposures, the TRVs for soluble nickel (including nickel sulphate and nickel chloride) from various agencies were considered. TRVs for soluble forms of nickel were identified from Health Canada (1994), US EPA (1996) and IOM (2001); however, a more recent evaluation from WHO (2005) with a Tolerable Daily Intake (TDI) of 11 µg Ni/kg bw/day, was used for the purpose of this assessment. WHO (2005) developed this TDI based on the EU (2004) re-analysis of the SLI (2000b) two-generation rat study, where a LOAEL of 2.2 mg/kg bw/day (for post-implantation loss and perinatal mortality) and a NOAEL of 1.1 mg/kg bw/day were derived. Using an uncertainty factor of 100 (10-fold for interspecies differences and 10-fold for intraspecies differences), the TDI for nickel, as nickel sulphate, was identified as 11 µg Ni/kg bw/day.

Nickel is not considered to be carcinogenic via the combined oral and dermal routes and, thus, the TDI of 11 µg Ni/kg bw/day is considered to be protective of all endpoints.

Since the estimated daily intake (EDI, an estimate of exposure) is larger than the TDI for certain exposure scenarios for nickel. An alternate approach (sections 8.5.1 and 8.5.2 and Appendix 11) was adopted that is based on a negligible increase to estimated exposure rather than tolerable intakes. This approach is considered conservative while technically applicable.

6.9.2 Inhalation Exposure – Non-Cancer Effects

For evaluation of inhalation exposures, the TRVs for nickel sulphate and nickel oxide from various agencies were considered. Although a TRV for nickel sulphate *via* the inhalation route was identified from Health Canada (EC and HC 1994), a series of more recent inhalation studies from the National Toxicology Program using nickel sulphate, nickel oxide and nickel subsulphide (NTP 1996a; 1996b; 1996c) have been identified (see Section 6.6.2). The OEHHA (2012) identifies inhalation TRVs for nickel and nickel compounds (except NiO) as well as a separate inhalation TRV for nickel oxide. The inhalation TRV for nickel sulphate and nickel oxide was based on a weight of evidence approach using Environment Canada and Health Canada (1994), ATSDR (2005) and European Commission (2001; 2007) information.

Health Canada (EC and HC 1994) recommended a Tolerable Concentration (TC) of 0.0035 µg Ni/m^3 for nickel sulphate based on a LOAEL of 20 µg/m^3 (Dunnick *et al*. 1989), adjustment for less than continuous experimental conditions, and application of a 1000-fold uncertainty factor (10 for interspecies differences, 10 for intraspecies differences and 10 for use of a subchronic study).

Health Canada (1996) recommended a TC of 0.02 µg Ni/m^3 for nickel oxide based on a LOAEL of 25 µg Ni/m^3 (Spiegelberg *et al*. 1984) and application of a 1000-fold uncertainty factor (10 for interspecies differences, 10 for intraspecies difference and 10 for use of a subchronic study and minimal effects at the LOAEL).

Since the publication of the above TCs, additional research has been completed by NTP (1996a, 1996b; 1996c) that is considered more appropriate for the selection of an inhalation toxicity value (EC 2007; Eur Comm 2001; ATSDR 2005). Consequently, the Health Canada values were not used in a direct quantitative manner as the inhalation TRVs for nickel sulphate and nickel oxide but were considered in the overall analysis.

For nickel sulphate, ATSDR (2005) developed a Minimal Risk Level (MRL) for chronic exposures (a TRV that is essentially equivalent to the Health Canada term "Tolerable Concentration" and defined as estimates of daily human exposures to a substance that would not cause appreciable risk of non-carcinogenic adverse human health effects over specified exposure durations [Chou *et al*. 1998] based on NTP (1996a). The ATSDR derives MRLs by dividing a NOAEL by an uncertainty factor. For inhalation exposures, a regional deposited dose ratio (RDDR) is used to derive a human equivalent concentration for particles from animal exposure studies when no adequate human data are available. The RDDR is used to adjust the exposure effect level for interspecies dosimetric differences for a given exposure in an animal species to the same exposure in a human (US EPA 1994).

The LOAEL based on active lung inflammation in the NTP (1996a) two-year nickel sulphate inhalation study on rats was reported to be 60 µg Ni/m^3, while the NOAEL was identified to be 30 µg Ni/m^3 (see Section 6.6.2). ATSDR (2005) then estimated a chronic MRL based on:

- Use of the NOAEL of 30 µg/m^3; a time adjusted NOAEL ($NOAEL_{ADJ}$) of 5.4 µg/m^3 (i.e., 30 µg/m^3 x 6 hr/24 hr x 5 days/7 days); a NOAEL human equivalent concentration ($NOAEL_{HEC}$) of 2.7 µg/m^3 (i.e., $NOAEL_{HEC}$ = $NOAEL_{ADJ}$ by the Regional Deposited Dose Ratio [RDDR], of 0.506) (i.e., 5.4 µg/m^3 x 0.506 = 2.7 µg/m^3); and, an uncertainty factor of 30 (3-fold for interspecies differences with dosimetric adjustment and 10-fold for intraspecies differences).

Based on the above NTP studies, ATSDR calculated a chronic MRL of 0.090 µg Ni/m^3 for nickel sulphate as follows:

$$\text{MRL} = \frac{\text{NOAEL} \times \text{Time Adjustment} \times \text{RDDR}}{\text{Uncertainty Factor}}$$

$$= \frac{30\ \mu\text{g/m}^3 \times 6\ \text{hr}/24\ \text{hr} \times 5\ \text{days}/7\ \text{days} \times \text{RDDR}}{30}$$

$$= 0.090\ \mu\text{g Ni/m}^3$$

Using the same NTP studies as above, the European Commission (2007) recommended an air quality standard of 0.020 µg Ni/m^3 for nickel (all forms) for protection of cancer and non-cancer effects. To develop a "limit value" for nickel sulphate (which is then assumed to represent all forms of nickel), the European Commission (2001) relied upon the NTP (1996a) nickel sulphate study. Contrary to the ATSDR (2005) interpretation, the European Commission (2001) concluded that there was no clear NOAEL in rats or mice, as they concluded that there was a possible increased rate of fibrosis in rats at 30 µg/m^3, and based their analysis on a statistically significant LOAEL of 60 µg/m^3 in both mice and rats. The European Commission (2001) then calculated an upper limit based on the following:

- Use of a LOAEL of 60 µg/m^3; a time adjusted LOAEL (LOAEL$_{ADJ}$) of 11 µg/m^3 (i.e., 60 µg/m^3 x 6 hr/24 hr x 5 days/7 days); and an uncertainty factor of 1000 (10-fold for interspecies differences, 10-fold for intraspecies differences and 10-fold for use of a LOAEL).

Based on the above, an upper limit was calculated as follows:

$$\text{UL} = \frac{\text{LOAEL} * \text{Time Adjustment}}{\text{Uncertainty Factor}}$$

$$= \frac{60\mu g/m^3 \times 6hr/24hr \times 5\ days/7days}{1000}$$

$$= 0.011\ \mu g\ Ni/m^3$$

The European Commission (2001) noted that if a NOAEL approach (i.e.,30 µg/m^3) was used, the upper limit would have been 0.05 µg/m^3 (same time adjustment but an uncertainty factor of 100). Thus, they (Eur Comm 2001) recommended that the upper limit value for nickel should be between 0.010 and 0.050 µg/m^3, which are also considered protective of an incremental lifetime cancer risk of 1 in 1 000 000.

Based on the above range, the EU (2008) recommended an air quality standard of 0.020 µg/m^3. It is not clear how this specific value was selected from the range of values available but this value lies toward the lower end of acceptable values.

Overall, for the purposes of SQG$_{HH}$ development, a Tolerable Concentration of 0.020 µg Ni/m^3 was assumed for both nickel sulphate and nickel oxide for protection of non-cancer effects. This value is based on the air quality standard recommended by the EU (2008) for nickel sulphate, as well as the TC of 0.02 µg Ni/m^3 for nickel oxide (HC 1994). The LOAEL and NOAEL derived from the NTP (1996a; 1996b; 1996c) studies are considered more relevant than the LOAEL from Dunnick *et al.* (1989) because the NTP studies were chronic studies (2 year study) compared to the subchronic study (13 weeks) by Dunnick *et al.* (1989). The TC of 0.02 µg Ni/m^3 recommended by the EU (2008) for all forms of nickel for the protection of non-cancer effects is the same value as the TC for nickel oxide based on Spiegelberg *et al*. (1984) established previously (HC 1996).

6.9.3 Inhalation - Carcinogenic Effects

Health Canada (1996) provided a TC$_{05}$ of 40 µg Ni/m^3 for exposure to combined oxidic, sulphidic and soluble nickel, based on the estimated TC$_{05}$ for lung cancer mortality for the same combination of compounds from concentrations of 40-1000 µg/m^3 in mining, smelting and refining operations in Ontario and Norway (IARC 1990). In calculating nickel cancer potency, Health Canada (1996) reported that lung cancer was a more sensitive endpoint than nasal cancer. The TC$_{05}$ corresponds to a unit risk value of 1.3 x 10^{-3} (µg Ni/m^3)$^{-1}$ and risk specific concentrations of 0.0008 µg/m^3 and 0.008 µg/m^3 for an incremental lifetime cancer risks of 1 x 10^{-6} and 1 x 10^{-5} respectively. The values for protection of carcinogenic effects are more stringent than the Tolerable Concentration of 0.02 µg Ni/m^3 for protection of non-cancer effects (see Section 6.9.2).

In addition to the TC_{05} for oxidic, sulphidic and soluble nickel, Health Canada (1996) provided a soluble nickel salts TC_{05} of 70 $\mu g/m^3$ for lung cancer mortality based on data from an epidemiology cohort study from Norway (IARC 1990). Soluble nickel was considered to consist primarily of nickel sulphate and nickel chloride. This TC_{05} corresponds to a unit risk value of 7.1×10^{-4} $(\mu g\ Ni/m^3)^{-1}$ and risk specific concentrations of 0.0014 $\mu g/m^3$ and 0.014 $\mu g/m^3$ for an incremental lifetime cancer risks of 1×10^{-6} and 1×10^{-5} respectively. These values are more stringent than the Tolerable Concentration of 0.02 $\mu g/m^3$ for protection of non-cancer effects (see Section 6.9.2).

Some research has indicated that soluble nickel salts may not be carcinogenic in the absence of other forms of nickel. Using US EPA guidelines for assessment of carcinogenicity, TERA (1999) concluded that soluble nickel by itself should be considered to be unclassifiable with respect to carcinogenic potential (i.e., Class D). Nevertheless, the more sensitive TRV for combined oxidic, sulphidic and soluble nickel was used for derivation of SQG_{HH} for nickel; therefore, this SQG_{HH} would be protective of potential carcinogenic effects associated with exposure to soluble nickel salts alone.

Overall, a unit risk value of 1.3×10^{-3} $(\mu g\ Ni/m^3)^{-1}$ was used for nickel sulphate and nickel oxide for the purposes of SQG_{HH} development, for protection of carcinogenic effects.

7 DERIVATION OF ENVIRONMENTAL SOIL QUALITY GUIDELINES

Canadian soil quality guidelines are derived for the protection of receptors under four different land uses: agricultural, residential/parkland, commercial and industrial. The derivation of the following environmental soil quality guidelines are based on "*A Protocol for the Derivation of Environmental and Human Health Soil Quality Guidelines*" (CCME 2006). The information presented in this chapter builds upon, and adds to, data collected and evaluated for the derivation of the original Canadian Soil Quality Guideline for nickel in 1999 (EC 1999), and first published in CCME (CCME 1999).

This chapter describes the derivation of the Soil Quality Guidelines for Soil Contact, Nutrient and Energy Cycling check, Soil Quality Guidelines for Soil and Food Ingestion and Off-site migration check. The Soil Quality Guidelines for the Protection of Freshwater Life and the Soil Quality Guidelines for the Protection of Livestock Watering and Irrigation Water were not derived because the soil protocol (CCME 2006) does not evaluate subsurface transport of inorganic compounds. Concerns about soil based inorganic contaminants impacting water resources should be addressed on a site-specific basis.

7.1 Agricultural and Residential/Parkland Land Uses

7.1.1 Soil Quality Guidelines for Soil Contact

The derivation of the soil quality guidelines for soil contact (SQG_{SC}) is based on toxicological data for vascular plants and soil invertebrates. The toxicological data available for plants and invertebrates are presented in Chapter 4 and Appendix 3 (plants) and Appendix 4 (invertebrates). Data in the Appendices that are listed as "Selected" were considered during guideline development, while those listed as "Consulted" were not considered acceptable for guideline derivation. Common reasons for classifying a study as consulted include test soil properties which may result in conditions of excessively high (e.g., <pH 4) or low bioavailability (e.g., high OM), study information lacking, improper or lacking statistics, controls, or replication, or no obvious dose-response relationship. A total of 12 plant studies covering 16 species and 147 endpoints, and 9 invertebrate studies covering 7 species and 51 endpoints were acceptable for use (i.e., toxicity studies that were classified as "Selected"). All acceptable endpoints were screened to ensure that only the most appropriate endpoints, and derivation method, were retained in guideline derivation. Briefly, the screening criteria are (see section 7.5.5.1 of CCME 2006);

- If multiple endpoints exist from a single study, only discrete endpoints were used, e.g., if a study reported an EC_{25} and EC_{50} from the same experiment, only one endpoint was used. EC_{25} and/or IC_{25} endpoints were preferred (or ECx or ICx where "X" is close to 25)
- Biologically relevant effects were preferred (e.g., growth over physiological)
- Studies with longer test durations were preferred
- Endpoints expressed as > X mg/kg were not used

Two EC_{25}s for alfalfa (Kapustka *et al*. 2006) were combined due to similar responses, and test conditions, in two separate soils (EC_{25} for alfalfa total dw/plant used in guideline derivation = 31.8 mg/kg = √(33.9 mg/kg × 29.8 mg/kg)). In contrast, oat and barley are represented more than once in the derivation data set (twice each) because of varying responses potentially due to

different soil conditions. Significant positive relationships between cation exchange capacity (CEC) and EC_{10} and EC_{50} 21-d tomato shoot growth were reported in 16 European soils ($p < 0.001$, each). The EC_{50} (50% inhibition) ranged from 17 to 920 mg/kg in the 16 soils (Rooney *et al*. 2007). To account for the variation in response due to different soil types, but not to bias the guideline data set with too many tomato data points, a total of two data points were selected from Rooney *et al.* (2007) as follows; a geometric mean of EC_{20}s were taken from soils with CEC <12 cmol/kg, and a separate geometric mean from soils with CEC >12 cmol/kg (CEC median value was ~12 cmol/kg). Four soils were omitted from the calculations because of, pH <4 (Houthalen, Belgium), elevated background levels of nickel (Souli, Greece; Brécy, France) and the estimated effect concentration is less than the lowest added nickel dose (Aluminusa, Italy). The resulting data points are 55 mg/kg and 280 mg/kg for 21-d EC_{20} tomato shoot growth.

The minimum data requirements for use of the preferred weight-of-evidence approach for guideline derivation were met using an EC_{25} (or IC_{25}) distribution. The resulting data-points for plants, 16 data-points from 13 species, and invertebrates, 5 data-points from 5 species, were combined in an “estimated species sensitivity distribution" in which the rank percentile was plotted against observed effect concentrations on a log scale (Figure 1). There were insufficient invertebrate data (minimum 10 data-points needed) to derive separate soil contact guidelines for plants and invertebrates.

The threshold effects concentration (TEC) was calculated as follows:

$$\mathrm{TEC} = \frac{\mathrm{ESSD}_{25}}{\mathrm{UF}}$$

where,

TEC = threshold effects concentration (mg/kg) - i.e., guideline value
$ESSD_{25}$ = estimated species sensitivity distribution - 25th percentile of the distribution (mg/kg)
UF = uncertainty factor (if needed); no uncertainty factor was applied.

A total of 21 acceptable EC_{20} or EC_{25} were ranked and the 25th percentile is used as the basis for the soil contact guidelines for agricultural and residential/parkland land uses (CCME 2006). The 25th percentile of the ESSD corresponds to a rank of 5.5. The 5th and 6th ranked data points in the distribution were 42 mg/kg and 47.3 mg/kg, respectively. A value was interpolated for rank 5.5 (25th percentile) as follows;

$ESSD_{25}$= rank 5 + 0.5 × (rank 6- rank 5)

= 42 mg/kg + 0.5 × (47.3 mg/kg – 42 mg/kg)

= 44.7 mg/kg

The Threshold Effects Concentration is calculated as 44.7 mg/kg, and is rounded to two significant figures to equal 45 mg/kg.

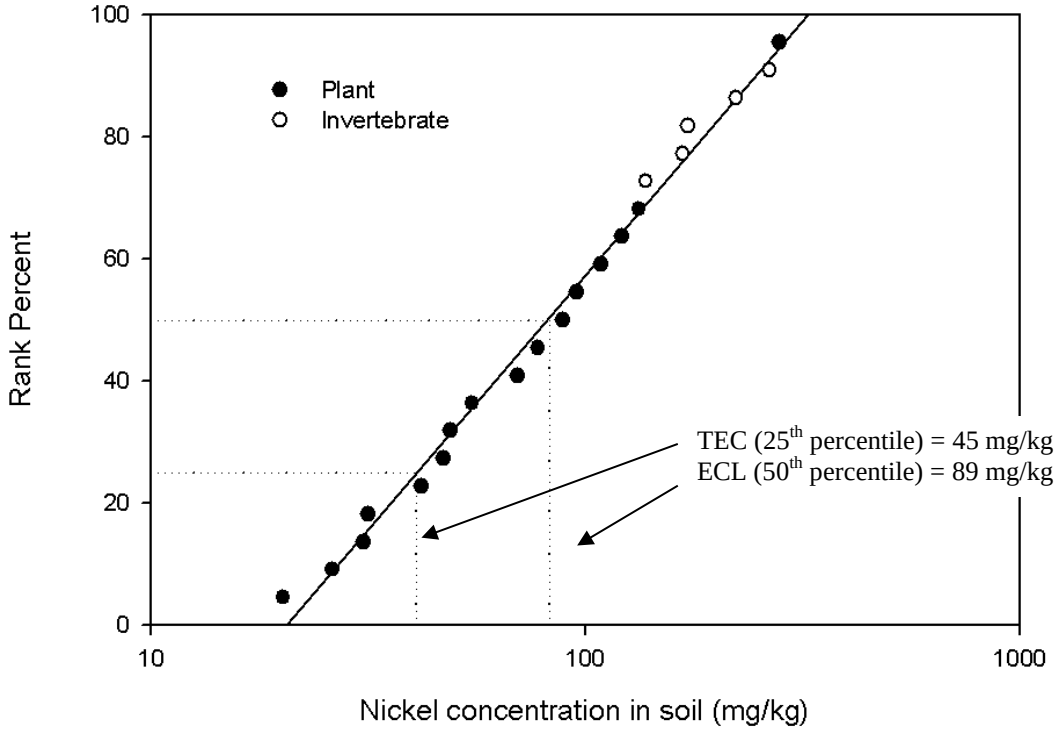

Figure 1: Rank probability plot of nickel bioassay data for plants and invertebrates.

Threshold Effects Concentration = TEC, Effects Concentration - Low = ECL. Straight line is for visual purposes only.

7.1.2 Soil Quality Guidelines for the Protection of Nutrient and Energy Cycling

The Soil Quality Guidelines for the Protection of Nutrient and Energy Cycling (SQG_{NEC}) is derived to protect microbes, and the vital soil functions they perform (e.g., nutrient fixation and recycling, decomposition, respiration). The toxicological data available for microbial processes are presented in Chapter 5 and Appendix 2. Data in Appendix 2 listed as "Selected" were considered during guideline development. Consulted studies were not considered during the guideline derivation process; common reasons for classifying microbial studies as consulted include test soil properties which may result in conditions of excessively high (e.g., <pH 4) or low bioavailability (e.g., high OM), study information lacking, improper or lacking statistics, controls, or replication, no obvious dose-response relationship, or endpoints which are not preferred (e.g. enzymatic effects, abundance and diversity). Nitrification and nitrogen fixation data are considered to be primary data, whereas nitrogen mineralisation, denitrification and carbon cycling data are considered secondary data (see soil protocol Appendix B for more detail on endpoint selection and guideline derivation). LOEC data, as reported by the author(s), are used directly, while effective concentration (EC) data producing ≥15 and ≤40% effects in primary data (i.e., EC_{15} to EC_{40}) and ≥15 and ≤25% effects in secondary data (i.e., EC_{15} to EC_{25}) are interpreted as LOEC values. The preferred Weight of Evidence method for guideline

derivation could not be used because no nitrogen fixation studies were available. The modified LOEC method was used to derive the guideline using both primary (1 nitrification data point) and secondary data (8 data points covering nitrogen or carbon mineralisation).

The Soil Quality Guideline for the Protection of Nutrient and Energy Cycling (SQG_{NEC}) was calculated as follows:

$$SQG_{NEC} = (LOEC_1 \times LOEC_2 \times LOEC_3 \times ... LOEC_n)^{1/n}$$

where,

SQG_{NEC} = nutrient and energy cycling check (mg/kg)
LOEC = lowest observed effect concentration, or EC_x equivalent (mg/kg)
n = number of available LOECs

thus,

$$NEC = (10 \times 100 \times 100 \times 100 \times 250 \times 294 \times 294 \times 583 \times 1000)^{1/9}$$

$$= 171 \text{ mg/kg}$$

The Soil Quality Guideline for the Protection of Nutrient and Energy Cycling (SQG_{NEC}) for agricultural and residential land uses is 171 mg/kg.

7.1.3 Soil Quality Guidelines for Soil and Food Ingestion

The soil quality guideline for soil and food ingestion (SQG_I) for nickel applies only to agricultural land use.

Calculation of the Daily Threshold Effect Dose

Calculation of the SQG_I is based on the lowest-observed-adverse-effects level (LOAEL) taken from the mammalian and avian toxicological data listed in Appendices 5 and 6. The lowest LOAEL was 14.6 mg Ni/kg bw/d, which resulted in a 44% reduction in growth rate for Holstein calves over an 8 week period (O'Dell *et al.* 1971). Two mammalian studies had lower LOECs, however they were not selected because the relevance of decreased sperm cell counts (Pandey & Srivastava 2000) to population viability is unknown, and the biological relevance of an 8% decrease in growth (Adjroud 2011) is considered negligible. For avian toxicity, a LOEC of 0.051 mg Ni/kg bw/d for reduced growth (36% reduction) in laying hens was calculated (Arpasova *et al*. 2007). This study was not used because there are no corroborating toxicity tests showing similar magnitude of effects at this dose level (see Appendix 6), and two publications by the same group of authors, with a similar experimental design, indicate that test concentrations reported in Arpasova *et al.* (2007) were likely incorrectly reported as 1000 times lower than the actual test concentrations used (Kolesarova *et al.* 2008; Capcarova *et al*. 2008).

The LOAEL is used to calculate the daily threshold effects dose (DTED) according to the equation:

$$DTED = \frac{\text{lowest LOAEL}}{UF}$$

where,

DTED = daily threshold effects dose (mg/kg bw/d)

LOAEL = lowest observed adverse effects level (mg/kg bw/d)
UF = uncertainty factor; no uncertainty factor was applied as the LOAEL was considered to be significant.

Thus,

$$\text{DTED} = 14.6 \text{ mg/kg bw/d}$$

An animal may be exposed to a contaminant by more than one route. Total exposure comes from a combination of contaminated food, direct soil ingestion, dermal contact, contaminated drinking water and inhalation of air and dust. Exposure from all of these routes should not exceed the DTED. Assuming that drinking water, dermal contact and inhalation account for 25% of the total exposure (CCME 2006), the remaining 75% of exposure is attributed to the ingestion of food and soil. It follows then, that exposure from soil and food ingestion should not exceed 75% of the DTED:

$$\text{Exposure from direct soil ingestion} + \text{Exposure from food ingestion} = 0.75 \times \text{DTED}$$

7.1.3.1 Exposure from Direct Soil Ingestion

To estimate the exposure of an animal from direct soil ingestion, the rate of soil ingestion must be calculated. The soil ingestion rate is usually calculated by multiplying the dry matter intake rate (DMIR; the ingestion rate of soil and forage together) by the proportion of soil ingested (PSI) (CCME 2006). As an alternative to estimating a DMIR for cattle from the literature, the soil ingestion rate was estimated from the PSI and food ingestion rate as follows:

$$\text{SIR} = \frac{\text{FIR} \times \text{PSI}}{1 - \text{PSI}}$$

where,

SIR = soil ingestion rate (kg dw soil/d)
FIR = food ingestion rate (kg dw food/d); 5.6 kg/d for Holstein calves (O'Dell *et al*. 1971)
PSI = geometric mean of available soil ingestion proportions reported with DMIR. As no information is available on the PSI for Holstein calves, a generic default value of 0.082 for cows (McMurter 1993) was used for the above equation.

Thus,

$$\text{SIR} = \frac{5.6 \text{ kg/d} \times 0.082}{1 - 0.082}$$

$$\text{SIR} = 0.5 \text{ kg dw soil/d}$$

The SIR can then be combined with the bioavailability factor (BF), body weight (BW) and a concentration of the contaminant in the soil (SQGI) to represent the exposure from soil ingestion:

$$\text{Exposure from soil ingestion} = \frac{\text{SQG}_\text{I} \times \text{SIR} \times \text{BF}}{\text{BW}}$$

where,

SIR = soil ingestion rate (kg dw soil/d)
BF = bioavailability factor; due to insufficient information on the bioavailability of nickel

from ingested soil for livestock and terrestrial wildlife, a BF of 1 is assumed

SQG_I = concentration of the contaminant in soil that will not result in >75% DTED (mg/kg)

BW = mean body weight (kg); 116 kg for Holstein calves (O'Dell *et al*. 1971)

The soil concentration at this point is unknown, but it should not be greater than 75% of the DTED when combined with the exposure calculated for food ingestion.

7.1.3.2 Exposure from Food Ingestion

Similar to SIR, the food ingestion rate (FIR) for livestock and wildlife, is expressed as a portion of DMIR (CCME 2006). However, the FIR was taken directly from O'Dell *et al*. (1971) which reported a food ingestion rate of 5.6 kg dw food/d for the Holstein calves control group. The FIR can then be combined with the bioconcentration factor (BCF), BW and the SQG_I to express the exposure from food ingestion:

$$\text{Exposure from food ingestion} = \frac{SQG_I \text{ x FIR x BCF}}{BW}$$

where,

FIR = food ingestion rate (kg dw food/d); 5.6 kg/d for Holstein calves (O'Dell *et al*. 1971)

BCF = bioconcentration factor; calculated from the data on plant accumulation of nickel to be 0.34 (see Appendix 7).

SQG_I = concentration of the contaminant in soil that will not result in greater than 75% DTED (mg/kg).

BW = mean body weight (kg); 116 kg for Holstein calves (O'Dell *et al*. 1971)

7.1.3.3 Calculation of the Soil Quality Guidelines for Soil and Food ingestion–Primary Consumers

The equations for exposure from soil ingestion and exposure from food ingestion can be combined and rearranged to solve for the SQG_I:

$$\frac{(SQG_I \times SIR \times BF)}{BW} + \frac{(SQG_I \times FIR \times BCF)}{BW} = 0.75 \times DTED$$

Thus,

$$SQG_I = \frac{0.75 \times DTED \times BW}{(SIR \times BF) + (FIR \times BCF)}$$

$$SQG_I = \frac{(0.75 \times 14.6 \text{ mg/kg bw/d} \times 116 \text{ kg})}{(0.5 \text{ kg dw soil/d} \times 1) + (5.6 \text{ kg dw food/d} \times 0.34)}$$

$$SQG_I = 528 \text{ mg/kg}$$

The Soil Quality Guideline for Soil and Food Ingestion (SQG_I) for agricultural land use is 528 mg/kg.

7.2 Commercial and Industrial Land Uses

7.2.1 Soil Quality Guidelines for Soil Contact

The derivation of the soil quality guideline for soil contact (SQG_{SC}) is based on toxicological data for vascular plants and soil invertebrates. The SQG_{SC} for commercial and industrial land uses was derived using the same data and weight-of-evidence approach for guideline derivation as described in section 7.1.1 of this chapter.

The effects concentration low (ECL) was calculated as follows:

$$ECL = ESSD_{50}$$

where,
ECL = effects concentration low (mg/kg) - i.e., guideline value
$ESSD_{50}$ = estimated species sensitivity distribution - 50th percentile of the distribution (mg/kg)

A total of 21 acceptable EC20 and EC25 were ranked and the 50th percentile is used as the basis for soil contact guidelines for commercial and industrial land uses (CCME 2006). The 50th percentile of the ESSD corresponds to a rank of 11. The 11th ranked data-point has a value of 89 mg/kg, therefore, the Effects Concentration - Low was calculated as 89 mg/kg (see Figure 1 from section 7.1.1).

7.2.2 Soil Quality Guidelines for the Protection of Nutrient and Energy Cycling

The Soil Quality Guideline for the Protection of Nutrient and Energy Cycling (SQG_{NEC}) is derived to protect microbes, and the vital soil functions they perform (e.g. nutrient fixation and recycling, decomposition, respiration). The toxicological data available for microbial processes are presented in Chapter 5 and Appendix 2. Data in Appendix 2 listed as "Selected" were considered during guideline development. Consulted studies were not considered during the guideline derivation process; common reasons for classifying microbial studies as consulted include test soil properties which may result in conditions of excessively high (e.g., <pH 4) or low bioavailability (e.g., high OM), study information lacking, improper or lacking statistics, controls, or replication, no obvious dose-response relationship and endpoints which are not preferred (e.g., enzymatic effects, abundance and diversity). Nitrification and nitrogen fixation data are considered to be primary data, whereas nitrogen mineralisation, denitrification and carbon cycling data are considered secondary data. LOEC data, as reported by the author(s), are used directly, while effective concentration (EC) data producing ≥15 and ≤50% effects in primary data (i.e., EC15 to EC50) and ≥15 and ≤35% effects in secondary data (i.e., EC15 to EC35) are interpreted as LOEC values. The preferred Weight of Evidence method for guideline derivation could not be used because no nitrogen fixation studies were available. The modified LOEC method was used to derive the guideline using both primary (13 nitrification data point) and secondary data (13 data points covering nitrogen or carbon mineralisation).

The Soil Quality Guideline for the Protection of Nutrient and Energy Cycling (SQG_{NEC}) was calculated as follows:

$$SQG_{NEC} = (LOEC_1 \times LOEC_2 \times LOEC_3 \times \ldots LOEC_n)^{1/n}$$

where,

SQG_{NEC} = nutrient and energy cycling check (mg/kg)
LOEC = lowest observed effect concentration, or EC_x equivalent (mg/kg)
n = number of available LOECs

thus,

$$SQG_{NEC} = (10\times72\times100\times100\times100\times106\times116\times172\times183\times183\times193\times224\times235\times250\times 294\times294\times294\times294\times294\times294\times309\times502\times583\times1000\times1982\times3086)^{1/26} = 235\ \text{mg/kg}$$

The Soil Quality Guideline for the Protection of Nutrient and Energy Cycling (SQG_{NEC}) for commercial and industrial land uses is 235 mg/kg.

7.2.3 Environmental Soil Quality Guidelines for Off-site Migration

When deriving soil quality guidelines for commercial and industrial sites, exposure scenarios only consider on-site exposure. However, transfers of contaminated soil from one property to another are possible by environmental routes such as wind and water erosion (CCME 2006).

The environmental soil quality guideline for off-site migration ($SQG_{OM\text{-}E}$) refers to the concentration in soil eroded from a commercial or industrial site that will raise the contaminant concentration in an adjacent, more sensitive land (e.g., agricultural property) within a specific time frame. The purpose or the $SQG_{OM\text{-}E}$ is to establish commercial or industrial soil guidelines that will not result in unacceptable adverse effects (i.e., not to exceed agricultural guideline) to more sensitive land uses due to contaminant migration over a specified time period. The $SQG_{OM\text{-}E}$ was derived as follows:

$$SQG_{OM-E} = 14.3 \times SQG_{E-\text{agricultural land use}} - 13.3 \times BSC$$

where,
$SQG_{OM\text{-}E}$ = environmental soil quality guideline for off-site migration (mg/kg);
$SQG_{E\text{-agricultural land use}}$ = environmental soil quality guideline (SQG_E) for agricultural land use (45 mg/kg; see Table 5);
BSC = background concentration of nickel in the receiving soil (26.8 mg/kg, see Section 2.5.4).

The environmental soil quality guideline for off-site migration ($SQG_{OM\text{-}E}$) is 287 mg/kg.

7.3 Final Environmental Soil Quality Guidelines

The environmental soil quality guidelines are derived using the available toxicological data to determine the threshold level of effects for key ecological receptors. Exposure from direct soil contact is the primary derivation procedure used for calculating environmental quality guidelines for residential/parkland, commercial and industrial land uses. Exposure from direct soil contact as well as soil and food ingestion are considered in calculating guidelines for agricultural land use, with the lower of the two values generated from these derivation procedures being recommended as the environmental soil quality guideline for this land use. In addition to these primary derivation procedures, check mechanisms such as the nutrient and energy cycling and off-site migration are used to consider additional important direct and indirect soil exposure pathways. The soil contact and nutrient and energy cycling guidelines are applicable to soils

within the pH range of 4.0 to 8.6, as the toxicological studies upon which these guidelines are based were conducted within this pH range.

Agricultural Land Use

The final environmental soil quality guideline (SQG_E) is the lowest of the values calculated for all exposure pathways applicable for nickel (i.e., the lower of the SQG_{SC}, SQG_{NEC} and SQG_I) for this land use. Therefore, the SQG_E for agricultural land use is 45 mg Ni/kg soil, based on the SQG_{SC}.

Residential/Parkland Land Use

For contaminants that do not bioaccumulate and/or biomagnify, the SQG_E is the lowest of the values calculated for all exposure pathways applicable for nickel (i.e., the lower of the SQG_{SC} and SQG_{NEC}) for this land use. Therefore, the SQG_E for residential/parkland use is 45 mg Ni/kg soil, based on the SQG_{SC}.

Commercial and Industrial land uses

The SQG_E is the lowest of the values calculated for all exposure pathways applicable for nickel (i.e., the lowest of the SQG_{SC} and SQG_{NEC}) for this land use. The SQG_E may also be modified by the environmental soil quality guideline for off-site migration (SQG_{OM-E}). Therefore, the SQG_E for commercial and industrial land uses is 89 mg Ni/kg soil, based on the SQG_{SC}.

8 DERIVATION OF HUMAN HEALTH SOIL QUALITY GUIDELINES

8.1 Protocol

Human health soil quality guidelines describe concentrations of substances in soil at or below which no appreciable risks to human health are expected. In order to derive a quantitative guideline, it is necessary to define one or more scenarios by which exposure will occur. This assessment has been prepared assuming an urban setting, because 80% of the Canadian population resides in urban and suburban areas (Statistics Canada 2005). Given that 84% of these urban dwellers receive treated water supplies, mostly from surface water sources (EC 2005), the most likely route of exposure to contaminants in soil is expected to be direct contact with soil.

Human health Canadian soil quality guidelines are defined for agricultural, residential/parkland, commercial and industrial land uses according to the *Protocol for the Derivation of Environmental and Human Health Soil Quality Guidelines* (CCME 2006). Receptor characteristics, typical intake values for environmental media and estimated daily intakes used to calculate the human health SQGs are summarised in Appendices 8, 9 and 10 and are discussed in the relevant sections of this document.

As per the CCME (2006) protocol for inorganic parameters, human health soil quality guidelines are developed for the following three direct exposure pathways: soil ingestion, dermal contact with soil and inhalation of soil particulates. Health effects were assumed to be similar for exposures via the ingestion and dermal contact pathways; therefore, a single direct human health-based soil quality guideline (SQG_{DH}) for combined ingestion and dermal contact exposures was developed for each land use category.

Exposure via the inhalation pathway is expected to result in different types of health effects. Therefore, separate soil quality guidelines were developed for exposures via inhalation of soil particles.

Nickel is not considered to be carcinogenic to humans via ingestion (see Section 6.2) and is therefore treated as a threshold toxicant for derivation of human health soil guidelines for soil ingestion and dermal contact (CCME 2006). For threshold toxicants two key factors are considered in the setting of soil guidelines in Canada. First, it is recognised that, exclusive of hazardous waste sites or any other point source of pollution or elevated exposure attributable to lifestyle choices, everyone is exposed to a "background" level of contamination that cannot be avoided. For nickel (as total), this background exposure arises primarily from foods. In setting soil quality guidelines for inorganic, threshold substances, the background estimated daily intake (EDI) is subtracted from the Tolerable Daily Intake (TDI) before guidelines are derived using the approach outlined by CCME (2006). In addition to using CCME (2006) approach, an alternative approach (Appendix 11) was also used to set soil quality guidelines for nickel (as total) to address issues when the EDI approaches or exceeds the TDI.

Secondly, a multimedia approach to guideline development has evolved whereby guidelines for one medium are established recognising that guidelines for other media may also be required. Guidelines must be established in a manner such that total simultaneous exposure at the guideline levels for all media will not result in exposure which exceeds the TDI. Therefore, in order to set soil guidelines for threshold contaminants, some portion of the residual tolerable daily intake (TDI-EDI) must be attributed to each medium. As recommended by CCME (2006),

20% of the residual tolerable daily intake for threshold (non-carcinogenic) toxicants was apportioned to each environmental medium, namely air, water, soil, food and consumer products.

Nickel is considered a potential carcinogen via the inhalation pathway. Therefore, for the derivation of the direct human health-based soil quality guideline for particulate inhalation pathway ($SQG_{DH\text{-}PI}$), nickel was treated as a non-threshold toxicant (a substance for which there is considered to be some probability of harm for the critical effect at any level of exposure). The appropriate derivation for a soil quality guideline, therefore, employs a critical RSD (risk specific dose), based on incremental lifetime cancer risks (ILCR) from inhalation of soil-borne particulates. For all land uses, the adult was chosen as the receptor when considering lifetime cancer risk (CCME 2006).

The CCME Soil Quality Guidelines Task Group recommends the development of a soil guideline for a non-threshold toxicant based on an incremental risk from soil exposure of 10^{-6} or 10^{-5} (CCME 2006) (i.e., an incremental risk of 1 in 1 000 000 or 1 in 100 000, respectively) above background. Health Canada considers an incremental risk of less than 10^{-5} to 10^{-6} to be "essentially negligible" for the purpose of deriving Maximum Acceptable Concentrations (MACs) for carcinogenic chemicals in drinking water (NHW Canada 1989). Some provinces in Canada have adopted through policy an acceptable incremental lifetime cancer risk (ILCR) of 10^{-5}, and others have chosen 10^{-6}. Therefore, soil quality guidelines that are based on a cancer endpoint in humans associated with ILCRs of both 10^{-6} and 10^{-5} are presented in this document.

In addition to the direct contact soil quality guidelines, 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 human health soil quality guideline, based on professional judgement and the information available on the substance under consideration.

8.2 Estimated Daily Intake

Estimated daily intakes (EDIs) for the Canadian population have been derived on the basis of the environmental concentrations of nickel in background environmental media that are not associated with contamination (see Section 2.5). In general, the EDI is an estimate (in µg/kg bw/day) of the typical total concurrent background exposure 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 or remediated site, or activities that may result in increased exposure of substances, not considered background exposure.

CCME prescribes the use of an EDI estimated using a deterministic approach (CCME 2006). Recently, Health Canada developed a probabilistic approach to estimating the EDI (HC 2011). In 2010, the CCME Soil Quality Guidelines Task Group (SQGTG) accepted that a probabilistic approach to estimate the EDI could be used instead of a deterministic approach as data and substance-specific characteristics warrant. In the case of nickel, data were sufficient to determine a probabilistic EDI and that approach was used herein to determine the SQG_{DH}. The EDI methodology is briefly described below and more information is available in Health Canada (2011).

The EDI calculation is illustrated in the equation below (CCME 2006):

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

The EDIs are intended to represent the average exposure that the Canadian general population may receive from nickel. The general population is subdivided into five age classes including infants (birth to 0.5 years), toddlers (>0.5 to 4 years), children (5 to 11 years), teenagers (12 to 19 years) and adults (>20 years). The following media were considered in calculating the EDI: ambient air, indoor air, indoor dust, soil, drinking water, food and breast milk (for breastfed infants). Consumer products were not included in the EDI estimate because there are limited data for this medium. 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-day)
C = contaminant concentration in medium (e.g., mg/L)
CR = media specific contact rate (e.g., L/day)
BF = bioavailability factor (unitless)
EF = exposure factor (i.e., exposure frequency (events/year) x exposure duration (years/lifetime))
BW = body weight (kg)

Appendices 8 and 9 list the receptor characteristics used to develop the EDIs including: body weights and intake rates of air, drinking water, soil and dust for each specified age group of the population. Appendix 10 summarises the typical concentrations of nickel in environmental media and the daily intake estimates for nickel via all media for four age classes of the Canadian general population.

The estimated median daily intakes for adults, teenagers, children and toddlers are 3.8, 4.7, 7.7 and 10.6 µg Ni/kg bw/d. For infants up to 6 months, the EDI can range from 1.8 µg Ni/kg bw/d, for exclusively breast fed infants to 12 µg Ni/kg bw/d for non-breast fed infants. For the purpose of soil quality guidelines derivation, the EDI for toddlers and adults were used.

8.3 Nickel Speciation in the Environment

Nickel may exist in a variety of forms, including soluble (primarily nickel sulphate and nickel chloride), oxidic, sulphidic and metallic species.

8.3.1 Soil and Dust

Data on nickel speciation in soil are limited to sites in the vicinity of nickel processing facilities. These data suggest that nickel in soil is predominantly in the form of oxides and hydroxides with smaller contributions of metallic nickel and nickel sulphide (SARA 2008; OMOE 2002) (section 3.5). Soil speciation data is not available for sites that are free of the influence of nickel processing facilities.

For the purposes of SQG development, soluble nickel species are considered the most relevant for development of the SQGs for oral and dermal exposure because they are generally considered more potent than insoluble species and soluble nickel species are expected to comprise a significant proportion of total nickel in soils. Nickel sulphate has been chosen for the development of the Tolerable Daily Intake (TDI) used in this SQG (section 6.9.1). Nickel sulphate serves as a surrogate, in this case, for soluble nickel species which are, generally, more bioaccessible than insoluble species (section 6.3).

8.3.2 Air

Speciation data from the PM_{10} fraction of ambient air samples collected in several locations in Ontario, Canada indicate that nickel is present primarily in soluble forms with a significant contribution of oxidic forms (OMOE 2004; 2011a) (section 3.1). The predominant forms of nickel in total suspended particulate samples collected from both urban and industrial sites in Germany were nickel oxides and soluble nickel species with a small fraction of sulphidic and metallic nickel species (Füchtjohann *et al*. 2001). Speciation data from ambient air samples suggest that soluble and oxidic forms would be the primary forms present.

For the purposes of SQG development, oxidic, sulphidic and soluble nickel species were considered most relevant for inhalation exposure based on the following:

- Nickel in ambient air is expected to exist primarily as a combination of oxidic and soluble species.
- Oxidic and sulphidic forms of nickel are also considered carcinogenic via inhalation and soluble nickel species are suspected to enhance the carcinogenicity of these insoluble species.
- For the purpose of SQG derivation, a conservative inhalation toxicity reference value was identified as the speciation of nickel is unknown at all sites. The inhalation toxicity reference value applies to nickel in fugitive dust from soils, where speciation is unknown, rather than the species of nickel which may be common in ambient air.

8.4 Relative Absorption Factors

Relative absorption factors (RAF) may be applied when the critical toxicological study used a different medium than that under investigation, in order to account for the difference in absorption of the contaminant by the body from the two different media (HC 2010).

An RAF of 100% was assumed for inhalation since inhalation epidemiological studies were used to derive the TRVs for inhalation exposure (section 6.9.2 and 6.9.3) and it is assumed that nickel adsorbed to soils in fugitive dust would have a similar bioavailability as that of nickel adsorbed to particles in the epidemiological studies.

Nickel was administered to test animals by gavage in water in the critical study used to develop the TRV for oral exposure (section 6.9.1) and this TRV was also used to assess dermal exposure since no dermal TRV was identified. The bioavailability of nickel in soil via oral exposure will vary significantly depending on factors such as soil conditions, the form of nickel present in the soil and gastrointestinal conditions. There is insufficient information to relate the bioavailability of nickel in Canadian soils for the purpose of guideline derivation to that of nickel in water

administered via gavage in the critical study used to derive the TRV. Therefore, a relative absorption factor of 100% was selected for exposure via ingestion.

Moody *et al.* (2009) derived a dermal absorption of 1% for nickel in soil based on *in vitro* dermal absorption of soluble nickel across human skin (section 6.4.2.3.1). The relative dermal absorption factor (e.g., dermal absorption relative to absorption via oral exposure) is calculated by adjusting for absorption efficiency in the principle study used to derive the oral TRV (section 6.9.1). This can be calculated according to the following formula:

$$\text{Relative dermal absorption factor} = \frac{\text{Absolute dermal absorption rate}}{\text{Absolute oral absorption rate in TRV study}}$$

A relative dermal absorption factor of 0.091 was calculated, based on the dermal absorption of 1.0% reported in Moody *et al.* (2009) for nickel in soils, divided by the estimated oral bioavailability of 9.8% for nickel in water (Ishimatsu *et al*. 1995) (see Section 6.4.2). This RAF was selected for the derivation of human health soil quality guidelines (i.e., 1.0/9.8 = 0.102).

8.5 Ingestion and Dermal Pathways

8.5.1 Agricultural and Residential/Parkland Land Uses

For purposes of determining an agricultural and residential/parkland soil guideline for a threshold substance, it has been assumed that the receptor with the greatest exposure per unit mass is the most likely to have adverse effects. Based on the general characteristics attributed to the Canadian population (HC 1994; Richardson *et al*. 1997), this is a toddler aged >6 months to 4 years.

Using the above assumption, a guideline for soil ingestion and dermal contact which applies to agricultural, residential/parkland soil can be determined as:

$$SQG_{DH} = \frac{(TDI - EDI) \times SAF \times BW}{[(AF_G \times SIR) + (AF_S \times SR)] \times ET} + BSC$$

where,

SQG_{DH} = agricultural and residential/parkland direct human health-based soil quality guideline for soil ingestion and dermal contact (mg/kg)
TDI = tolerable daily intake (total nickel as soluble salts) = 11 µg/kg bw/day (WHO 2005)
EDI = estimated daily intake for toddler = 10.6 µg/kg bw/day (Section 8.2)
SAF = soil allocation factor = 20% by default (CCME 2006)
BW = body weight for toddler = 16.5 kg (CCME 2006)
AF_G = absorption factor from gut (medium specific) = 1 by default
AF_S = relative absorption factor for skin = 0.102 (Section 8.4)
SIR = soil ingestion rate for toddler = 0.08 g/day (CCME 2006)
SR = soil dermal contact rate for toddler

= 6.88 x 10^{-2} g/d [surface area of hands of 0.043 m^2 x soil adherence factor of 0.001 kg/m^2/d + surface of arms & legs of 0.258 m^2 x soil adherence factor of 0.0001 kg/m^2/d] (CCME 2006)

ET = exposure term (unitless) = 1 (7/7 d/wk x 52/52 wk/yr at the site, CCME 2006)

BSC = background soil concentration = 26.8 mg/kg dw (Section 2.5.4)

As shown above, the background soil concentration is added back into the equation to calculate the SQG. It is initially removed when the exposure resulting from it is subtracted out along with the estimated daily intake. If the estimated daily intake of nickel, as total nickel is greater or equal to the TDI for total nickel, as soluble salts (i.e., EDI ≥11 µg/kg bw/day) the human health soil quality guideline derived using the CCME (2006) protocol would be set to the background soil concentration of nickel. However,

- Recently, alternative approaches to address issues when the EDI approaches or exceeds the TDI have been considered (Appendix 11). Under such circumstances, soil quality guidelines (and risk assessments) could be based on an acceptable level of exposure that would be equal to the lower of the following: 20% of the TDI; or 10% of the EDI.

For nickel, "10% of the EDI" (i.e., 1.06 µg/kg bw/day for toddlers) represents a more conservative value than "20% of the TDI" (i.e., 2.2 µg/kg bw/day) for the toddler age group (for adults considered for industrial land use guidelines, the EDI does not exceed the TDI and, thus, this adjustment is not applicable). Using this approach, the value of "10% of the EDI" is recommended for use in derivation of the soil quality guideline for nickel. Consequently, the SQG_{DH} may be modified to:

$$SQG_{DH} = \frac{(0.1 \times EDI) \times BW}{[(AF_G \times SIR) + (AF_S \times SR)] \times ET}$$

where,

SQG_{DH} = agricultural and residential/parkland direct human health-based soil quality guideline for soil ingestion and dermal contact (mg/kg)

EDI = estimated daily intake for toddler =10.6 µg/kg bw/d (Section 8.2)

BW = body weight for toddler =16.5 kg (CCME 2006)

SIR = soil ingestion rate for toddler = 0.08 g/d (CCME 2006)

SR = soil dermal contact rate for toddler = 6.88 x 10^{-2} g/d (surface area of hands of 0.043 m^2 x soil adherence factor of 0.001 kg/m^2/d + surface of arms & legs of 0.258 m^2 x soil adherence factor of 0.0001 kg/m^2/d) (CCME 2006)

AF_G = relative absorption factor for nickel across the gut = 1 (100%, assumed by default)

AF_S = relative absorption factor for skin = 0.102 (Section 8.4)

ET = exposure term (unitless) = 1 (7 d/wk x 52 wk/yr at the site) (CCME 2006)

The agricultural and residential/parkland SQG_{DH} for nickel based on the 10% of the EDI approach is recommended for use. This approach is considered to be scientifically defensible and will provide adequate protection for the health of Canadians. Therefore, using the above approach, the SQG_{DH} for nickel at agricultural and residential/parkland sites is 200 mg/kg.

8.5.2 Commercial Land Use

Commercial lands are generically defined as sites at which commercial activities predominate. No manufacturing activities and no residential occupancy are expected to take place at

commercial sites. A commercial site is fully accessible to all age classes but it is used with less intensity, duration and frequency than a residential site. An example of a commercial site would be a typical urban shopping mall.

For threshold contaminants, it is assumed that a toddler is the most sensitive receptor but with access restricted to 10 hours per day, 5 days per week and 48 weeks per year (e.g., daycare). Using the above assumptions, a guideline which applies to commercial soil can be determined as:

$$SQG_{DH} = \frac{(TDI - EDI) \times SAF \times BW}{[(AF_G \times SIR) + (AF_S \times SR)] \times ET} + BSC$$

where,

SQG_{DH} = commercial direct human health-based soil quality guideline for soil ingestion and dermal contact (mg/kg)
TDI = tolerable daily intake (total nickel as soluble salts) = 11 µg/kg bw/day (WHO 2005)
EDI = estimated daily intake by ingestion for toddlers = 10.6 µg/kg bw/day (Section 8.2)
SAF = soil allocation factor = 20% by default (CCME 2006)
BW = body weight for toddler = 16.5 kg (CCME 2006)
AF_G = relative absorption factor for nickel across the gut = 1 (100%, assumed by default)
AF_S = relative absorption factor for skin = 0.102 (Section 8.4)
SIR = soil ingestion rate for toddler = 0.08 g/day (CCME 2006)
SR = soil dermal contact rate for toddler = 6.88 x 10^{-2} g/d [surface area of hands of 0.043 m^2 x soil adherence factor of 0.001 kg/m^2/d + surface of arms & legs of 0.258 m^2 x soil adherence factor of 0.0001 kg/m^2/d] (CCME 2006)
ET = exposure term (unitless) = 0.66 (5/7 d/wk x 48/52 wk/yr at site) (CCME 2006)
BSC = background soil concentration = 26.8 mg/kg dw (Section 2.5.4).

As with residential land use, the EDI is greater than the TDI under the commercial land use scenario. Therefore, the human health soil quality guideline derived using the CCME (2006) protocol would be set to the background soil concentration of nickel.

As discussed above, an alternate approach is to use the value of "10% of the EDI" and this approach is recommended for use in soil quality guideline development. Consequently, the SQG_{DH} may be modified to:

$$SQG_{DH} = \frac{(0.1 \times EDI) \times BW}{[(AF_G \times SIR) + (AF_S \times SR)] \times ET}$$

where,

SQG_{DH} = commercial direct human health-based soil quality guideline for soil ingestion and dermal contact (mg/kg)
EDI = estimated daily intake for toddler = 10.6 µg/kg bw/d (Section 8.2)
BW = body weight for toddler = 16.5 kg (CCME 2006)
SIR = soil ingestion rate for toddler = 0.08 g/d (CCME 2006)
SR = soil dermal contact rate for toddler = 6.88 x 10^{-2} g/d (surface area of hands of 0.043 m^2 x soil adherence factor of 0.001 kg/m^2/d + surface of arms & legs of 0.258 m^2 x soil adherence factor of 0.0001 kg/m^2/d) (CCME 2006)
AF_G = relative absorption factor for nickel across the gut = 1 (100%, assumed by default)

AF_S = relative absorption factor for skin = 0.102 (Section 8.4)
ET = exposure term 1 (unitless) = 0.66 (5/7 d/wk x 48/52 wk/yr at the site) (CCME 2006)

The commercial SQG_{DH} for nickel based on the 10% of the EDI approach is recommended for use as this approach is scientifically defensible and will provide adequate protection to the health of Canadians. Therefore, using the above approach, the SQG_{DH} for nickel in dry soil at commercial sites is calculated to be 310 mg/kg.

8.5.3 Industrial Land Use

Industrial lands typically have limited or restricted access to the public so that adult, occupational exposure will predominate. The typical exposure period for an adult at an industrial site is assumed to be 10 hours per day, 5 days per week and 48 weeks per year. For industrial land use, only adult receptors are considered. The industrial soil guideline is derived as:

$$SQG_{DH} = \frac{(TDI - EDI) \times SAF \times BW}{[(AF_G \times SIR) + (AF_S \times SR)] \times ET} + BSC$$

where,
SQG_{DH} = industrial direct human health-based soil quality guideline for soil ingestion and dermal contact (mg/kg)
TDI = tolerable daily intake (total nickel as soluble salts) = 11 µg/kg bw-day (WHO 2005)
EDI = estimated daily intake by ingestion for adult = 3.8 µg/kg bw-day (Section 8.2)
SAF = soil allocation factor (unitless) = 20% by default (CCME 2006)
BW = body weight for adult = 70.7 kg (CCME 2006)
AF_G = relative absorption factor for nickel across the gut = 1 (100%, assumed by default)
AF_S = relative absorption factor for skin = 0.102 (Section 8.4)
SIR = soil ingestion rate for adult = 0.02 g/d (CCME 2006)
SR = soil dermal contact rate for adult = 1.14×10^{-1} g/day [surface area of hands of 0.089 m^2 x soil adherence factor of 0.001 $kg/m^2/d$ + surface of arms of 0.25 m^2 x soil adherence factor of 0.0001 $kg/m^2/d$] (CCME 2006)
BSC = background soil concentration = 26.8 mg/kg (Section 2.5.4)
ET = exposure term (unitless) = 0.66 (5/7 d/wk x 48/52 wks/yr at the site) (CCME 2006)

Therefore, using the above approach, the SQG_{DH} for nickel at industrial sites is calculated to be 5100 mg/kg.

8.6 Inhalation Pathway (All land uses)

For the derivation of an SQG where speciation is unknown, a conservative approach was taken, assuming that the nickel species present may be potential carcinogens via the inhalation pathway and therefore, to have non-threshold health effects. It is noted that there are also threshold-based effects associated with exposure to nickel via inhalation. For this reason, nickel soil quality guidelines for soil inhalation were developed by adapting the indoor air quality equation specified in the protocol (CCME 2006) for both non-threshold and threshold substances. Adults are considered the most appropriate receptor for evaluating life-time cancer risk for non-threshold substances. Given that the exposure period is greater than the likely latency period for most carcinogens, the CCME (2006) default exposure term for all land uses is one. The non-

threshold soil quality guideline for nickel based on inhalation of soil particles is calculated as follows:

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

(This is a mathematical re-arrangement of the CCME equation for estimation of soil quality guidelines for carcinogens when the cancer potency factor is expressed as a unit risk factor.)

where,

SQG_{DH-PI} = direct human health-based soil quality guideline for particulate inhalation - non-threshold effects (mg/kg)
TILCR = Target Incremental Lifetime Cancer Risk (10^{-6} or 10^{-5})
UR = unit risk = 1.3 x 10^{-3} $(\mu g/m^3)^{-1}$ (Section 6.9.3)
AF_L = relative absorption factor for lungs = 1 (100% assumed by default) (CCME 2006)
DC = dust concentration from resuspension of soil = 7.6 x 10^{-7} g/m^3 (CCME 2006)
ET = exposure term (unitless) =1 (i.e., continuous lifetime exposure for an individual)
BSC = background soil concentration = 26.8 mg/kg (Section 2.5.4)

Derivations are provided based on incremental lifetime cancer risks (ILCR) of both 10^{-6} and 10^{-5}.

The inhalation SQG_{DH-PI} for soil-borne particulates for all land uses are 1000 mg Ni/kg for incremental lifetime cancer risk (ILCR) of 10^{-6} and 10 000 mg Ni/kg for an ILCR of 10^{-5}.

The threshold soil quality guidelines for nickel based on inhalation of soil particles are calculated as follows:

$$SQG_{DH-PI} = \frac{TC \times SAF}{(DC \times AF_L) \times ET_1 \times ET_2} + BSC$$

(This is a mathematical re-arrangement of the CCME equation for estimation of soil quality guidelines for non-carcinogens when the toxicity reference value is expressed as a tolerable concentration instead of a risk-specific dose.)

where,

SQG_{DH-PI} = direct human health-based soil quality guideline for particulate inhalation – threshold effects (mg/kg)
TC = tolerable concentration in air = 0.020 $\mu g/m^3$ (Section 6.9.2)
SAF = soil allocation factor = 20% by default (CCME 2006)
AF_L = absorption factor from lung (medium specific) = 1 (100% assumed by default)
DC = dust concentration from resuspension of soil = 7.6 x 10^{-7} g/m^3 (CCME 2006)
BSC = background soil concentration = 26.8 mg/kg (Section 2.5.4)
ET_1 = exposure term 1 (unitless) = 1 for residential land use (24 hr/d)
ET_1 = 0.66 (unitless) for commercial and industrial land use (5/7 d/wk x 48/52 wk/yr at the site) (CCME 2006)

ET_2 = exposure term 2 (unitless) = 1 for residential land use; 0.42 for commercial and industrial land use - 10/24 hr/d at the site (CCME 2006)

The $SQG_{DH\text{-}PI}$ for inhalation of soil-borne particulates for protection of non-cancer risks are 5300 mg/kg for agricultural and residential/park land uses, and 19 000 mg/kg for commercial and industrial land uses.

A summary of SQGs for inhalation of fugitive dust (*i.e* $SQG_{DH\text{-}PI}$s) is provided in Table 3 below along with the overall inhalation of fugitive dust SQG for each land use category.

Table 3. Summary of human health soil quality guidelines for the inhalation of fugitive dust (mg/kg).

	Land Use			
Target risk	Agricultural	Residential/Parkland	Commercial	Industrial
Overall inhalation SQG protective of both threshold and non-threshold effects				
10^{-5} ILCR & threshold	5300[a]	5300[a]	10 000	10 000
10^{-6} ILCR & threshold	1000	1000	1000	1000
Separate inhalation SQGs to protect against either threshold or non-threshold effects				
Non-Threshold (10^{-5})	10 000	10 000	10 000	10 000
Non-Threshold (10^{-6})	1000	1000	1000	1000
Threshold	5300	5300	19 000	19 000

[a] The guideline values is set at the lowest of the guideline values. For the soil inhalation pathway, the threshold guideline value is lower than the non-threshold value for an incremental lifetime cancer risk of 10^{-5} and is therefore, set as the guideline value for this land use.

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

No guideline for protection of groundwater used as a source of raw water as drinking was derived for nickel (as total) due to constraints on the mathematical model when applied to inorganic compounds (CCME 2006).

8.8 Guideline for Off-site Migration for Commercial and Industrial Land Uses

When deriving soil quality guidelines for commercial and industrial sites, exposure scenarios only consider on-site exposure. Transfers of contaminated soil, from one property to another are possible by environmental routes such as wind and water erosion (CCME 2006).

The human health soil quality guideline for off-site migration ($SQG_{OM\text{-}HH}$) refers to the concentration in soil eroded from the site that will raise the contaminant concentration in the receiving soil to the level of the agricultural guideline within a specific time frame. The $SQG_{OM\text{-}HH}$ was derived as follows:

$$SQG_{OM-HH} = 14.3 \times SQG_{A-HH} - 13.3 \times BSC$$

where,

$SQG_{OM\text{-}HH}$ = Human health-based soil quality guideline for off-site migration (mg/kg)
$SQG_{A\text{-}HH}$ = Human health-based soil quality guideline for agricultural land use (200 mg/kg)
BSC = Background concentration of nickel in the receiving soil (26.8 mg/kg, Section 2.5.4).

Therefore, using the above approach, the human health-based soil quality guideline for off-site migration (SQG_{OM-HH}) is calculated to be 2500 mg/kg. It was derived for protection of an off-site property with a SQG_{A-HH} of 200 mg/kg (Section 8.5.1).

8.9 Final Human Health Soil Quality Guidelines

Human health soil quality guidelines were derived for nickel at agricultural, residential/parkland, commercial and industrial sites, based on ingestion, dermal contact and inhalation of soil. Nickel was assumed to behave as a threshold substance via the ingestion, dermal contact and inhalation pathways and a non-threshold substance via the inhalation pathway. For the ingestion, dermal contact pathways and non-cancer inhalation-related effects, soluble nickel salts toxicity data were used for guideline development. For the inhalation pathway, the SQG_{DH-PI} was developed based on combined soluble, oxidic and sulphidic nickel toxicity data. The soil quality guidelines calculated for each land use are presented in Table 4 below.

The overall human health soil quality guideline (SQG_{HH}) is set as the lowest of the human health guidelines and checks derived for the land use. Based on this, the overall SQG_{HH} based on ingestion and dermal contact pathways are: 200 mg/kg for agricultural land use, 200 mg/kg for residential/parkland land use and 310 mg/kg for commercial land use. For industrial land, the SQG_{HH} is 1000 mg/kg for industrial land use based on an incremental lifetime cancer risk of 10^{-6} or 2500 mg/kg for industrial land use based on an incremental lifetime cancer risk of 10^{-5} based on the check mechanism for the migration of eroded soil from off-site commercial and industrial and use deposited onto adjacent agricultural land use.

Table 4. Exposure Pathways for the Development of the Human Health Soil Quality Guidelines

Pathway	Agricultural (mg/kg)	Residential/ Parkland (mg/kg)	Commercial (mg/kg)	Industrial (mg/kg)
Overall SQG_{HH} or $PSQG_{HH}$				
Non-Cancer and 10^{-6} ILCR	200	200	310	1000[b, c]
Non-Cancer and 10^{-5} ILCR	200	200	310	2500[b, d]
Direct contact				
Ingestion + Dermal contact (SQG_{DH})	200[a]	200[a]	310[a]	5100
Inhalation[c] (SQG_{DH-PI})				
Non-threshold				
10^{-6} ILCR	1000	1000	1000	1000
10^{-5} ILCR	10 000	10 000	10 000	10 000
Threshold	5300	5300	19 000	19 000
Potable groundwater (SQG_{PW})	NC	NC	NC	NC
Consumption of produce, meat and milk (SQG_{FI})	NC[,d]	NC[,d]		
Offsite migration (SQG_{OM-HH})			2500	2500

Notes: NC = not calculated
a – pathway is required (i.e. final guideline cannot be developed without it)
b – the SQG_{HH} is the lowest of the human health guidelines and check values
c – Ni forms included in the development of the inhalation guideline based on combined soluble, oxidic and sulphidic nickel.
d – Applies to non-polar organic compounds and is not calculated for metal substances. Concerns about metal substances should be addressed on a site specific basis.

It is noted that the SQG_{HH} provided above are considered to be protective at most sites; however, certain exposure pathways have not been evaluated in the development of the SQG_{HH}. More

specifically, the SQG_{HH} have not evaluated garden produce consumption or drinking water consumption (see footnotes in Table 5).

For dermal exposure, it is noted that persons particularly sensitive to nickel (e.g., contact dermatitis) may not be adequately protected by the SQG provided above. Appropriate TRVs for evaluating this type of scenario were not identified in the literature. Furthermore, nickel concentrations in soil that are developed to be protective of such effects were not identified in the literature.

With the above in mind, the SQG_{HH} are considered to be protective of human health at most sites.

9 RECOMMENDED CANADIAN SOIL QUALITY GUIDELINES

According to the soil protocol (CCME 2006), both environmental and human health soil quality guidelines are developed for four land uses: agricultural, residential/parkland, commercial, and industrial. The lower value generated by the two approaches for each of the four land uses is recommended by CCME as the Canadian Soil Quality Guideline. The environmental soil quality guidelines, presented in Chapter 7, were considered along with the human health guidelines, presented in Chapter 8, in making final recommendations for Canadian Soil Quality Guidelines for the protection of environmental and human health (CCME 2006). The recommended Canadian Soil Quality Guidelines for the protection of environmental and human health are presented below in Table 5. The interim remediation criteria (CCME 1991) and previous soil quality guidelines for nickel (EC 1999) are replaced by the soil quality guidelines recommended in this document. Human health soil quality guidelines were not developed for the previous soil quality guidelines for nickel (EC 1999), thus, the current soil quality guidelines represent a first time that the soil quality guidelines for nickel are based on considerations of both environmental and human health.

Table 5. Canadian soil quality guidelines for nickel (mg/kg)

	Land use			
	Agricultural	**Residential/ Parkland**	**Commercial**	**Industrial**
Guideline	**45**[a]	**45**[a]	**89**[a]	**89**[a]
Human health guidelines/check values				
SQG_{HH} Non-Cancer and 10^{-6} ILCR	200	200	310	1000[b]
SQG_{HH} Non-Cancer and 10^{-5} ILCR	200	200	310	2500[c]
Direct contact guideline (ingestion and dermal)	200	200	310	5100
Direct contact guideline (particulate inhalation)[d]				
10^{-6} ILCR	1000	1000	1000	1000
10^{-5} ILCR	10 000	10 000	10 000	10 000
Threshold	5300	5300	19 000	19 000
Groundwater check (drinking water)	NC[e]	NC[e]	NC[e]	NC[e]
Produce, meat and milk check	NC[f]	NC[f]	-	-
Off-site migration check	-	-	2500	2500
Environmental health guidelines/check values				
SQG_E	45	45	89	89
Soil contact guideline	45	45	89	89
Soil and food ingestion guideline	528	-	-	-
Nutrient and energy cycling check	171	171	235	235
Off-site migration check	-	-	287	287
Groundwater check (aquatic life)	NC[e]	NC[e]	NC[e]	NC[e]
Guideline derived in 1999 (original Ni SQG)	50	50	50	50
Interim Soil Quality Criteria (CCME 1999)	150	100	500	500

Notes: NC = not calculated; ILCR = Incremental Lifetime Cancer Risk; SQG_E = soil quality guideline for environmental health; SQG_{HH} = soil quality guideline for human health.

[a] Data are sufficient and adequate to calculate a SQG_E and SQG_{HH} for this land use. Therefore the soil quality guideline is the lower of the two (CCME 2006). The original nickel soil quality guideline derived in 1999 (and the interim soil quality criteria (CCME 1991) are superseded by the 2011 nickel soil quality guideline (this document).

[b] The SQG_{HH} is set at the non-threshold direct contact guideline for particulate inhalation because it is the lowest of the of the human health guidelines and check mechanisms for this land use at an ILCR of 1 in 1 000 000.

[c] The SQGHH is set at the off-site migration check value because it is the lowest of the human health guidelines and check values for this land use at an ILCR of 1 in 100 000.

[d] Inhalation pathway was developed for combined soluble, oxidic and sulphidic nickel.

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

REFERENCES

ABC, 1988. Ninety day gavage study in albino rats using nickel. Draft final report submitted to Research Triangle Institute and U.S. EPA, Office of Solid Waste. Study 410-2520.

Abdel-Rahman, M.S and R.M. Turkall. 2011. Nickel Dermal Bioavailability in Pig Skin Increased by a Chemical Mixture: Role of Gender. Proceedings of the Annual International Conference on Soils, Sediments, Water and Energy. Vol. 16, Article 4. 29-36.

Abdel-Sabour, M.F., A.S. Abdel-Haleem, A.Sroor & R.A. Zaghloul. 1997. Accumulation of heavy metals in two crop seeds due to soil contamination as determined by neutron activation analysis techniques. *Environmental Sciences*. 10(2)

AB Health, 1998. Assessing air quality in high level report 1: A preliminary analyses of physician vists and air particulate data. Prepared for Northwestern Health Services Region #17 AB Health, Health Surveillance, as cited in Health Canada (2011) .

Adamo, P. *et al*., 1996. Chemical and mineralogical forms of Cu and Ni in contaminated soils from the Sudbury mining and smelting region, Canada. *Environmental Pollution*, 91(1), pp.11-19.

Adgate, J.L. *et al.*, 1998. Chemical mass balance of lead in house dust. *Environ. Sci. Technol.* 32, pp.108-114.

Adgate, J.L. *et al*., 2007. Relationships between personal, indoor, and outdoor exposures to trace elements in PM2.5. *Science of the Total Environment*, 386(1-3), pp.21-32.

Adjroud, O., 2011. The toxic effects of nickel chloride on liver, erythropoiesis, and development in Wistar albino preimplanted rats can be reversed with selenium pretreatment. *Environmental Toxicology*, 13(4).

Adriano, D.C., 2001. *Trace Elements in the Terrestrial Environments: Biogeochemistry, Bioavailability and Risk Assessments. 2nd edition*, Berlin Heidelberg: Springer-Verlag.

AENV, 2010. Alberta Tier 1 Soil and Groundwater Remediation Guidelines E. A. D. AB Environment Air, Land and Waste Policy Branch, ed.

Agner, T. *et al.*, 2002. Combined effects of irritants and allergens: Synergistic effects of nickel and sodium lauryl sulfate in nickel-sensitized individuals. *Contact Dermatitis*, 47(1), pp.21-26.

Åkerblom, S., E. Bååth & L. Bringmark, 2007. Experimentally induced effects of heavy metal on microbial activity and community structure of forest mor layers. *Biology and Fertility of Soils*, 44, pp.79-91.

Akesson, B. & S. Skerfving, 1985. Exposure in welding of high nickel alloy. *International Archives of Occupational and Environmental Health*, 56(2), pp.111-117, as cited in Roels *et al.* (1993).

Al-Khafaji, A.A. & M.A. Tabatabai, 1979. Effects of trace elements on arylsulfatase activity in soils. *Soil Sci.* , 127, pp.129-133.

Allan, M. & G.M. Richardson, 2008. Probability Density Functions Describing 24-Hour Inhalation Rates for Use in Human Health Risk Assessments: An Update and Comparison. *HERA*, 14(2), pp.372-391.

Allen-Gil, S.M. *et al*., 1997. Heavy metal accumulation in sediment and freshwater fish in U.S. Arctic lakes. *Environmental Toxicology and Chemistry*, 16(4), pp.733-741.

Allenby, C.F. & B.F.J. Goodwin, 1983. Influence of detergent washing powders on minimal eliciting patch test concentrations of nickel and chromium. *Contact Dermatitis*, 9(6), pp.491-499.

Aller, A.J. *et al*., 1990. Effects of selected trace elements on plant growth. *Journal of the Science of Food and Agriculture*, 51(4), pp.447-479. Available at: http://dx.doi.org/10.1002/jsfa.2740510404.

Allinson, D.W. & C. Dzialo, 1981. The influence of lead, cadmium, and nickel on the growth of ryegrass and oats. *Plant and Soil*, 62, pp.81-89.

Almeida, A.A. *et al*., 2008. Trace elements in human milk: Correlation with blood levels, inter-element correlations and changes in concentration during the first month of lactation. *Journal of Trace Elements in Medicine and Biology*, 22(3), pp.196-205.

Ambrose, A.M., P.S. Larson & J.R. Borzelleca, 1976. Long term toxicologic assessment of nickel in rats and dogs. *J. Food Sci. Technol.*, 13, pp.181-187.

Andersen, A. *et al.*, 1996. Exposure to nickel compounds and smoking in relation to incidence of lung and nasal cancer among nickel refinery workers. *Occupational and Environmental Medicine*, 53(10), pp.708-713.
Andersen, I. & K.B. Svenes, 1989. Determination of nickel in lung specimens of thirty-nine autopsied nickel workers. *International Archives of Occupational and Environmental Health*, 61(4), pp.289-295.
Anderson, A-M., 2004. Unpublished monitoring data for ambient metal concentrations in Alberta surface waters. AB Environment, Edmonton, AB.
Anderson, P.R. & T.H.Christensen, 1988. Distribution coefficients of Cd, Co, Ni and Zn in soils . *Journal of Soil Science*, 39, pp.15-22.
Anke, M. *et al.*, 1984. Nickel-an essential element. *IARC Scientific Publications*, (53), pp.339-365.
Anke, M. *et al.*, 1995. The biological importance of nickel in the food chain. *Fresenius' Journal of Analytical Chemistry*, 352(1-2), pp.92-96.
Anke, M. *et al.*, 2000. Intake of nickel in Germany: Risk or normality? *Journal of Trace and Microprobe Techniques*, 18(4), pp.549-556.
Ankley, G.T. *et al.*, 1991. Acid volatile sulphide as a factor mediating cadmium and nickel bioavailability in contaminated sediments. *Environmental Toxicology and Chemistry*, 10, pp.1299-1307.
Annora, S. *et al.*, 2009. *Advanced Nutrition and Human Metabolism. 5th Edition* , Belmont, CA: Wadsworth, Cenege Learning .
Anttila, A. *et al.*, 1998. Update of cancer incidence among workers at a copper/nickel smelter and nickel refinery. *International Archives of Occupational and Environmental Health*, 71(4), pp.245-250.
Apostoli, P. *et al.*, 2006. Elemental speciation in human health risk assessment. *Environmental Health Criteria (World Health Organization)*, 234, p.ix-235.
Arafat, N. & J.O. Nriagu, 1986. Simulated mobilization of metals from sediments in response to lake acidification. *Water, Air, and Soil Pollution*, 31(3-4), pp.991-998.
Archambault, D.J.P., 1991. *Metal tolerance studies on populations of Agrostis scabra (Tickle grass) from Sudbury area*. Laurentian Univ. Sudbury, ON.
Arena, V.C. *et al.*, 1998. Using alternative comparison populations to assess occupation-related mortality risk. Results for the high nickel alloys workers cohort. *Journal of Occupational and Environmental Medicine*, 40(10), pp.907-916.
Arocena, J.M., S.K. Nepal & M. Rutherford, 2006. Visitor-induced changes in the chemical composition of soils in back country areas of Mt Robson Provincial Park, BC, Canada. *J. Environ. Management*, 79(1), pp.10-19.
Arpasova, H. *et al.*, 2007. Nickel induced alteration of hen body weight, egg production and egg quality after an experimental peroral administration. *Journal of Environmental Science and Health - Part B Pesticides, Food Contaminants, and Agricultural Wastes*, 42(8), pp.913-918.
Arrandale, V. *et al.*, 2012. Occupational contact allergens: Are they also associated with occupational asthma? *American Journal of Industrial Medicine*.
Artik, S. *et al.*, 1999. Nickel allergy in mice: enhanced sensitization capacity of nickel at higher oxidation states. *Journal of Immunology*, 163(3), pp.1143-1152. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10415008.
Aschmann, S.G. & R.J. Zasoski, 1987. Nickel and rubidium uptake by whole oat plants in solution culture. *Physiologia Plantarum*, 71, pp.191-196.
ATSDR, 2005. Toxicological Profile for Nickel US Department of Health and Human Services Public Health Service, ed. Available at: http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=245&tid=44.
Australia. 2010. NEPC (National Environment Protection Council) ASC (Assessment of Site Contamination) NEPM_Schedule B7_Appendix A1 (Metals and Inorganics), pp 64-71
Bååth, E., 1989. Effects of heavy metals in soil on microbial processes and populations (a review). *Water Air Soil Pollution*, 47, pp.335-379.

Babich, H. & G. Stotzky, 1982. Toxicity of nickel to microorganisms in soil: Influence of some physicochemical characteristics. *Environmental Pollution Series A, Ecological and Biological*, 29(4), pp.303-315. Available at: http://www.sciencedirect.com/science/article/pii/0143147182900691.

Babich, H. & G. Stotzky, 1983a. Further studies on environmental factors that modify the toxicity of nickel to microbes. *Regulatory Toxicology and Pharmacology*, 3(1), pp.82-99. Available at: http://www.ncbi.nlm.nih.gov/pubmed/6412320.

Babich, H. & G. Stotzky, 1983b. Nickel toxicity to estuarine/marine fungi and its amelioration by magnesium in seawater. *Water Air Soil Pollut.*, 19, pp.193-202, as cited in Environment Canada and Health Canada.

Bábiková, L., R. Toman, S. Hluchý & P. Massányi, 2007. Quantitative Morphometry Analysis of the Rat Epididymis After A Peroral Administration Of Nickel. Lucrări ştiinţifice Zootehnie şi Biotehnologii (Scientific Papers, Animal Science and Biotechnologies), vol. 40(1): 330-334. Available at: http://www.spasb.ro/index.php/spasb/article/view/1595

Baker, A.J.M. & R.R. Brooks, 1989. Terrestrial higher plants which hyperaccumulate metallic elements - A review of their distribution, ecology and phytochemistry. *Biorecovery*, 1, pp.81-126.

Balasubramanian, R. & S.S. Lee, 2007. Characteristics of Indoor Aerosols in Residential Homes in Urban Locations: A Case Study in Singapore. *Journal of the Air & Waste Management Association*, 57(8), pp.981-990. Available at: http://www.tandfonline.com/doi/abs/10.3155/1047-3289.57.8.981.

Barashkov, G.K. *et al*., 2003. Distribution of chemical elements in whole blood and plasma. *Biomeditsinskaya Khimiya*, 49(3), pp.297-302.

Basketter, D.A. *et al*., 1993. Nickel, cobalt and chromium m consumer products: A role in allergic contact dermatitis? *Contact Dermatitis*, 28(1), pp.15-25.

Bazzaz, F.A., R.W. Carlson & G.L. Rolfe, 1974. The effect of heavy metals on plants: Part I. Inhibition of gas exchange in sunflower by Pb, Cd, Ni and Tl. *Environmental Pollution*, 7, pp.241-246.

BCMOE, 1999. Protocol 4 Determining background soil quality prepared pursuant to Section 53 of the Contaminated Sites Regulation under the Environmental Management Act. BCMOE Environmental Protection Division Land Remediation Section, ed.

BCMOE, 2008. Water and Sediment Quality Monitoring Reports. State of Water Quality Reports for some BC locations BCMOE Environmental Protection Division. Available at: http://www.env.gov.bc.ca/wat/wq/quality/sowq.html.

BCMOE, 2011. Environmental Management Act: Contaminated Sites Regulation. Available at: http://www2.gov.bc.ca/gov/topic.page?id=9A8B9BE814A1471F86EF4CA87BCE0CE2

Beckerton, J., 2004. pers. comm. Unpublished data for metal concentrations in Yukon groundwater samples (1995 to 2001). Environment Yukon, Whitehorse, Yukon Territory.

Bedello, P.G. *et al*., 1985. Nickel: Ubiquitary hapten. *NICHEL: APTENE UBIQUITARIO*, 120(4), pp.293-296.

Bednarska, A.J. & R. Laskowski, 2008. Effects of nickel and temperature on the ground beetle *Pterostichus oblongopunctatus* (Coleoptera: Carabidae). *Ecotoxicology*, 17(3), pp.189-198.

Beijer, K. & A. Jernelov, 1986. Sources, transport and transformation of metals in the environment. In L. Friberg, G.F. Nordberg & V.B. Vouk, eds. *Handbook on the Toxicology of Metals*. New York, Oxford, Amsterdam: Elsevier Science Publ, pp. 68-84.

Bell, R.W. *et al*., 1994. Windsor Air Quality Study: Personal Exposure Survey Results.

Belzile, N., Chen, Y-W. & Gunn, J.M., 2004. Sediment trace metal profiles in lakes of Killarney Park, Canada: from regional to continental influence. *Environmental Pollution*, 130, pp.239-248.

Benfeldt, E., J. Serup, & T. Menne, 1999. Microdialysis vs. suction blister technique for in vivo sampling of pharmacokinetics in the human dermis. *Acta Dermato-Venereologica*, 79(5), pp.338-342.

Bennett, B.G., 1982. Exposure of man to environmental nickel - An exposure commitment assessment. *Science of the Total Environment*, 22(3), pp.203-212.

Benson, J.M. *et al*., 1994. Fate of inhaled nickel oxide and nickel subsulfide in F344/N rats. *Inhalation Toxicology*, 6(2), pp.167-183.
Benson, J.M. *et al*., 1995. Particle clearance and histopathology in lungs of F344/N rats and B6C3F1 mice inhaling nickel oxide or nickel sulfate. *Fundamental and Applied Toxicology*, 28(2), pp.232-244.
Berg, T. *et al*., 2000. The release of nickel and other trace elements from electric kettles and coffee machines. *Food Additives and Contaminants*, 17(3), pp.189-196.
Berge, S.R. & K. Skyberg, 2003. Radiographic evidence of pulmonary fibrosis and possible etiologic factors at a nickel refinery in Norway. *Journal of Environmental Monitoring*, 5(4), pp.681-688, in ATSDR (2005).
Bergsam, E., 2004. Unpublished data for metal concentrations in Yukon drinking water (1999 to 2003). Yukon Department of Environmental Health, Whitehorse, YT.
Berry, J.P. *et al*., 1988. Inhaled soluble aerosols insolubilised by lysosomes of alveolar cells. Application to some toxic compounds; electron microprobe and ion microprobe studies. *Toxicology*, 52(1-2), pp.127-139.
Berry, J.P. *et al*., 1997. Role of alveolar macrophage lysosomes in metal detoxification. *Microscopy Research and Technique*, 36(4), pp.313-323.
Berry, J.P., F. Bertrand & P. Galle, 1993. Selective intra-lysosomal concentration of niobium in kidney and bone marrow cells: a microanalytical study. *BioMetals*, 6(1), pp.17-23.
Beyer, W.N. & G. Miller, 1990. Trace elements in soil and biota in confined disposal facilities for dredged material. *Environmental Pollution*, 65, pp.19-32.
Beyersmann, D. & A. Hartwig, 2008. Carcinogenic metal compounds: Recent insight into molecular and cellular mechanisms. *Archives of Toxicology*, 82(8), pp.493-512.
Bhuiya, M.R.H., 1972. Effects of addition of 1000 ppm Cu, Ni, Pb, and Zn on carbon dioxide release during incubation of soil alone and after treatment with straw. *Environmental Pollution*, 3, pp.173-177.
Birmingham, B. & D. McLaughlin, 2006. Soil investigation and human health risk assessment for nickel in community soils near a former nickel refinery in southern Ontario, Canada. *Journal of Toxicology and Environmental Health - Part A*, 69(9), pp.845-892.
Biró, B., K. Köves-Péchy & I. Vörös, 1998. Toxicity of some field applied heavy metal salts to the rhizobial and fungal microsymbionts of alfalfa and red clover. *Agrokémia és Talajtan*, 1-4, pp.265-276.
Bisessar, S., 1989. Effects of lime on nickel uptake and toxicity in celery grown on muck soil contaminated by a nickel refinery. *Science of the Total Environment*, 84, pp.83-90.
Bisson, M., 2004. Statistical data on elemental concentrations in suspended particulate matter (PM10) at different industrial sites in Québec (1999-2002). Ministère de l'Environnement du Québec, Quebec City, QC.
Block, G.T. & M. Yeung, 1982. Asthma induced by nickel. *Journal of the American Medical Association*, 247(11), pp.1600-1602.
Bocca, B. *et al*., 2007. Levels of nickel and other potentially allergenic metals in Ni-tested commercial body creams. *Journal of Pharmaceutical and Biomedical Analysis*, 44(5), pp.1197-1202.
Bocio, A. *et al*., 2005. Monitoring metals in the population living in the vicinity of a hazardous waste incinerator: Concentrations in autopsy tissues. *Biological Trace Element Research*, 106(1), pp.41-50.
Bodo, B.A., 1989. Heavy metals in water and suspended particulates from an urban basin impacting lake Ontario. *Science of the Total Environment*, 87-88, pp.329-344.
Boyd, D, 1991-92. Personal communication. ON Ministry of the Environment, Toronto, ON.
Boyd, D., 2004. Unpublished data on metal concentrations in surface waters and sediments from lakes and rivers sampled across Ontario (1994 to 2003). ON Ministry of the Environment, Toronto, ON.

Boyd, W.A. & P.L. Williams, 2003. Availability of metals to the nematode Caenorhabditis elegans: toxicity based on total concentration in soil and extracted fractions. *Environmental Toxicology and Chemistry*, 22(5), pp.1100-1106.
Boyle, D.R., W.A. Spirito, and S.W. Adcock, 1994. Groundwater hydrogeochemical survey of southeastern New Brunswick (211I/1; 21I/2; 21I/3; 21H/15; 21H/16; 11L/4). Open File 2912 Geological Survey of Canada, ed. Available at: geoscan.nrcan.gc.ca
Boyle, D.R., W.A. Spirito and S.W. Adcock, 1996. Groundwater hydrogeochemical survey of central New Brunswick. Open File 3306. Available at: geoscan.nrcan.gc.ca
Bradley, R.W. & J.R. Morris, 1986. Heavy metals in fish from a series of metal-contaminated lakes near Sudbury, Ontario. *Water, Air, and Soil Pollution*, 27(3-4), pp.341-354.
Brassard, P., J.R. Kramer & P.V. Collins, 1997. Dissolved metal concentrations and suspended sediment in Hamilton harbour. *Journal of Great Lakes Research*, 23(1), pp.86-96.
Brecher, R.W. *et al*., 1989. Eco Logic Inc., Contract report for the Environmental Substances Division, Environmental Health Centre, Health and Welfare Canada, Ottawa, ON, Canada.
Brera, S. & A. Nicolini, 2005. Respiratory manifestations due to nickel. *Acta otorhinolaryngologica Italica : organo ufficiale della Societa italiana di otorinolaringologia e chirurgia cervico-facciale*, 25(2), pp.113-115.
Broerse, M. & C.A.M. van Gestel, 2010. Chlorpyrifos reduces nickel-induced growth retardation of the soil dwelling collembolan *Folsomia candida*. *Ecotoxicology and Environmental Safety*, 73, pp.1051-1056.
Brookes, P.C. & S.P. McGrath, 1984. Effects of metal toxicity on the size of the soil microbial biomass. *J. Soil. Sci.* , 35, pp.341-346.
Brooks, N.N., 1980. Accumulation of nickel by terrestrial plants. In J.O. Nriagu, ed. *Nickel in the Environment*. New York: Wiley and Sons .
Brown, P.H., R.M. Welch *et al*., 1987a. Beneficial effects of nickel on plant growth. *Journal of Plant Nutrition*, 10, pp.2125-2135.
Brown, P.H., R.M.Welch, E.E. Cary *et al*., 1987b. Micronutrients. *Journal of Plant Nutrition*, 10(9-16), pp.2125-2135. Available at: http://www.tandfonline.com/doi/abs/10.1080/01904168709363763.
Brown, P.H., R.M. Welch & E.E. Cary, 1987c. Nickel: A Micronutrient Essential for Higher Plants. *Plant Physiology*, 85(3), pp.801-803. Available at: http://www.plantphysiol.org/content/85/3/801.abstract.
Bruland, K.W. *et al*., 1979. Sampling and analytical methods for the determination of copper, cadmium, zinc, and nickel at the nanogram per liter level in seawater. *Analytica Chimica Acta*, 105, pp.233-245.
Burnett, R.T. *et al*., 2000. Association between particulate- and gas-phase components of urban air pollution and daily mortality in eight Canadian cities. *Inhalation Toxicology*, 12(4), pp.15-39.
CCME, 1991. Interim Canadian environmental quality criteria for contaminated sites CCME.
CCME, 1993. Guidance manual on sampling, analysis and data management guidelines for contaminated sites. Vol. 1: Main Report, Vol. II: Analytical Method Summaries CCME CCME, 2007. A Protocol for the Derivation of Water Quality Guidelines for the Protection of Aquatic Life 2007.
CCME, 1996a. A Protocol for the Derivation of Environmental and Human Health Soil Quality Guidelines CCME.
CCME, 1996b. Guidance Manual for Developing Site-Specific Soil Quality Remediation Objectives for Contaminated Sites in Canada CCME.
CCME, 2006. A Protocol for the Derivation of Environmental and Human Health Soil Quality Guidelines CCME.
CCME, 1999. Canadian Environmental Quality Guidelines CCME. Available at: ccme.ca
CCREM, 1987. Canadian Water Quality Guidelines Task Force on Water Quality Guidelines.
Cain, B.W. & E.A. Pafford, 1981. Effects of dietary nickel on survival and growth of mallard ducklings. *Environ. Contam. Toxicol.*, 10, pp.737-745.

Calderón-Garcidueñas, L. *et al*., 2003. DNA damage in nasal and brain tissues of canines exposed to air pollutants is associated with evidence of chronic brain inflammation and neurodegeneration. *Toxicologic Pathology*, 31(5), pp.524-538.

Callahan, M.A. *et al*., 1979. Nickel: Water-related environmental fate of 129 priority pollutants, Vol. 1: Introduction and technical background, metals and inorganics, pesticides and PCBs U.S. Environmental Protection Agency Office of Water and Waste Management.

Cameron, K.S., V. Buchner & P.B. Tchounwou, 2011. Exploring the molecular mechanisms of nickel-induced genotoxicity and carcinogenicity: A literature review. *Reviews on Environmental Health*, 26(2), pp.81-92.

Capcarova, M., A. Kolesarova, H. Arpasova, P. Massanyi, N. Lukac, J. Kovacik, A. Kalafova & M. Schneidgenova. 2008. Blood biochemical dynamics and correlations in laying hens after experimental nickel administration. *Int. J. Poultry Sci.* 7:538-547.

Carlson, C.L. *et al*., 1991. Effects of selected trace metals on germinating seeds of six plant species. *Water Air Soil Pollut.*, 59, pp.231-240.

Carvalho, S.M.M. & P.L. Ziemer, 1982. Distribution and clearance of ^{63}Ni administered as $^{63}NiCl_2$ in the rat: Intratracheal study. *Archives of Environmental Contamination and Toxicology*, 11(2), pp.245-248. Available at: http://dx.doi.org/10.1007/BF01054903.

Casey, C.E. & M.C. Neville, 1987. Studies in human lactation 3: Molybdenum and nickel in human milk during the first month of lactation. *American Journal of Clinical Nutrition*, 45(5), pp.921-926.

Cataldo, D.A. *et al*., 1978. Nickel in plants: I. Uptake kinetics using intact soybean seedlings. *Plant Physiology*, 62, pp.563-565.

Cempel, M. & K. Janicka, 2002. Distribution of nickel, zinc, and copper in rat organs after oral administration of nickel(II) chloride. *Biological Trace Element Research*, 90(1-3), pp.215-226.

Cha, N.R. *et al*., 2010. Determination of iron, copper, zinc, lead, nickel and cadmium in cosmetic matrices by flame atomic absorption spectroscopy. *Analytical Letters*, 43(2), pp.259-268.

Chan, W.H. & M.A. Lusis, 1988. Smelting operations and trace metals in air and precipitation in the Sudbury Basin. In *Adv. Environ. Sci. Tech.* Toronto, ON: Ontario Ministry of the Environment, pp. 113-143.

Chang, A.C. *et al*., 1984. Sequential extraction of soil heavy metals following a biosolids applciation. *Journal of Environment Quality*, 13, pp.33-38.

Chapman, P. & R. Wang, 2000. Issues in ecological risk assessment of metals and metalloids . *HERA* , 6, p.6.

Chattopadhyay, G., K.C.P. Lin & A.J. Feitz, 2003. Household dust metal levels in the Sydney metropolitan area. *Environmental Research*, 93(3), pp.301-307.

Chaudri, A.M. & S.P. McGrath, 1992. Survival of the indigenous population of *Rhizobium leguminosarum biovar trifolii* in soil spiked with Cd, Zn, Cu, and Ni salts. *Soil Biology and Biochemistry*, 24(7), pp.625-632.

Chen, J.R., R.B. Francisco & T.E. Miller, 1977. Legionnaires' disease: nickel levels. *Science*, 196(4292), pp.906-908, in Rezuke *et al*. (1987).

Cheung, P., 2004. Unpublished summary of data on ambient metal concentrations in Ontario drinking water monitored by the Ontario Drinking Water Surveillance Program (DWSP) from 1990 to 2002. ON Ministry of the Environment, Toronto, ON.

Choinière, J. & M. Beaumier, 1997. Bruits de Fond Geochimiques pour Differents Environnements Geologiques au Québec. Ministère Des Ressources Naturelles du Québec.

Chou, C.H.S.J., J. Holler & C.T. De Rosa, 1998. Minimal risk levels (MRLs) for hazardous substances. *Journal of Clean Technology, Environmental Toxicology and Occupational Medicine*, 7(1), pp.1-24.

Christensen, O.B. *et al*., 1979. Nickel concentration of blood, urine and sweat after oral administration. *Contact Dermatitis*, 5(5), pp.312-316.

Christensen, O.B. *et al*., 1981. Micromorphology and specificity of orally induced flare-up reactions in nickel-sensitive patients. *Acta Dermato-Venereologica*, 61(6), pp.505-510.

Christensen, O.B. & V. Lagesson, 1981. Nickel concentration of blood and urine after oral administration. *Annals of Clinical and Laboratory Science*, 11(2), pp.119-125, as cited in CalEPA OEHHA (2011).
Christensen, O.B. & H. Moller, 1975. External and internal exposure to the antigen in the hand eczema of nickel allergy. *Contact Dermatitis*, 1(3), pp.136-141.
Christensen, O.B. & H. Moller, 1978. Release of nickel from cooking utensils. *Contact Dermatitis*, 4(6), pp.343-346.
Christensen, O.B. & L.M. Wall, 1987. Open, closed and intradermal testing in nickel allergy. *Contact Dermatitis*, 16(1), pp.21-26.
Clary, J.J., 1975. Nickel chloride induced metabolic changes in the rat and guinea pig. *Toxicology and Applied Pharmacology*, 31(1), pp.55-65.
Connell, D.W., 1990. *Bioaccumulation of Xenobiotic Compounds*, Boca Raton, FL: CRC Press.
Corazza, M. *et al*., 2009. Measurement of nickel, cobalt and chromium in toy make-up by atomic absorption spectroscopy. *Acta Dermato-Venereologica*, 89(2), pp.130-133.
Cornfield, A.H., 1977. Effects of addition of 12 metals on carbon dioxide release during incubation of an acid sandy soil. *Geoderma* , 19, pp.199-203.
Costa, M. *et al*., 2005. Nickel carcinogenesis: Epigenetics and hypoxia signaling. *Mutation Research - Fundamental and Molecular Mechanisms of Mutagenesis*, 592(1-2), pp.79-88.
Costa, M., J. Simmons-Hansen & C.W.M. Bedrossian, 1981. Phagocytosis, cellular distribution, and carcinogenic activity of particulate nickel compounds in tissue culture. *Cancer Research*, 41(7), pp.2868-2876.
Cottenie, A.R. *et al*., 1979. Fractionation and determination of trace elements in plants, soils and sediments. *Pure and Applied Chemistry*, 52, pp.45-53.
Cotton, F.A. & G. Wilkinson, 1988. *Advanced Inorganic Chemistry: A Comprehensive Text, 5th edition.* Wiley-Interscience, New York, NY, in Environment Canada and Health Canada (1994).
Covington, J.S. *et al*., 1985. Quantization of nickel and beryllium leakage from base metal casting alloys. *The Journal of Prosthetic Dentistry*, 54(1), pp.127-136.
Cox, R.M. & T.C. Hutchinson, 1981. Environmental factors influencing the rate of spread of the grass Deschampsia Cespitosa invading areas around the Sudbury nickel-copper smelters. *Water Air Soil Pollution*, 16, pp.83-106.
Cronin, E., A.D. Di Michiel & S.S. Brown, 1980. Oral challenge in nickel-sensitive women with hand eczema. In S.S. Brown & F.W. Sunderman, eds. *Nickel Toxicology*. London, UK: Academic Press Inc. (London) Ltd, in OEHHA (2011, draft).
Culbard, E.B. *et al*., 1988. Metal contamination in British urban dusts and soils. *J. Environ Qual.*, 17, pp.226-234.
Dabeka, R., 2004. Data on trace elements in food from the 2000-2004 Canadian Total Diet Study Health Canada. Available at: http://www.hc-sc.gc.ca/fn-an/surveill/total-diet/concentration/index-eng.php.
Dabeka, R., 2009. Food Research Division, Bureau of Chemical Safety, Food Directorate, Health Products and Food Branch, Health Canada. Various emails.
Dabeka, R.W., 1989. Survey of lead, cadmium, cobalt and nickel in infant formulas and evaporated milks and estimation of dietary intakes of the elements by infants 0-12 months old. *Science of the Total Environment*, 89(3), pp.279-289.
Dabeka, R.W. *et al*., 2002. Survey of bottled drinking waters sold in Canada for chlorate, bromide, bromate, lead, cadmium and other trace elements. *Food Additives and Contaminants*, 19(8), pp.721-732.
Dabeka, R.W. & A.D. McKenzie, 1995. Survey of lead, cadmium, fluoride, nickel, and cobalt in food composites and estimation of dietary intakes of these elements by Canadians in 1986-1988. *Journal of AOAC International*, 78(4), pp.897-909.
Daldrup, T., K. Haarhoff & S.C. Szathmary, 1983. Toedliche nickel sulfaye-intoxikation. Berichte zur Serichtlichen Medizin., 41, pp.141-144, in ATSDR (2005).

Dang, Y.P., R. Chabra & K.S. Verna, 1990. Effects of Cd, Ni, Pb, and Zn on growth and chemical composition of onion and fenugreek. *Comm. Soil Sci. Plant Anal.*, 21, pp.717-735.
Dann, T., 1991. Measurement Program for toxic contaminants. In *Environment Canada. Canadian Urban Air. Update and summary report. Pollution measurement division.*, Rep. PMD #91-2. Ottawa, ON: Environment Canada.
Dann, T., 2007. Environmental Technology Centre, Environment Canada, Ottawa, ON.
Dann, T., 2010. Head, Air Toxics, Analysis and Air Quality, Environment Canada, Ottawa ON. NAPS data for Nickel 01 Jan 2007 - 31 Dec 2009 PM2.5 (via email) To Deanna Lee.
Davies, J.E., 1986. Occupational asthma caused by nickel salts. *Journal of the Society of Occupational Medicine*, 36(1), pp.29-31.
Davis, J.J. & B.L. Gulson, 2005. Ceiling (attic) dust: A "museum" of contamination and potential hazard. *Environmental Research*, 99(2), pp.177-194.
Davis, R.D., P.H.T. Beckett & E. Wollan, 1978. Critical levels of twenty potentially toxic elements in young spring barley. *Plant and Soil*, 49, pp.395-408.
De Brouwere, K, J.Buekers, C. Cornelis, C.E. Schlekat and A.R. Oller. 2012. Assessment of indirect human exposure to environmental sources of nickel: Oral exposure and risk characterization for systemic effects. Science of the Total Environment 419(2012): 25-36
deCatanzaro, J.B. & T.C. Hutchinson, 1985. Effects of nickel addition on nitrogen mineralization, nitrification, and nitrogen leaching in some boreal forest soils. *Water, Air, and Soil Pollution*, 24, pp.153-164.
Degtiareva, A. & M. Elektorowica, 2001. Change in the water quality of industrial channels due to resuspension of sediments contaminated with heavy metals. *Water Sci.Tech: Water Supply* , 1(2), pp.27-35.
De Hauteclocque, C. *et al*., 2002. Occupational asthma due to hard metals hypersensitivity. *Asthme professionnel par hypersensibilité aux métaux durs*, 19(3), pp.363-365.
de Lafontaine, Y. *et al*., 2000. Biomarkers in zebra mussels (*Dreissena polymorpha*) for the assessment and monitoring of water quality of the St Lawrence River (Canada). *Aquat. Toxicol.* 50(1-2), pp.51-71.
Denkhaus, E. & K. Salnikow, 2002. Nickel essentiality, toxicity, and carcinogenicity. *Critical Reviews in Oncology/Hematology*, 42(1), pp.35-56.
DEPA, 1995. Soil Quality Criteria for Selected Inorganic Compounds Ministry of Environment and Energy DEPA, ed.
Desrosiers, M. *et al.*, 2008. Relationships among total recoverable and reactive metals and metalloid in St. Lawrence River sediment: bioaccumulation by chironomids and implications for ecological risk assessment. *Science of the Total Environment*, 389(1), pp.101-114.
Dickel, H. *et al*., 2010. Increased sensitivity of patch testing by standardized tape stripping beforehand: A multicentre diagnostic accuracy study. *Contact Dermatitis*, 62(5), pp.294-302.
Dieter, M.P. *et al*., 1988. Evaluation of tissue disposition, myelopoietic, and immunologic responses in mice after long-term exposure to nickel sulphate in the drinking water. *Journal of Toxicology and Environmental Health*, 24, pp.357-372.
Dinwoodie, G., 2004 pers comm. AB Environment .
DiToro, D.M. *et al*., 1986. Effects of nonreversibility, particle concentration and ionic strength on heavy metal sorption. *Environmental Science & Technology*, 20, pp.55-61.
Diwan, B.A., K.S. Kasprzak & J.M. Rice, 1992. Transplacental carcinogenic effects of nickel(II) acetate in the renal cortex, renal pelvis and adenohypophysis in F344/NCr rats. *Carcinogenesis*, 13(8), pp.1351-1357.
Dixit, S.S., A.S. Dixit & J.P. Smol, 1991. Multivariable environmental interferences based on diatom assemblages from Sudbury (Canada) lakes . *Freshwater Biol*, 26, pp.251-266.
Dixon, N.E. *et al*., 1975. Letter: Jack bean urease (EC 3.5.1.5). A metalloenzyme. A simple biological role for nickel? *Journal of the American Chemical Society*, 97(14), pp.4131-4133.

Dixon, R.K., 1988. Response of ectomycorrhizal *Quercus rubra* to soil cadmium, nickel and lead. *Soil Biology and Biochemistry*, 20, pp.555-559.
Dixon, R.K. & C.A. Bushena, 1988. Response of ectomycorrhizal *Pinus banksiana* and *Picea glauca* to heavy metals in soil. *Plant and Soil*, 105, pp.265-271.
Dobrin, D.J. & R.Potvin, 1992. Air Quality Monitoring Studies in the Sudbury Area: 1978 to 1988. Ontario Ministry of the Environment, Technical Assessment Section, Northeastern Region, Toronto, ON. in Environment Canada and Health Canada (1994).
Doelman, P. & L. Haanstra, 1984. Short- term and long-term effects of cadmium, chromium, copper, nickel, lead and zinc on soil microbial respiration in relation to abiotic soil factors. *Plant and Soil*, 79, pp.317-327.
Doelman, P. & L. Haanstra, 1986. Short- and long-term effects of heavy metals on urease activity in soils. *Biol. Fertil. Soils*, 2, pp.213-218.
Doelman, P. & L. Haanstra, 1989. Short- and long-term effects of heavy metals on phosphatase activity in soils: An ecological dose-response model approach. *Biol. Fertil. Soils*, 8, pp.235-241.
Dolovich, J., S.L. Evans & E. Nieboer, 1984. Occupational asthma from nickel sensitivity: I. Human serum albumin in the antigenic determinant. *British Journal of Industrial Medicine*, 41(1), pp.51-55.
Doyle, P., 1991. Nickel and chromium in Canadian soil: Natural variations and anthropogenic additions, Contract Report with Environment Canada.
Dryfhout-Clark, H., 2004. Unpublished monitoring data on air quality of the Great Lakes Basin from the Integrated Atmospheric Deposition Network (IADN). Environment Canada, Egbert, ON .
Drysdale, M. *et al*., 2011. Evaluating the respiratory bioaccessibility of nickel in soil through the use of a simulated lung fluid. *Environmental Geochemistry and Health*, pp.1-10.
Dumonet, S., H.Dinel & P.E.N. Lévesque, 1992. The distribution of pollutant heavy metals and their effect on soil respiration and acid phosphatase activity in mineral soils of the Rouyn-Noranda region, Québec. *Science of the Total Environment*, 121, pp.231-245.
Dunnick, J.K. *et al*., 1989. Lung toxicity after 13-week inhalation exposure to nickel oxide, nickel subsulfide, or nickel sulfate hexahydrate in F344/N rats and B6C3F1 mice. *Fundamental and Applied Toxicology*, 12(3), pp.584-594.
Dunnick, J.K. *et al*., 1995. Comparative carcinogenic effects of nickel subsulfide, nickel oxide, or nickel sulfate hexahydrate chronic exposures in the lung. *Cancer Research*, 55(22), pp.5251-5256.
Eastin Jr., W.C. & T.J. O'Shea, 1981. Effects of dietary nickel on mallards. *Journal of Toxicology and Environmental Health*, 7, pp.883-892.
Easton, D.F., J. Peto & L.G. Morgan, *et al*., 1992. Respiratory cancer mortality in Welsh nickel refiners: Which nickel compounds are responsible?. In E. Niebor & J. Nrigau, eds. *Nickel and Human Health: Current Perspectives. Advances in Environmental Sciences and Technology*. New York: Wiley & Sons, pp. 603-619, as cited in IARC (2011).
EC, 1989a. Atlantic region federal-provincial toxic chemical survey of municipal drinking water sources. Data summary report, Province of New Brunswick, 1985-1988 EC Environmental Protection Service Water Quality Branch, Atlantic Region.
EC, 1989b. Atlantic region federal-provincial toxic chemical survey of municipal drinking water sources. Data summary report, Province of Nova Scotia, 1985-1988 EC Environmental Protection Service Water Quality Branch, Atlantic Region.
EC, 1994. Priority Substances List Supporting Documentation - Environmental Sections: Nickel and its Compounds Canadian Environmental Protection Act.
EC, 1996. The State of Canada's Environment - 1996 Environment Canada.
EC, 1999. Canadian Soil Quality Guidelines for Nickel: Environmental Effects. Scientific Supporting Document Environment Canada National Guidelines and Standards Office.
EC, 2003a. National Air Pollution Surveillance (NAPS) Network EC Analysis and Air Quality Division. Available at: www.ec.gc.ca/rnspa-naps/.

EC, 2003b. Phytorem and phytopet - selecting plants for site decontamination, *in* Environmental solutions through technology innovation and partnerships. Environment Canada, Innovative Solutions Division. ISBN: 0-662-67115-5. p 33.
EC, 2005. 2004 Municipal Water Use Report: Municipal Water Use 2001 Statistics. Available at: www.ec.gc.ca/eau-water/default.asp?lang=En&n=ED0E12D7-1
EC, 2007. National Pollutant Release Inventory (NPRI). Available at: http://www.ec.gc.ca/pdb/querysite/query_e.cfm.
EC, 2011. The National Air Pollution Surveillance (NAPS) network - Integrated sampling air monitoring data, as cited in Health Canada (2011).
EC and HC, 1994. Priority Substances List Assessment Report: Nickel and its Compounds Canadian Environmental Protection Act. Available at: http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/psl1-lsp1/compounds_nickel_composes/index-eng.php.
Echevarria, G. *et al*., 2006. Assessment and control of the bioavailability of nickel in soils. *Environmental Toxicology and Chemistry*, 25(3), pp.643-651.
Edwards, D.L., J.C. Wataha & C.T. Hanks, 1998. Uptake and reversibility of uptake of nickel by human macrophages. *Journal of Oral Rehabilitation*, 25(1), pp.2-7.
Efroymson, R.A., B.E. Sample & G.W.S. II, 2004. Bioaccumulation of inorganic chemicals from soil by plants: Spiked soils vs. field contamination or background. *HERA*, 10(6), pp.1117-1127.
Elkin, B., 2001. Heavy Metal and Radionuclide Contaminants in Caribou. In *INAC (Indian and Northern Affairs Canada). Abstracts of Synopsis of Research (2000-2001)* Conducted under the Northern Contaminants Program - Biotic Monitoring. Indian and Northern Affairs Canada.
Elmosly, W.A. & M.F. Abdel-Sabour, 1997. Transfer characteristics and uptake of nickel by red clover grown on nickel amended alluvial soils of an arid zone. *Agri. Ecosystems Environ.* , 65(1), pp.49-57.
Emmett, E.A. *et al*., 1988. Allergic contact dermatitis to nickel: Bioavailability from consumer products and provocation threshold. *Journal of the American Academy of Dermatology*, 19(2 I), pp.314-322.
English, J.C. *et al*., 1981. Toxicokinetics of nickel in rats after intratracheal administration of a soluble and insoluble form. *American Industrial Hygiene Association Journal*, 42(7), pp.486-492, in OEHHA (2011, draft).
Environment Agency (UK), 2009. Contaminants in soil: updated collation of toxicological data and intake values for humans. Nickel. Science report: SC050021/ Tox 8. Bristol: Environment Agency. Available at: www.gov.uk/government/uploads/system/uploads/attachment_data/file/291234/scho0409bpvz-e-e.pdf
Ermolli, M. *et al*., 2001. Nickel, cobalt and chromium-induced cytotoxicity and intracellular accumulation in human hacat keratinocytes. *Toxicology*, 159(1-2), pp.23-31.
Eskew, D.L., R.M. Welch & E.E. Cary. 1983. Nickel: An essential micronutrient for legumes and possibly all higher plants. *Science*, 222(4624), pp. 621-623.
EU, 2004. Nickel sulphate risk assessment. Draft RAR. Prepared by the Danish Environmental Protection Agency for the EU.
EU, 2004a. Commission Directive 2004/96/EC, 27 September 2004. *Official Journal of the European Union*. Available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:301:0051:0052:EN:PDF. Accessed 15 Aug. 2013.
EU, 2008. European Union risk assessment report - nickel and nickel compounds. Section 3.2 Effects Assessment. Final Version.
EU, 2008b. European Union risk assessment report-Nickel; Nickel Carbonate; Nickel Chloride; Nickel Dinitrate; Nickel Sulphate CAS No: 7440-02-0; 333-67-3; 7718-54-9; 13138-45-9; 7786-81-4; EINECS No: 231-111-4; 222-068-2; 231-743-0; 236-068-5; 232-104-9 Risk Assessment. Humans exposed indirectly via the environment and combined exposure-exposure assessment and risk characterization Final version April 2008. Danish Environmental Protection Agency in collaboration

with NiPERA and VITO. Final approved version. Available at: http://echa.europa.eu/documents/10162/cefda8bc-2952-4c11-885f-342aacf769b3
Eur Comm, 2001. European Commission DG Environment. Ambient Air Pollution by As, Cd and Ni compounds. Position Paper. Final Version. Eur Comm Working Group on Arsenic Cadmium and Nickel Compounds, Available at: http://www.ec.europa.eu/environment/air/pdf/pp_as_cd_ni.pdf.
Eur Comm, 2007. Air Quality Standards Eur Comm DG Environment. Available at: http://ec.europa.eu/environment/air/quality/standards.htm.
Evans, M.S. *et al*., 2005. Persistent organic pollutants and metals in the freshwater biota of the Canadian Subarctic and Arctic: An overview. *Sci. Tot. Environ.*, 351-352, pp.94-147.
Evans, P., 2004. Unpublished data on metal concentrations in British Columbia groundwater. BC Ministry of Water, Land, and Air Protection, Victoria, BC.
Everhart, J.L. *et al*., 2006. Assessing nickel bioavailability in smelter-contaminated soils. *Sci.Tot. Environ.*, 367(2-3), pp.732-744.
Fait, G. *et al*., 2006. Tolerance of nitrifying bacteria to copper and nickel. *Environmental Toxicology and Chemistry*, 25(8), pp.2000-2005.
Fancey, L., 2004. Unpublished monitoring data on metal concentrations in crab and clam tissue collected by S. Ray, L.L. Fancey & D. Scruton for the National Contaminants Information System (NCIS). Fisheries and Oceans Canada, St. John's, NF.
Feisthauer, N.C. *et al*., 2006. Effects of metal-contaminated forest soils from the Canadian shield to terrestrial organisms. *Environmental Toxicology and Chemistry*, 25(3), pp.823-835.
Fergusson, J.E. & N.D. Kim, 1991. Trace elements in street and house dusts: Sources and speciation. *Science of the Total Environment*, 100, pp.125-150.
Fischer, L.A. *et al*., 2009. The dose-response relationship between the patch test and ROAT and the potential use for regulatory purposes. *Contact Dermatitis*, 61(4), pp.201-208.
Fischer, L.A., T. Menné & J.D. Johansen, 2005. Experimental nickel elicitation thresholds - A review focusing on occluded nickel exposure. *Contact Dermatitis*, 52(2), pp.57-64.
Fischer, L.A., T. Menné & J.D. Johansen, 2007a. Dose per unit area - A study of elicitation of nickel allergy. *Contact Dermatitis*, 56(5), pp.255-261.
Fischer, L.A., J.D. Johansen & T. Menne, 2007b. Nickel allergy: relationship between patch test and repeated open application test thresholds. *British Journal of Dermatology*, 157(4), pp.723-729.
Fisher, J.R., G.A. Rosenblum & B.D. Thomson, 1982. Asthma induced by nickel. *Journal of the American Medical Association*, 248(9), pp.1065-1066.
Fleet, J.C. *et al*., 1990. Induction of hepatic metallothionein by intraperitoneal metal injection: An associated inflammatory response. *American Journal of Physiology - Gastrointestinal and Liver Physiology*, 258(6 21-6), pp.G926-G933.
Fletcher, G.G. *et al*., 1994. Toxicity, uptake, and mutagenicity of particulate and soluble nickel compounds. *Environmental Health Perspectives*, 102(Supp. 3), pp.69-79.
Flint, G.N. & S. Packirisamy, 1995. Systemic nickel: The contribution made by stainless-steel cooking utensils. *Contact Dermatitis*, 32(4), pp.218-224.
Flint, G.N. & S. Packirisamy, 1997. Purity of food cooked in stainless steel utensils. *Food Additives and Contaminants*, 14(2), pp.115-126.
Flora, C.J. & E. Nieboer, 1980. Determination of Nanogram Quantities of Nickel by Differential Pulse Polarography at a Dropping Mercury Electrode and Selected Application. *Analytical Chemistry*, 52, pp.1013-1020.
Frank, R., K.I. Stonefield & P. Suda, 1982. Impact of nickel contamination on the production of vegetables on an organic soil, Ontario, Canada, 1980-1981. *Science of the Total Environment*, 26, pp.41-65.
Freedman, B. & T.C. Hutchinson, 1980. Effects of smelter pollutants on forest leaf litter decomposition near a nickel-copper smelter at Sudbury, Ontario. *Can. J. Bot.*, 58, pp.1722-1736.

Friel, J.K. *et al*., 1999. Elemental composition of human milk from mothers of premature and full- term infants during the first 3 months of lactation. *Biological Trace Element Research*, 67(3), pp.225-247.

Friske, P.W.B. *et al*., 1993. A detailed lake sediment and water geochemical survey, central Labrador. Open file 2650 Geological Survey of Canada.

FSANZ, 2008. The 22nd Australian Total Diet Study FSANZ. Available at: http://www.foodstandards.gov.au.

Füchtjohann, L., N. Jakurbowski, D. Gladtke, D. Klockow & J. A. C. Broekaert. 2001. Speciation of nickel in airborne particulate matter by means of sequential extraction in a micro flow system and determination by graphite furnace absorption spectrometry and inductively coupled mass spectrometry. J. Environ. Monit. 3, pp.681-687.

Fullerton, A. *et al*., 1986. Permeation of nickel salts through human skin in vitro. *Contact Dermatitis*, 15(3), pp.173-177.

Fullerton, A., J.R. Andersen & A. Hoelgaard, 1988. Permeation of nickel through human skin in vitro - Effect of vehicles. *British Journal of Dermatology*, 118(4), pp.509-516, in Hostynek *et al*. (2003).

Fullerton, A., T. Menne & A. Hoelgaard, 1989. Patch testing with nickel chloride in a hydrogel. *Contact Dermatitis*, 20(1), pp.17-20.

Füchtjohann, L. *et al.*, 2001. Speciation of nickel in airborne particulate matter by means of sequential extraction in a micro flow system and determination by graphite furnace atomic absorption spectrometry and inductively coupled plasma mass spectrometry. *Journal of Environmental Monitoring*, 3(6), pp.681-687, in OMOE.

Gallagher, L. & R.W. Macdonald, 2004. The historical record of metals in sediments from six lakes in the Fraser River Basin, BC. *Water Air Soil Pollut.*, 152(1-4), pp.257-278.

Galbreath, K.C., C.R. Crocker, C.M. Nyberg, F.E. Huggins, G.P. Huffman & K.P. Larson. 2003. Nickel speciation measurements of urban particulate matter: method evaluation and relevance to risk assessmente. J. Environ. Monit. 5(3):56N-61N.

Galle, P., J.P. Berry & C. Galle, 1992. Role of alveolar macrophages in precipitation of mineral elements inhaled as soluble aerosols. *Environmental Health Perspectives*, 97, pp.145-147.

Garrett, R., 2004. Summary statistics for nickel concentrations in stream sediment according to EcoRegion and EcoDistrict. Data on nickel concentrations in Prairie and Ontario soils. NRCan, Ottawa, ON .

Garrett, R., 2010. Summary statistics for nickel concentrations in stream sediment according to EcoRegion and EcoDistrict. Data on nickel concentrations in Yukon streams. Natural Resources Canada, Geological Survey of Canada E-mail to Deanna Lee.

Gawkrodger, D.J. *et al*., 1986. Nickel dermatitis: The reaction to oral nickel challenge. *British Journal of Dermatology*, 115(1), pp.33-38, as cited in Cal EPA OEHHA (2011 draft).

Gawkrodger, D.J., C.W. McLeod & K. Dobson, 2012. Nickel skin levels in different occupations and an estimate of the threshold for reacting to a single open application of nickel in nickel-allergic subjects. *British Journal of Dermatology*, 166(1), pp.82-87.

Gawkrodger, D.J., I.A. Shuttler & H.T. Delves, 1988. Nickel dermatitis and diet: Clinical improvement and a reduction in blood and urine nickel levels with a low-nickel diet. *Acta Dermato-Venereologica*, 68(5), pp.453-456.

Ge, Y., P. Murray & W.H. Hendershot, 2000. Trace metal speciation and bioavailability in urban soils. *Environmental Pollution*, 107(1), pp.137-144.

Gelinas, Y., M. Lucotte & J.P. Schmit, 2000. History of the atmospheric deposition of major and trace elements in the industrialized St. Lawrence Valley, QC, Canada. *Atmospheric Environment*, 34(11).

Gelinas, Y. & J.P. Schmit, 1998. Estimation of the bulk atmospheric deposition of major and trace elements to a rural watershed. *Atmospheric Environment*, 32 (9), pp.1473-1483.

Gewurtz, S.B. *et al*., 2008. Spatial distribution of legacy contaminants in sediments of Lakes Huron and Superior. *Journal of Great Lakes Research*, 34(1), pp.153-168.

Ghezzi, I. *et al*., 1989. Behaviour of urinary nickel in low-level occupational exposure. *Medicina del Lavoro*, 80(3), pp.244-50, in ATSDR (2005). Available at: http://www.ncbi.nlm.nih.gov/pubmed/2796834.
Giashuddin, M. & A.H. Cornfield, 1978. Incubation study on effects of adding varying levels of nickel (as sulphate) on nitrogen and carbon mineralisation in soil. *Environmental Pollution*, 15, pp.231-234.
Giashuddin, M. & A.H. Cornfield, 1979. Effects of adding nickel (as oxide) to soil to nitrogen and carbon mineralization at different pH values. *Environmental Pollution*, 19, pp.67-70.
Gibbs, R.J., 1977. Transport phases of transition metals in the Amazon and Yukon Rivers. *Geol. Soc. Am. Bull.*, 88, pp.829-843.
Gilman, J.P. & G.M. Ruckerbauer, 1962. Metal carcinogenesis. I. Observations on the carcinogenicity of a refinery dust, cobalt oxide, and colloidal thorium dioxide. *Cancer Research*, 22, pp.152-157.
Giroux, M. *et al*., 1992. Caractérisation de la teneur en métaux lourds totaux et disponibles des sols du Québec. *Agrosol*, 5(2), pp.46-55.
Gish, C.D. & R.E. Christensen, 1973. Cadmium, nickel, lead, and zinc in earthworms from roadside soil. *Environmental Science & Technology*, 7, pp.1060-1062.
Gizyn, W.I., 1994. Windsor Air Quality Study: Soil and Garden Produce Survey Results. Fall 1994 Phytotoxicology Section Standards Development Branch, OMEE.
Gizyn, W.I., 2002. Phytotoxicology 1999, 2000 and 2001 Investigations: Safety-Kleen Limited - Moore Township.
Gong, S-L., 2004. Unpublished monitoring data on metal concentrations in aerosol samples collected at Alert, NT. Environment Canada, Downsview, ON.
Goodman, J.E., 2011. Nickel metal not associated with lung cancer risk. *American Journal of Industrial Medicine*, 54(5), p.419.
Goodman, J.E. *et al*., 2009. Carcinogenicity assessment of water-soluble nickel compounds. *Critical Reviews in Toxicology*, 39(5), pp.365-417.
Goodman, J.E. *et al*., 2011. The nickel ion bioavailability model of the carcinogenic potential of nickel-containing substances in the lung. *Critical Reviews in Toxicology*, 41(2), pp.142-174.
Graham, H., 1995. Drinking Water Surveillance Program summary for 1993/1994 for nickel. Unpublished OMEE data received by Richard Carrier, Health Canada.
Grandjean, P., G.D. Nielsen & O. Andersen, 1989. Human exposure and chemobiokinetics. In T. Menne & H.I. Maibach, eds. *Nickel and the Skin: Immunology and Toxicology*. Boca Raton, FL: CRC Press, pp. 9-34.
Granero, S. *et al*., 1998. Biological monitoring of environmental pollution and human exposure to metals in Tarragona, Spain. I. Levels in hair of school children. *Trace Elements and Electrocytes*, 15(1), pp.39-43.
Graney, J.R., M.S. Landis & G.A. Norris, 2004. Concentrations and solubility of metals from indoor and personal exposure PM2.5 samples. *Atmospheric Environment*, 38(2), pp.237-247.
Grant, B.D. & J.G. Donaldson, 2009. Pathways and mechanisms of endocytic recycling. *Nature Reviews Molecular Cell Biology*, 10(9), pp.597-608.
Gratton, W.S., K.K. Nkongolo & G.A. Spiers, 2000. Heavy metal accumulation in soil and jack pine (Pinus banksiana) needles in Sudbury, ON, Canada. *Bulletin of Environmental Contamination and Toxicology*, 64(4), pp.550-557.
Greger, M., 1999. Metal availability and bioconcentration in plants. In M.N. Prasad & J. Hagemeyer, eds. *Heavy Metal Stress in Plants*. Berlin, Heidelberg: Springer-Verlag, pp. 1-27.
Griffin, S.R. *et al*., 1990. *Bioavailability in rats of metals adsorbed to soils*. USEPA DC, Hazleton Laboratories, America, Inc. Poster presented at the Society of Toxicology 29th Annual Meeting, Miami Beach, FL. February 12-16, 1990. Poster paper no. 623., in Birmingham & McLaughlin (2006).

Griffith, M.A., T. Spires & P. Barclay, 1984. Ontario Soil Baseline Survey, Analytical Data 1980-1981, Vol. 3, Analytical Data for Northern Ontario OMOE, Toronto, ON, in Environment Canada and Health Canada (1994).
Grimsrud, T.K. *et al*., 2000. Assessment of historical exposures in a nickel refinery in Norway. *Scandinavian Journal of Work, Environment and Health*, 26(4), pp.338-345.
Grimsrud, T.K. *et al*., 2002. Exposure to different forms of nickel and risk of lung cancer. *American Journal of Epidemiology*, 156(12), pp.1123-1132.
Grimsrud, T.K. *et al*., 2003. Lung cancer incidence among Norwegian nickel-refinery workers 1953-2000. *Journal of Environmental Monitoring*, 5(2), pp.190-197.
Grimsrud, T.K. *et al*., 2005. Can lung cancer risk among nickel refinery workers be explained by occupational exposures other than nickel. *Epidemiology*, 16(2), pp.146-154.
Grimsrud, T.K. & A. Andersen, 2010. Evidence of carcinogenicity in humans of water-soluble nickel salts. *Journal of Occupational Medicine and Toxicology*, 5(1).
Grimsrud, T.K. & J. Peto, 2006. Persisting risk of nickel related lung cancer and nasal cancer among Clydach refiners. *Occupational and Environmental Medicine*, 63(5), pp.365-366.
Grunsky, E.C., 2010. Geochemical Background in Soil and Till from Selected Areas Across Canada, including New Brunswick and the Maritime Provinces Soil Survey. Part 1: Till Geochemistry from Selected Areas in Canada.
Gül, Ü. *et al*., 2007. Nickel sensitivity in asthma patients. *Journal of Asthma*, 44(5), pp.383-384.
Gupta, S.K. *et al*., 1987. The effect of graded doses of nickel on the yield, the nickel content of lettuce and the soil respiration. *Toxicology and Environmental Chemistry*, 14, pp.1-9.
Gupta, V.K. & R. Kala, 1996. Effect of nickel on yield and its concentration in some rabi crops grown on typic ustipsamment. *J. Indian Soc. Soil Sci.*, 44(2), pp.348-349.
Haanstra, L. & P. Doelman, 1984. Glutamic acid decomposition as a sensitive measure of heavy metal pollution in soil. *Soil Biology and Biochemistry*, 16(6), pp.595-600.
Hachimi, A. *et al*., 1995. Interaction study of αNi_3S_2 with guinea pig alveolar macrophages by resonance ionization mass spectrometry. *Journal of Mass Spectrometry*, 30, pp.S183-S191.
Hack, A. P. Welge, J. Wittsiepe, M. Wilhelm & B. Marschner. 2002. Balance study for estimation of bioavaliability of soilborne contaminants in young minipigs. Contract report from Ruhr-Universität, Bochum to the German Umweltbundesamt, Berlin (in German with English summary). Available at: http://www.opengrey.eu/partner/fiz.
Hack, C.E. *et al*., 2007. A pharmacokinetic model of the intracellular dosimetry of inhaled nickel. *Journal of Toxicology and Environmental Health - Part A: Current Issues*, 70(5), pp.445-464.
Haq, A.U., T.E. Bates & Y.K. Soon, 1980. Comparison of extractants for plant-available zinc, cadmium, nickel and copper in contaminated soils. *Soil Science Society of America Journal*, 44, pp.772-777.
Halliwell, D.R. & S. Catto, 2003. How and why is aquatic quality changing at Nahanni National Park Reserve, NWT, Canada. *Environ. Monitor. Assess.*, 88(1-3), pp.243-281.
Halstead, R.L., B.J. Finn & A.J. MacLean, 1969. Extractability of nickel added to soils and its concentration in plants. *Canadian Journal of Soil Science*, 49, pp.335-342.
Hammond, D. & R.J. O'Connor, 2008. Constituents in tobacco and smoke emissions from Canadian cigarettes. *Tobacco Control*, 17(supp. 1), pp.i24-i31.
Hansen, K. & R.M. Stern, 1983. In vitro toxicity and transformation potency of nickel compounds. *Environmental Health Perspectives*, 51, pp.223-226.
Haro, R.T. *et al*., 1968. Studies on the acute toxicity of nickelocene. *Proc. West Pharmacol. Soc.*, 11, pp.39-42.
Harris, G., 2004. Unpublished data on metal concentrations in British Columbia soils. BC Ministry of Water, Land, and Air Protection, Victoria, BC.
Hase, S., 2004. Unpublished monitoring data for ambient metal concentrations in Saskatchewan surface waters. SK Environment, Regina, SK .

Hassler, E. *et al*., 1983. Urinary and fecal elimination of nickel in relation to air-borne nickel in a battery factory. *Annals of Clinical Laboratory Science*, 13(3), pp.217-224. Available at: http://www.ncbi.nlm.nih.gov/pubmed/6870185.

Havas, M. & T.C. Hutchinson, 1983. The Smoking Hills: natural acidification of an aquatic ecosystem. *Nature*, 301, pp.23-27.

Haynes, W.M., 2011. Section 4. Properties of the elements and inorganic compounds. In *CRC Handbook of Chemistry and Physics*. Boca Raton, FL: CRC Press/Taylor and Francis.

HC, 1994. Canadian Environmental Protection Act. Human health risk assessment for priority substances HC.

HC, 1996. Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances HC. Available at: http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/hbct-jact/index-eng.php.

HC, 2010. Federal Contaminated Site Risk Assessment in Canada, Part I: Guidance on Human Health Preliminary Quantitative Risk Assessment (PQRA), Version 2.0 HC Safe Environments Directorate Contaminated Sites Division.

HC, 2011 Draft. Estimated Daily Intake Development Methodology Nickel HC Safe Environments Directorate Contaminated Sites Division.

He, Z.L., X.E. Yang & P.J. Stofella, 2005. Trace elements in agroecosystems and impacts on the environment. *J. Trace Elements Med. Biol.*, 19(2-3), pp.125-140.

Heale, E.L. & D.P. Ormrod, 1982. Effects of nickel and copper on *Acer rubrum*, *Cornus stolonifera*, *Lonicera tatarica* and *Pinus resinosa*. *Can. J. Bot.*, 60, pp.2674-2681.

Heim, K.E. *et al*., 2007. Oral carcinogenicity study with nickel sulfate hexahydrate in Fischer 344 rats. *Toxicology and Applied Pharmacology*, 224(2), pp.126-137.

Henderson, R.G. *et al*., 2012. Oral bioaccessibility testing and read-across hazard assessment of nickel compounds. *Regulatory Toxicology and Pharmacology*, 63(1), pp.20-28.

Henriksson, J., J. Tallkvist & H. Tjälve, 1997. Uptake of nickel into the brain via olfactory neurons in rats. *Toxicology Letters*, 91(2), pp.153-162.

Henry, W.M. & K.T. Knapp, 1980. Compound forms of fossil fuel fly ash emissions. *Environmental Science and Technology*, 14(4), pp.450-456.

Heon, D., 2003. Yukon Regional Geochemical Database 2003 - Stream sediment analyses Exploration and Geological Services Division (Whitehorse) Yukon Region, Indian and Northern Affairs Canada.

Hesterberg, D., 1998. Biogeochemical cycles and processes leading to changes in mobility of chemicals in soils. *Agri. Ecosystems Environ.*, 67(2-3), pp.121-133.

Hickey, M.F. & J.A. Kittrick, 1984. Chemical partitioning of cadmium, copper, nicle and zinc in soils and sediments containing high levels of heavy metals. *J. Environ. Qual.*, 13, pp.372-376, in McGrath (1995).

Hildebrand, H.F. *et al*., 1990. Uptake and biological transformation of βNiS and αNi_3S_2 by human embryonic pulmonary epithelial cells (L132) in culture. *Carcinogenesis*, 11(11), pp.1943-1950.

Hildebrand, H.F. *et al*., 1991. In vitro and in vivo uptake of nickel sulfides by rat lymphocytes. *Archives of Toxicology*, 65(4), pp.324-329.

Hill, C.H., 1979. The effect of dietary protein levels on mineral toxicity in chicks. *The Journal of nutrition*, 109(3), pp.501-7. Available at: http://www.ncbi.nlm.nih.gov/pubmed/430253.

Hindsén, M. & M. Bruze, 1998. The significance of previous contact dermatitis for elicitation of contact allergy to nickel. *Acta Dermato-Venereologica*, 78(5), pp.367-370.

Hindsén, M., M. Bruze & O.B. Christensen, 1999. Individual variation in nickel patch test reactivity. *American Journal of Contact Dermatitis*, 10(2), pp.62-67.

Hindsén, M., M. Bruze & O.B. Christensen, 2001. Flare-up reactions after oral challenge with nickel in relation to challenge dose and intensity and time of previous patch test reactions. *Journal of the American Academy of Dermatology*, 44(4), pp.616-623.

Hindsén, M., M. Bruze & O.B. Christensen, 1997. The significance of previous allergic contact dermatitis for elicitation of delayed hypersensitivity to nickel. *Contact Dermatitis*, 37(3), pp.101-106.
Hindsén, M., A. Spirén & M. Bruze, 2005. Cross-reactivity between nickel and palladium demonstrated by systemic administration of nickel. *Contact Dermatitis*, 53(1), pp.2-8.
Hirano, S. *et al*., 1994. Pulmonary clearance and inflammatory potency of intratracheally instilled or acutely inhaled nickel sulfate in rats. *Archives of Toxicology*, 68(9), pp.548-554.
Ho, W. & A. Furst, 1973. Nickel excretion by rats following a single treatment. *Proceedings of the Western Pharmacology Society*, Vol.16, pp.245-248, in OEHHA (2011 draft).
Hoff, R.M. & L.A. Barrie, 1986. Air chemistry observations in the Canadian Arctic. *Water Science and Technology*, 18(2), pp.97-107.
Hohnadel, D.C. *et al*., 1973. Atomic absorption spectrometry of nickel, copper, zinc, and lead in sweat collected from healthy subjects during sauna bathing. *Clinical Chemistry*, 19(11), pp.1288-1292.
Holt-Oduro, C., 2004. Unpublished data on metal concentrations in Alberta groundwater. AB Environment, Edmonton, AB.
Hong, C.S. *et al*., 1986. Occupational asthma caused by nickel and zinc. *Korean Journal of Internal Medicine*, 1(2), pp.259-262.
Hopfer, S.M., W.P. Fay & F.W. Sunderman, 1989. Serum Nickel Concentrations in Hemodialysis Patients with Environmental Exposure. *Annals of Clinical Laboratory Science*, 19, pp.161-167.
Hopkin, S.P., 1989. *Ecophysiology of Metals in Terrestrial Invertebrates* , Barking, UK: Elsevier Appl. Science.
Horak, E. & F.W. Sunderman Jr, 1973. Fecal nickel excretion by healthy adults. *Clinical Chemistry*, 19(4), pp.429-430. A
Horie, M. *et al*., 2009. Ultrafine NiO particles induce cytotoxicity in vitro by cellular uptake and subsequent Ni(II) release. *Chemical Research in Toxicology*, 22(8), pp.1415-1426.
Hostýnek, J.J., 2003. Factors determining percutaneous metal absorption. *Food and Chemical Toxicology*, 41(3), pp.327-345.
Hostýnek, J.J., F. Dreher, A. Pelosi, *et al*., 2001a. Human stratum corneum penetration by nickel: In vivo study of depth distribution after occlusive application of the metal as powder. *Acta Dermato-Venereologica, Supplement*, (212), pp.5-10.
Hostýnek, J.J., F. Dreher, T. Nakada, *et al*., 2001b. Human stratum corneum adsorption of nickel salts: Investigation of depth profiles by tape stripping in vivo. *Acta Dermato-Venereologica, Supplement*, (212), pp.11-18.
Hostýnek, J.J., K.E. Reagan & H.I. Maibach, 2002. Oxidative properties of skin exudates - A determinant for nickel diffusion: A review. *Exogenous Dermatology*, 1(1), pp.7-17.
Hsieh, T.H., 1999. A dosimetry model of nickel compounds in the rat lung. *Inhalation Toxicology*, 11(3), pp.229-248. Available at: http://informahealthcare.com/doi/abs/10.1080/089583799197168.
Hu K., Z. *et al*., 2002. Effect of nickel and cadmium speciation on nitrification inhibition. *Environmental Science & Technology*, 36(14), pp.3074-3078.
Hung, G.A., 2007. Metal accumulation in surface salt marsh sediments of the Bay of Fundy, Canada. *Estuaries and Coasts*, 30(4), pp.725-734.
Hunter, J.G. & O. Vergnano, 1952. Nickel toxicity in plants. *Proceedings of the Association of Applied Biologists*, pp.279-284.
Hutchinson, T.C., B. Freedman & L. Whitby, 1981. Nickel in Canadian soils and vegetation. In *Effects of Nickel in the Canadian Environment*. Ottawa, ON: National Research Council of Canada, pp. 119-157.
Hutchinson, T.C. & M. Havas, 1986. Recovery of previously acidified lakes near Coniston, Canada following reductions in atmospheric sulphur and metal emissions. *Water, Air, and Soil Pollution*, 28(3-4), pp.319-333.
Hutzell, W.T. & D.J. Luecken, 2007. Fate and transport of emissions for several trace metals over the United States. *Science of the Total Environment*, 396(2-3), pp.164-179.

IARC, 1990. Chromium, Nickel and Welding. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, 49.
IARC, 2011. Nickel and nickel compounds. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Supplement*, 100 C, pp.169-218.
ICRP, 1981. Limits for intakes of radionuclides by workers. ICRP Publication 30, Part 2.
Ikem, A. *et al*., 2002. Levels of 26 elements in infant formula from USA, UK, and Nigeria by microwave digestion and ICP-OES. *Food Chemistry*, 77(4), pp.439-447.
INAC, 2003. Canadian Arctic Contaminants Assessment Report II INAC., pp.148-152.
IOM, 2001. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc IOM Food and Nutrition Board.
Ishimatsu, S. *et al*., 1995. Distribution of various nickel compounds in rat organs after oral administration. *Biological Trace Element Research*, 49(1), pp.43-52.
Jackson, M.B., 1988. The dominant attached filamentous algae of Georgian Bay, the North Channel and Eastern Lake Huron: Field ecology and biomonitoring potential during 1980. *Hydrobiologia*, 163(1), pp.149-171.
Jacques, A.P., 1987. Summary of emissions of antimony, arsenic, cadmium, chromium, copper, lead, manganese, mercury and nickel in Canada.Environment Canada. 44 p.
Janssen, R.P., W.J.G. Peijnenburg & L. Posthuma, 1997. Equilibrium partitioning of heavy metals in Dutch field soils. I. Relationship between metal partition coefficients and soil characteristics. *Environ. Toxicol. and Chem.*, 16(12), pp.2470-2478.
Jenkins, G., 1992. Ontario Ministry of the Environment, Water Resources, Toronto, ON.
Jensen, C.S. *et al.*, 2003. Experimental systemic contact dermatitis from nickel: A dose-response study. *Contact Dermatitis*, 49(3), pp.124-132.
Jensen, C.S., T. Menné & J. Duus Johansen, 2006. Systemic contact dermatitis after oral exposure to nickel: A review with a modified meta-analysis. *Contact Dermatitis*, 54(2), pp.79-86.
Jensen, P. *et al*., 2011. Excessive nickel release from mobile phones-a persistent cause of nickel allergy and dermatitis. *Contact Dermatitis*, 65(6), pp.354-358.
Jøhnke, H. *et al*., 2004. Reactivity to patch tests with nickel sulfate and fragrance mix in infants. *Contact Dermatitis*, 51(3), pp.141-147.
Johnson, D. & B. Hale, 2004. White birch (*Betula papyrifera Marshall*) foliar litter decomposition in relation to trace metal atmospheric inputs at metal-contaminated and uncontaminated sites near Sudbury, ON and Rouyn-Noranda, QC, Canada. *Environmental Pollution*, 127(1), pp.65-72.
Jones Geoff (via Edwin Yee), 2004. Unpublished monitoring data for ambient metal concentrations in soils across the province of Manitoba (1995 to 2003). MB Conservation, Winnipeg, MB.
Jones-White, D., 1992. Ontario Ministry of the Environment database on drinking water. Various paginations.
Kaaber, K. *et al*., 1979. Antabuse® treatment of nickel dermatitis. Chelation - a new principle in the treatment of nickel dermatitis. *Contact Dermatitis*, 5(4), pp.221-228.
Kaaber, K., N.K. Veien & J.C. Tjell, 1978. Low nickel diet in the treatment of patients with chronic nickel dermatitis. *British Journal of Dermatology*, 98(2), pp.197-201.
Kabata-Pendias, A. & A.B. Mukherjee, 2007. *Trace Elements from Soil to Human*, Berlin Heidelberg: Springer-Verlag.
Kabata-Pendias, A. & H. Pendias, 1984. *Trace Elements in Soils and Plants*, Boca Raton, FL: CRC Press Inc.
Käkelä R, A. Käkelä & H.Hyvärinen, 1999. Effects of nickel chloride on reproduction of the rat and possible antagonistic role of selenium. Comp Biochem Physiol C Pharmacol Toxicol Endocrinol. 23(1), 27-37.
Kalimo, K., K. Lammintausta & J. Maki, 1985. Nickel penetration in allergic individuals: Bioavailability versus X-ray microanalysis detection. *Contact Dermatitis*, 12(5), pp.255-257.

Kapustka, L.A., D. Eskew & J.M. Yocum, 2006. Plant toxicity testing to derive ecological soil screening levels for cobalt and nickel. *Environmental Toxicology and Chemistry*, 25(3), pp.865-874.
Kasprzak, K.S. & F.W. Sunderman Jr, 1969. The metabolism of nickel carbonyl-14C. *Toxicology and Applied Pharmacology*, 15(2), pp.295-303.
Kasprzak, K.S., F.W. Sunderman Jr & K. Salnikow, 2003. Nickel carcinogenesis. *Mutation Research - Fundamental and Molecular Mechanisms of Mutagenesis*, 533(1-2), pp.67-97.
Kaszycki, C.A., 1986. Surficial geology and till geochemistry, Lynn Lake - Leaf Rapids Region, Manitoba, in Current Research, Part B, Geological Survey of Canada Paper 861-B, 245-256.
Ke, Q. *et al*., 2007. Fluorescent tracking of nickel ions in human cultured cells. *Toxicology and Applied Pharmacology*, 219(1), pp.18-23.
Keller, W., J.R. Pitblado & J. Carbone, 1992. Chemical responses of acidic lakes in the Sudbury, Ontario, area to reduced smelter emissions, 1981-89. *Canadian Journal of Fisheries and Aquatic Sciences*, 49(Supp.1), pp.25-32.
Kelly, S.J., C. Hertzman & M. Wiens, 1991. *Element Analysis of 198 Soil Samples Collected in Trail B.C.* Prepared for the B.C. Ministry of Environment.
Khalid, B.Y. & J. Tinsley, 1980. Some effects of nickel toxicity on rye grass. *Plant and Soil*, 55, pp.139-144.
Kilburn, K.H. *et al*., 1989. Respiratory symptoms and functional impairment from acute (cross-shift) exposure to welding gases and fumes. *American Journal of the Medical Sciences*, 298(5), pp.314-319.
Kim, N. & J. Fergusson, 1993. Concentrations and sources of cadmium, copper, lead, and zinc in house dust in Christchurch, New Zealand. *Science of the Total Environment*, 138, pp.1-21.
Kimber, I. *et al*., 2002. Allergic contact dermatitis. *International Immunopharmacology*, 2(2-3), pp.201-211.
Kissel, J.C. *et al*., 1998. Empirical investigation of hand-to-mouth transfer of soil. *Bulletin of environmental contamination and toxicology*, 60(3), pp.379-86. Available at: http://link.springer.com/journal/128/60/3.
Kissel, J.C., K.Y. Richter & R. Fenske, 1996. Field measurement of dermal soil loading attributable to various activities: implications for exposure assessment. *Risk analysis: an official publication of the Society for Risk Analysis*, 16(1), pp.115-25. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8868226.
Klassen, R.A. & F.J. Thompson, 1990. Glacial history, drift composition and till geochemistry, Labrador. GSC-Open File 2170.
Koch, I., K. Reimer & C. Ollson. 2005. Application of Bioaccessibility for Contaminated Site Risk Assessment. Presentation at Health Canada Bioaccessibility Workshop. August 30-31, 2005. Delta Chelsea Hotel, Toronto. Available at: http://www.bioavailabilityresearch.ca/Final%20Bio%20Workshop%20Proceedings%20Jan06.pdf.
Kodama, Y. *et al*., 1993. Comparative deposition and clearance of various nickel compounds exposed by inhalation in rats. *Biological Trace Element Research*, 36(3), pp.257-269.
Kodama, Y., S. Ishimatsu & K. Matsuno, 1985. Pulmonary deposition and clearance of a nickel oxide aerosol by inhalation. *Biological Trace Element Research*, 7(1), pp.1-9.
Koizumi, C. *et al*., 2004. Urinary nickel: Measurement of exposure by inductively coupled plasma argon emission spectrometry. *Toxicology and Industrial Health*, 20(6-10), pp.103-108.
Kolesarova, A., M. Capcarova, H. Arpasova, A. Kalafova, P. Massanyi, N. Lukac, J. Kovacik & M. Schneidgenova. 2008. Nickel-induced blood biochemistry alterations in hens after an experimental peroral administration. *J. Environ. Sci. Health* B43:625-632.
Kollmeier, H. *et al*., 1990. Age, sex, and region adjusted concentrations of chromium and nickel in lung tissue. *British Journal of Industrial Medicine*, 47(10), pp.682-687.

Konhauser, K.O. *et al*., 2009. Oceanic nickel depletion and a methanogen famine before the Great Oxidation Event. *Nature*, 458(7239), pp.750-753.
Korthals, G.W. *et al*., 1996. Short-term effects of cadmium, copper, nickel, and zinc on soil nematodes from different feeding and life-history strategy groups. *Applied Soil Ecology*, 4, pp.107-117.
Koutrakis, P., S.L.K. Briggs & B.P. Leaderer, 1992. Source apportionment of indoor aerosols in suffolk and onondaga counties, New York. *Environmental Science and Technology*, 26(3), pp.521-527.
Kukier, U. & R.L. Chaney, 2001. Amelioration of nickel phytotoxicity in muck and mineral soils. *Journal of Environment Quality*, 30(6), pp.1949-1960.
Kuligowski, J. & K.M. Halperin, 1992. Stainless steel cookware as a significant source of nickel, chromium, and iron. *Archives of Environmental Contamination and Toxicology*, 23(2), pp.211-215, in Environment Canada and Health Canada.
Kurowska, E. & W. Bal, 2010. Recent advances in molecular toxicology of cadmium and nickel. , 4, pp.85-126.
Kutman, B.Y., U.B Kutman & I. Cakmak. 2013. Nickel-enriched seed and externally supplied nickel to improve growth and alleviate foliar urea damage in soybean. *Plant Soil*, 363, pp. 61-75.
Lacy, S.A. *et al*., 1996. Distribution of nickel and cobalt following dermal and systemic administration with in vitro and in vivo studies. *Journal of Biomedical Materials Research*, 32(2), pp.279-283.
Laliberté, D., 2004. Teneurs en métaux dans les sédiments et les poissons des lacs aux Dorés, Chibougamau, Obatogamau et Waconichi en 2002. Ministère de l'Environnement du Québec, Direction du suivi de l'état de l'environnement.
Laliberté, D. & G. Trembaly, 2002. Teneurs en métaux, en BPC et en dioxines et furanes dans les poissons et les sédiments de quatre lacs du nord du Québec en 2001. Ministère de l'Environnement du Québec, Direction du suivi de l'état de l'environnement.
Lamoureux, M., 2005. Report on nickel (Ni) speciation in particulate matter collected on filters. Enviroanalytix Services. October 5, 2005, in OMOE (2011) .
Lamoureux, M., 2003. The characterization of nickel and arsenic species in air filters for the Ministry of Environment of Ontario. Preliminary report on nickel speciation. Environanalytix Services. March 25, 2002, in OMOE (2011).
Larsen, E.H. *et al*., 2002. Monitoring the content and intake of trace elements from food in Denmark. *Food Additives Contamin.*, 19, pp.33-46.
Larter, N.C. & J.A. Nagy, 2000. A comparison of heavy metal levels in the kidneys of High Arctic and mainland caribou populations in the Northwest Territories of Canada. *Science of the Total Environment*, 246(2-3), pp.109-119.
Lee, S.Z. *et al*., 2001. The effect of hydration on adsorption and desorption of heavy metals in soils. *J. Environ. Sci. Health Part A Toxic/Hazardous Substances and Environmental Engineering*, 36 (1), pp.63-74.
Leece, B. & S. Rifat, 1997. Technical Report. Assessment of Potential Health Risk of Reported Soil Levels of Nickel, Copper and Cobalt in Port Colborne and Vicinity May 1997. Available at: http://booksnow1.scholarsportal.info/ebooks/oca5/5/ome/pdf/assessmentofpote00ontauoft.pdf.
Leger, D.A., 1991. Data summary report on nickel in Atlantic Canada (1973-1990). IWD-AR-WQR-91-60 Environment Canada Inland Water Directorate, Water Quality Branch.
Lehnert, B.E., Y.E. Valdez & G.L. Tietjen, 1989. Alveolar macrophage-particle relationships during lung clearance. *American Journal of Respiratory Cell and Molecular Biology*, 1(2), pp.145-154.
Li, B. *et al*., 2011. Influences of soil properties and leaching on nickel toxicity to barley root elongation. *Ecotoxicology and Environmental Safety*, 74, pp.459-466.
Li, C.S., L.Y. Hsu & Y.Y.T. Chuang, 1993. Elemental profiles of indoor and outdoor particulate matter less than 10 μm (PM_{10}) and 2.5 μm ($PM_{2.5}$) in Taipei. *Chemosphere*, 27(11), pp.2143-2154.
Li, Z., H. Wang, & W.S. Wu, 2008. Pharmacokinetic parameter and residua of ^{63}Ni-$NiCl_2$ in rat. *Yaoxue Xuebao*, 43(2), pp.224-226.

Liang, C.N. & M.A. Tabatabai, 1977. Effects of trace elements on nitrogen mineralization in soils. *Environmental Pollution*, 12, pp.141-147.
Liang, C.N. & M.A. Tabatabai, 1978. Effects of trace elements on nitrification in soils. *Journal of Environment Quality*, 7, pp.291-293.
Liang, J. & J.J. Schoenau, 1995. Development of resin membranes as a sensitive indicator of heavy metal toxicity in the soil environment. *International Journal of Environmental Analytical Chemistry*, 59, pp.265-275.
Lighthart, B., J. Bahim & V.V. Volk, 1983. Microbial respiration and chemical speciation in metal-amended soils. *Journal of Environment Quality*, 12.
Ling, J.R. & R.M. Leach, 1979. Studies on nickel metabolism: Interaction with other mineral elements . *Poultry Sci.*, 58, pp.591-596.
Lisiewicz, M., R. Heimburger & J. Golimowski, 2000. Granulometry and the content of toxic and potentially toxic elements in vacuum-cleaner collected, indoor dusts of the city of Warsaw. *Science of the Total Environment*, 263(1-3), pp.69-78.
Llobet, J.M. *et al.*, 1998. Biological monitoring of environmental pollution and human exposure to metals in Tarragona, Spain. III. Blood levels. *Trace Elements and Electrocytes*, 15(2), pp.76-80.
Lloyd, G.K., 1980. Dermal absorption and conjugation of nickel in relation to the induction of allergic contact dermatitis: Preliminary results . In S.F.W. Brown (Jr.), ed. *Nickel Toxicology*. London, England: Academic Press, pp. 145-148, in R.H. Guy, J.J. Hosty.
Lock, K. & C.R. Janssen, 2002. Ecotoxicity of nickel to *Eisenia fetida, Enchytraeus albidus*, and *Folsomia candida*. *Chemosphere*, 46, pp.197-200.
Lucassen, M. & B. Sarkar, 1979. Nickel(II)-binding constituents of human blood serum. *Journal of Toxicology and Environmental Health*, 5(5), pp.897-905.
Lumb, A., D. Halliwell & T. Sharma, 2006. Application of CCME water quality index to monitor water quality: a case study of the Mackenzie River Basin, Canada. *Environ. Monitor. Assess.*, 113(1-3), pp.411-429.
Lutwick, G., 1994. Unpublished data on nickel levels in Alberta agricultural soils. AB Environment, Environmental Protection Services, Wastes and Chemicals Division, Soil Protection Branch, Lethbridge, AB Received by Sylvie Coad and Victoria Laube.
Ma, L.Q., 1997. Chemical fractionation of cadmium, copper, nickel, and zinc in contaminated soils. *J. Environ. Qual.*, 26(1), pp.259-264.
Ma, W.C., 1982. The influence of soil properties and worm-related factors on the concentration of heavy metals in earthworms. *Pedobiologia*, 24, pp.109-119.
MAC, 1991. *Mining in Canada: Facts and figures*, Ottawa, ON.
MacLatchy, J., 1992. Environment Canada, Industrial Programs Branch, Hull, QC, unpublished information.
MacLean, A.J. & A.J. Dekker, 1978. Availability of zinc, copper, and nickel to plants grown in sewage-treated soils. *Canadian Journal of Soil Science*, 58, pp.381-389.
Maciariello, S.L. *et al.*, 2010. Nickel allergy: Description of a case of rhinitis and atypical professional Asthma [Allergia da nichel: Presentazione di un caso di rinite e di asma professionale Atipico]. *Capsula Eburnea* , 2010, pp.45-49.
Macomber, L. & R.P. Hausinger, 2011. Mechanisms of nickel toxicity in microorganisms. *Metallomics*, 3(11), pp.1153-1162.
Madany, I.M., M.S. Akhter & O.A. Al Jowder, 1994. The correlations between heavy metals in residential indoor dust and outdoor street dust in Bahrain. *Environment International*, 20(4), pp.483-492.
Madrid, F., M. Biasioli & F. Ajmone-Marsan, 2008. Availability and bioaccessibility of metals in fine particles of some urban soils. *Archives of Environmental Contamination and Toxicology*, 55(1), pp.21-32.

Malecki, M.R., E.F. Neuhauser & R.C. Loehr, 1982. The effect of metals on the growth and reproduction of *Eisenia foetida* (*Oligochaeta, Lumbricidae*). *Pedobiologia*, 24, pp.129-137.
Mallory, M.L. *et al*., 1998. Chemical trends and status of small lakes near Sudbury, ON, 1983-1995: Evidence of continued chemical recovery. *Canadian Journal of Fisheries and Aquatic Sciences*, 55(1), pp.63-75.
Malo, J.L., A. Cartier & M. Doepner, 1982. Occupational asthma caused by nickel sulfate. *Journal of Allergy and Clinical Immunology*, 69(1 I), pp.55-59.
Malo, J.L., A. Cartier & G. Gagnon, 1985. Isolated late asthmatic reaction due to nickel sulphate without antibodies to nickel. *Clinical Allergy*, 15(2), pp.95-99.
Manchananda, D. 2011. Nickel Release Regulations, EN 1811:2011 - What's New? The Laboratory at the Birmingham Assay Office. Birmingham.
Mandal, R. *et al*., 2002. Chemical speciation and toxicity of nickel species in natural waters from the Sudbury area (Canada). *Environmental Science & Technology*, 36(7), pp.1477-1484.
Marsalek, J., W.E. Watt & B.C. Anderson, 2006. Trace metal levels in sediments deposited in urban stormwater management facilities. *Water Science & Technology*, 53(2), pp.175-183.
Martinez, D. & G. Diaz, 1996. Effect of graded levels of dietary nickel and manganese on blood haemoglobin content and pulmonary hypertension in broiler chickens Effect of graded levels of dietary nickel and manganese on blood haemoglobin content and pulmonary hypertension in broiler chickens. *Avian Pathology*, 25(3), pp. 37-41.
Marvin, C. *et al*., 2007. Metals associated with suspended sediments in Lakes Erie and Ontario, 2000-2002. *Environ. Monitor. Assess.*, 130(1-3), pp.149-161.
Marvin, C., L. Grapentine & S. Painter, 2004. Application of a sediment quality index to the lower Laurentian Great Lakes. *Environ. Monitor. Assess.*, 91, pp.1-16.
Marzouk, A. & F.W. Sunderman Jr, 1985. Biliary excretion of nickel in rats. *Toxicology Letters*, 27(1-3), pp.65-71. Available at: http://www.sciencedirect.com/science/article/pii/0378427485901213.
Massoura, S.T. *et al*., 2006. Control of nickel availability by nickel bearing minerals in natural and anthropogenic soils. *Geoderma*, 136(1), pp.28-37.
McConnell, L.H. *et al*., 1973. Asthma caused by nickel sensitivity. *Annals of Internal Medicine*, 78(6), pp.888-890.
McGrath, S.P., 1995. Nickel. In B. J. Alloway, ed. *Heavy Metals in Soils*. London UK: Blackie Academic & Professional, pp. 152-174.
McIlveen, W.D., 1998. Investigation into Chemical Composition of Shales in Ontario. OMOE, Phytotoxicology Section, Standards Development Branch.
McIlveen, W.D. & J.J. Negusanti, 1993. Nickel in the terrestrial environment. In E. Nieboer, ed. *Proceedings of the Fifth International conference on Nickel Metabolism and Toxicity*. Sudbury, ON, Canada, Sept. 1992.
McKeague, J.A. & M.S. Wolynetz, 1980. Background levels of minor elements in some Canadian soils. *Geoderma*, 24(4), pp.299-307.
McMurter, H.J.G., 1993. Soil ingestion estimates for livestock and wildlife (unpublished report) Environment Canada Eco-Health Branch.
MEF, 1998. Politique de protection des sols et de réhabilitation des terrains contaminés - Nouvelle politique. Available at: http://www.mddelcc.gouv.qc.ca/sol/terrains/politique-en/appendix2.htm.
Melluzi, A., F. Simoncini, F. Sirri, L. Vandi & G. Giordani, 1996. Feeding hens diets supplemented with heavy metals (chromium, nickel and lead). *Archiv fuer Gelfuegelkunde*. 603(3), pp. 119-125.
Menne, T. & G. Calvin, 1993. Concentration threshold of non-occluded nickel exposure in nickel-sensitive individuals and controls with and without surfactant. *Contact Dermatitis*, 29(4), pp.180-184.
Menne, T., H.I. Mikkelsen & P. Solgaard, 1978. Nickel excretion in urine after oral administration. *Contact Dermatitis*, 4(2), pp.106-108.

Menon, C.R. & E. Nieboer, 1986. Uptake of nickel(II) by human peripheral mononuclear leukocytes. *Journal of Inorganic Biochemistry*, 28(2-3), pp.217-225.
Menzel, D.B. *et al*., 1987. Pharmacokinetic modeling of the lung burden from repeated inhalation of nickel aerosols. *Toxicology Letters*, 38(1-2), pp.33-43.
Menzies, N.W., M.J. Donn & P.M. Kopittke. 2007. Evaluation of extractants for estimation of the phytoavailable trace metals in soils. *Environmental Pollution*, 145(1), 121-130.
Méranger, J.C., K.S. Subramanian & C. Chalifoux, 1981. Survey for cadmium, cobalt, chromium, copper, nickel, lead, zinc, calcium, and magnesium in Canadian drinking water supplies. *J. Assoc. Analytic Chem*, 64, pp.44-53.
Mertz, W., 1979. The newer trace elements. *Biological Trace Element Research*, 1(3), pp.259-270.
Meyer, J.D. *et al.*, 2000. Occupational contact dermatitis in the UK: A surveillance report from EPIDERM and OPRA. *Occupational Medicine*, 50(4), pp.265-273.
MHSPE, 1994. Environmental Quality Objectives in the Netherlands Risk Assessment and Environmental Quality Division Directorate for Chemicals, External Safety and Radiation Protection.
Mills, J.G. & M.A. Zwarich, 1975. Heavy metal content of agricultural soils in Manitoba. *Canadian Journal of Soil Science*, 55, pp.295-300.
Molas, J. & S. Baran, 2004. Relationship between the chemical form of nickel applied to the soil and its uptake and toxicity to barley plants (*Hordeum vulgare L.*). *Geoderma*, 122(2-4), pp.247-255.
Molnár, P. *et al*., 2006. Personal exposures and indoor, residential outdoor, and urban background levels of fine particle trace elements in the general population. *Journal of Environmental Monitoring*, 8(5), pp.543-551.
Moman, S.A., G.S. Plumlee & D.B. Smith, 2009. Application of in vitro extraction studies to evaluate element bioaccessibility in soils form a transect across the United States and Canada. Applied Geochemistry. 24(2009): 1454-1463.
Moody, R.P. *et al*., 2009. Contaminated soils (II): In vitro dermal absorption of nickel (Ni-63) and mercury (Hg-203) in human skin. *Journal of Toxicology and Environmental Health Part A*, 72(8), pp.551-559.
Moon, J. *et al*., 1988. Correlation clusters in the accumulation of metals in human scalp hair: Effects of age, community of residence, and abundances of metals in air and water supplies. *Science of the Total Environment*, 72(1), pp.87-112.
Moore, J.W. & S. Ramamoorthy, 1984. Heavy metals in natural waters: applied monitoring and impact assessment.
Moreno, J.L., A. Pérez & A. Aliaga, 2003. The ecological dose of nickel in a semiarid soil amended with sewage sludge related to the unamended soil. *Water, Air, and Soil Pollution*, 143, pp.289-300.
Morgan, L.G. & P.J.C. Rouge, 1984. Biological monitoring in nickel refinery workers. In F.W. Sunderman, ed. *Nickel in the Human Environment. IARC Scientific Publications*. Lyon, France: International Agency for Research on Cancer, pp. 507-20, in Roels *et al*. (1993).
Morvai, V. *et al*., 1992. The role of maternal and placental circulation in the embryotoxic and teratogenic effects induced by nickel sulphate. *Reproductive Toxicology*, 6(2), pp.183-184.
Muir, D. *et al.*, 1993. Prevalence of small opacities in chest radiographs of nickel sinter plant workers. *British Journal of Industrial Medicine*, 50(5), pp.428-431.
Muir, D. *et al.*, 2005. Spatial and temporal trends of mercury and other metals in landlocked char from lakes in the Canadian Arctic archipelago. *Sci Total Environ.*, 351-352, pp.464-478.
Murdoch, A., L. Sarazin & T. Lomas, 1988. Summary of surface and background concentrations of selected elements in the Great Lakes sediments. *Journal of Great Lakes Research*, 14(2), pp.241-251.
Murray, Y.G. & W.H. Hendershot, 2000. Trace metal speciation and bioavailabiliy in urban soils. *Environmental Pollution*, 107(1), pp.137-144.
NAS, 1975. Medical and biological effects of environmental pollutants: Nickel Academy of Sciences.

Nason, T., 2004. pers. comm. Alberta Environmental Protection.
Nava, C. *et al.*, 1987. Chromium and nickel salts: a cause of allergic contact dermatitis due to detergents. *Medicina del Lavoro*, 78(5), pp.405-412, in Environment Canada and Health Canada.
Neuhauser, E.F. *et al*., 1985. Toxicity of metals to the earthworm *Eisenia foetida*. *Biol. Fert. Soils*, 1, pp.149-152.
Neuhauser, E.F., M.R. Malecki & R.C. Loehr, 1984. Growth and reproduction of the earthworm *Eisenia fetida* after exposure to sublethal concentrations of metals. *Pedobiologia*, 27, pp.89-97.
NHW Canada, 1989. Guidelines for Canadian drinking water quality - Supporting documentation. Updated November 1990, December 1992 and February 1995.
Nieboer, E. *et al.*, 1984. Cellular binding and/or uptake of nickel(II) ions. *IARC Scientific Publications*, (53), pp.321-331.
Nieboer, E., 1992. McMaster University, Hamilton, ON, in Environment Canada and Health Canada (1994) .
Nielsen, F.H. *et al*., 1984. Nickel influences iron metabolism through physiologic, pharmacologic and toxicologic mechanisms in the rat. *Journal of Nutrition*, 114(7), pp.1280-1288.
Nielsen, F.H., 1986. Nickel. In W. Mertz, ed. *Trace Elements in Human and Animal Nutrition, Volume 1, 5th edition.* New York: Academic Press, pp. 245-273.
Nielsen, F.H., 1991. Nutritional requirements for boron, silicon, vanadium, nickel, and arsenic: current knowledge and speculation. *FASEB Journal*, 5(12), pp.2661-2667.
Nielsen, F.H. & H.H. Sandstead, 1974. Are nickel, vanadium, silicon, fluorine, and tin essential for man? A review. *American Journal of Clinical Nutrition*, 27(5), pp.515-520.
Nielsen, G.D., U. Søderberg, *et al*., 1999. Absorption and retention of nickel from drinking water in relation to food intake and nickel sensitivity. *Toxicology and Applied Pharmacology*, 154(1), pp.67-75.
Nielsen, G.D. *et al.*, 1990. Nickel-sensitive patients with vesicular hand eczema: Oral challenge with a diet naturally high in nickel. *British Journal of Dermatology*, 122(3), pp.299-308.
Nielsen, G.D., O. Andersen & M. Jensen, 1993. Toxicokinetics of nickel in mice studied with the γ-emitting isotope ^{57}Ni. *Fundamental and Applied Toxicology*, 21(2), pp.236-243.
Nielsen, G.D. & M. Flyvholm, 1984. Risks of high nickel intake with diet. *IARC Scientific Publications*, (53), pp.333-338.
Nielsen, N.H., T. Menné, *et al*., 1999. Effects of repeated skin exposure to low nickel concentrations: A model for allergic contact dermatitis to nickel on the hands. *British Journal of Dermatology*, 141(4), pp.676-682.
Nielsen, N.H. *et al*., 2001. Persistence of contact allergy among Danish adults: An 8-year follow-up study. *Contact Dermatitis*, 45(6), pp.350-353.
Niu, J., P.E. Rasmussen, N.M. Hassan, *et al*., 2010b. Concentration distribution and bioaccessibility of trace elements in nano and fine urban airborne particulate matter: Influence of particle size. *Water, Air, and Soil Pollution*, 213(1-4), pp.211-225.
Niu, J., P.E. Rasmussen, A. Wheeler, *et al.*, 2010a. Evaluation of airborne particulate matter and metals data in personal, indoor and outdoor environments using ED-XRF and ICP-MS and co-located duplicate samples. *Atmospheric Environment*, 44(2), pp.235-245.
Nkongolo, K.K. *et al*., 2008. Metal content in soil and black spruce (*Picea mariana*) trees in the Sudbury region (Ontario, Canada): low concentrations of arsenic, cadmium, and nickel detected near smelter sources. *Bulletin of Environmental Contamination and Toxicology*, 80(2), pp.107-111.
Noble, D.G., 1990. *Contaminants in Canadian Seabirds. State of the Environment Report no. 90-2*, Canadian Wildlife Service, Environment Canada.
Noel, L., J.C. Leblanc & T. Guerin, 2003. Determination of several elements in duplicate meals from catering establishments using closed vessel microwave digestion with inductively coupled plasma mass spectrometry detection: estimation of daily dietary intake. *Food Additives Contamin.*, 20, p.44.

Nomoto, S. *et al*., 1973. Isolation of ^{63}Ni-labeled nickeloplasmin from rabbit serum. *Biochemical Medicine*, 8(2), pp.171-181.
Nomoto, S., M.D. McNeely & F.W. Sunderman Jr, 1971. Isolation of a nickel α2-macroglobulin from rabbit serum. *Biochemistry*, 10(9), pp.1647-1651.
Norgaard, O., 1955. Investigations with radioactive Ni 57 into the resorption of nickel through the skin in normal and in nickel-hypersensitive persons. *Acta Dermato-Venereologica*, 35(2), pp.111-7, in R.H. Guy, J.J. Hostyne.
Norgaard, O., 1957. Investigations with radioactive nickel, cobalt and sodium on the resorption through the skin in rabbits, guinea-pigs and man. *Acta Dermato-Venereologica*, 37(6), pp.440-445, in R.H. Guy, J.J. Hostyne.
Novey, H.S., M. Habib & I.D. Wells, 1983. Asthma and IgE antibodies induced by chromium and nickel salts. *Journal of Allergy and Clinical Immunology*, 72(4), pp.407-412.
NRCan, 2009. Canadian Minerals Yearbook (CMY) - 2009 Nickel. Minerals and Metals Sector Natural Resources Canada. Available at: www.nrcan.gc.ca/mining-materials/markets/canadian-minerals-yearbook/2009/8466
NRCC, 1981. Effects of nickel in the Canadian environment NRCC Associate Committee on Scientific Criteria for Environment Quality.
Nriagu, J.O., 1980. Global cycle and properties of nickel. In J.O. Nriagu, ed. *Nickel in the Environment*. New York: Wiley, pp. 1-26.
Nriagu, J.O., H.K. Wong & R.D. Coker, 1982. Deposition and chemistry of pollutant metals in lakes around the smelters at Sudbury, ON. *Environmental Science & Technology*, 16(9), pp.551-560.
NTP, 1996a. Toxicology and carcinogenesis studies of nickel oxide (CAS NO. 1313-99-1) in F344/N rats and B6C3F1 mice (Inhalation Studies). NTP TR 451 US Deparment of Health and Human Services National Toxicology Program.
NTP, 1996b. Toxicology and carcinogenesis studies of nickel subsulfide (CAS NO. 12035-72-2) in F344/N rats and B6C3F1 mice (Inhalation Studies). NTP TR 453 US Deparment of Health and Human Services National Toxicology Program.
NTP, 1996c. Toxicology and carcinogenesis studies of nickel sulfate hexahydrate (CAS NO. 10101-97-0) in F344/N rats and B6C3F1 mice (Inhalation Studies). NTP TR 454 US Deparment of Health and Human Services National Toxicology Program.
Oberdorster, G., R.B. Baggs & J. Finkelstein, 1995. Pulmonary retention and effects of inhaled NiO and Ni_3S_2 in rats and mice: indicators of maximum tolerated dose? *Annals of Clinical Laboratory Science*, 25, p.441.
Oberdorster, G., 1995b. Lung Particle Overload: Implications for Occupational Exposures to Particles. *Regulatory Toxicology and Pharmacology*. 21(1), pp.123-135.
Obone, É. *et al*., 1999. Toxicity and bioaccumulation of nickel sulfate in Sprague-Dawley rats following 13 weeks of subchronic exposure. *Journal of Toxicology and Environmental Health - Part A*, 57(6), pp.379-401.
O'Dell, G.D. *et al*., 1971. Effect of dietary nickel level on excretion and nickel content of tissues in male calves. *Journal of Animal Science*, 32(4), pp.769-773.
OEHHA, 2012. Nickel Reference Exposure Levels. Nickel and Nickel Compounds. Nickel Oxide. Reference Exposure Levels (RELs). Office of Environmental Health Hazard Assessment. California Environmental Protection Agency. February 2012. Available at: http://oehha.ca.gov/air/chronic_rels/pdf/032312NiREL_Final.pdf
Oller, A.R., 2002. Respiratory carcinogenecity assessment of soluble nickel compounds. *Environmental Health Perspectives*, 110(Supp. 5), pp.841-844.
Oller, A.R. *et al.*, 2008. Inhalation carcinogenicity study with nickel metal powder in Wistar rats. *Toxicology and Applied Pharmacology*, 233(2), pp.262-275.

Oller, A.R. *et al*., 2009. Comparison of nickel release in solutions used for the identification of water-soluble nickel exposures and in synthetic lung fluids. *Journal of Environmental Monitoring*, 11(4), pp.823-829.
Oller, A.R., M. Costa & G. Oberdörster, 1997. Carcinogenicity assessment of selected nickel compounds. *Toxicology and Applied Pharmacology*, 143(1), pp.152-166.
Ollson, C.A., W. Chi Wan, C.E. Willert, E. Veska, I. Koch & K. Reimer. 2003. Bioavailability of Nickel from Port Colborne Soils: A comparison of in vivo and in vitro Methodologies. 19th Annual International Conference on Soils, Sediments, Water and Energy. University of Massachusetts. Tuesday, Oct. 21, 2003. Available at: http://www.tandfonline.com/doi/abs/10.1080/10588330408984085#
OMEE (Ontario Ministry of Environment and Energy), 1994. Ontario Typical Range of Chemical Parameters in Soil, Vegetation, Moss Bags and Snow. April, 1994 (Version 1.0a) OMEE.
OMOE (Ontario Ministry of the Environment). 1992. Air Quality in Ontario: 1990. Queen's Printer for Ontario. ISSN 0840-9366, PIBS 1804-01/02, A86-A88. In: Environment Canada and Health Canada) 1994. Priority Substances List Assessment Report: Nickel and its Compounds. Canadian Environmental Protection Act. Ministry of Supply and Services Canada Catalogue No. En 40-215/43E. 82 pp.
OMOE, 1999. Large volume sampling at six Lake Ontario tributaries during 1997 and 1998: Project synopsis and summary of selected results OMOE. Available at: http://agrienvarchive.ca/download/large_vol_samp_L.Ont_trib_1997-98.pdf.
OMOE, 2002. Soil investigation and human health risk assessment for the Rodney Street community, Port Colborne, ON OMOE.
OMOE, 2004. Information Draft on the Development of Ontario Air Standards for Nickel and its Compounds OMOE Standards Development Branch.
OMOE, 2011a. Ontario air standards for nickel and nickel compounds OMOE Standards Development Branch. Available at: http://www.downloads.ene.gov.on.ca/envision/env_reg/er/documents/2011/010-7188.pdf.
OMOE, 2011b. Soil, Ground Water and Sediment Standards for Use Under Part XV.1 of the Environmental Protection Act OMOE. Available at: http://www.ontario.ca/document/soil-ground-water-and-sediment-standards-use-under-part-xv1-environmental-protection-act
Onkelinx, C., J. Becker & F.W. Sunderman Jr, 1973. Compartmental analysis of the metabolism of 63Ni(II) in rats and rabbits. Res. Commun. Chem. Path. Pharmacol., 6(2), pp.663-676, as cited in OEHHA (2011, draft) and WHO (2005).
Oorts, K. *et al*., 2006. Soil properties affecting the toxicity of $CuCl_2$ and $NiCl_2$ for soil microbial processes in freshly spiked soils. *Environmental Toxicology and Chemistry*, 25(3), pp.836-844.
Oorts, K., U. Ghesquiere & E. Smolders, 2007. Leaching and aging decrease nickel toxicity to soil microbial processes in soils freshly spiked with nickel chloride. *Environmental Toxicology and Chemistry*, 26(6), pp.1130-1138.
Oosting, J.S. *et al*., 1991. Iron, copper, and zinc status in rats fed supplemental nickel. *Biological Trace Element Research*, 31(1), pp.63-70.
Oskarsson, A. & H. Tjalve, 1979a. An autoradiographic study on the distribution of $^{63}NiCl_2$ in mice. *Annals of Clinical and Laboratory Science*, 9(1), pp.47-59.
Oskarsson, A. & H. Tjalve, 1979b. Binding of ^{63}Ni by cellular constituents in some tissues of mice after the administration of $^{63}NiCl_2$ and $^{63}Ni(CO)^4$. *Acta Pharmacologica et Toxicologica*, 45(4), pp.306-314.
Ottolenghi, A.D., J.K. Haseman & W.W. Payne, 1975. Inhalation studies of nickel sulfide in pulmonary carcinogenesis of rats. *Journal of the National Cancer Institute*, 54(5), pp.1165-1172, in IARC (2011).
Outridge, P.M. & A.M. Scheuhammer, 1993. Bioaccumulation and toxicology of nickel: implications for wild mammals and birds. *Environmental Reviews*, 1, pp.172-197.

Painter, S. *et al*., 1994. Reconnaissance geochemistry and its environmental relevance. *J. Geochem. Explor.* 51(3), pp.213-246.
Pandey R., R. Kumar, S.P. Singh, D.K. Saxena & S.P. Srivastava 1999. Male reproductive effect of nickel sulphate in mice. BioMetals, 12(4), Dec. 1999, pp. 339-346(8)
Pandey, R. & S.P. Srivastava, 2000. Spermatotoxic effects of nickel in mice. *Bulletin of Environmental Contamination and Toxicology*, 64(2), pp.161-167.
Parida, B.K., I.M. Chhibba & V.K. Nayyar, 2003. Influence of nickel-contaminated soils on fenugreek (*Trigonella corniculata L.*) growth and mineral composition. *Scientia Horticulturae*, 98(2), pp.113-119.
Parker, G.H., 2001. Metal levels in body tissues, forage and fecal pellets of elk (*Cervus elaphus*) living near the ore smelters at Sudbury, ON. *Environmental Pollution*, 113(3), pp.347-355.
Parker, G.H., 2004. Tissue metal levels in Muskrat (*Ondatra zibethica*) collected near the Sudbury (Ontario) ore-smelters; prospects for biomonitoring marsh pollution. *Environmental Pollution*, 129(1), pp.23-30.
Parr, R.M. *et al*., 1991. Minor and trace elements in human milk from Guatemala, Hungary, Nigeria, Philippines, Sweden, and Zaire: Results from a WHO/IAEA joint project. *Biological Trace Element Research*, 29(1), pp.51-75.
Pastorek, L. 1995. pers. comm. Ontario Ministry of Environment and Energy. Laboratory Services Branch, Personal communication from Liz Pastorek on March 24, 1995.
Patel, M.M. *et al.*, 2009. Ambient metals, elemental carbon, and wheeze and cough in New York city children through 24 months of age. *American Journal of Respiratory and Critical Care Medicine*, 180(11), pp.1107-1113.
Patriarca, M. & G.S. Fell, 1996. Monitoring of sources of clinical exposure to nickel. *Mikrochimica Acta*, 123(1-4), pp.261-269.
Patriarca, M., T.D.B. Lyon & G.S. Fell, 1997. Nickel metabolism in humans investigated with an oral stable isotope. *American Journal of Clinical Nutrition*, 66(3), pp.616-621.
Patterson, W.A.I.I.I. & Olson, J.J., 1982. Effects of heavy metals on radicle growth of selected woody species germinated on filter paper, mineral and organic soil substrates. *Can. J. For. Res.*, 13, pp.233-238.
Peiser, M. *et al*., 2012. Allergic contact dermatitis: Epidemiology, molecular mechanisms, in vitro methods and regulatory aspects. *Cellular and Molecular Life Sciences*, 69(5), pp.763-781.
Pennington, J.A.T. & J.W. Jones, 1987. Molybdenum, nickel, cobalt, vanadium, and strontium in total diets. *Journal of the American Dietetic Association*, 87(12), pp.1644-1650, in IOM (2001).
Peredney, C.L. & P.L. Williams, 2000a. Comparison of toxicological effects of nitrate versus chloride metallic salts on *Caenorhabditis elegans* in soil. In F.T. Price & K.V. Brix, eds. *Environmental Toxicology and Risk Assessment: Recent Achievements in Environmental Fate and Transport*. West Conshohocken, PA: American Society for Testing and Materials.
Peredney, C.L. & P.L. Williams, 2000b. Utility of *Caenorhabditis elegans* for assessing heavy metal contamination in artificial soil. *Archives of Environmental Contamination and Toxicology*, 39, pp.113-118.
Peris, M., 2004. Unpublished data on elemental concentrations in coarse particulate matter (PM10) from the National Air Pollution Surveillance (NAPS) Program. Environment Canada, Gloucester, ON.
Petruzzelli, G., L. Lubrano & G. Guidi, 1989. Uptake by corn and chemical extractability of heavy metals from a four year compost treated soil. *Plant and Soil*, 116, pp.23-27.
Phillips, J.I. *et al*., 2010. Pulmonary and systemic toxicity following exposure to nickel nanoparticles. *American Journal of Industrial Medicine*, 53(8), pp.763-767.
Phipps, T. *et al*., 2002. Essentiality of nickel and homeostatic mechanisms for its regulation in terrestrial organisms. *Environmental Reviews*, 10(4), pp.209-261.
Picarelli, A. *et al*., 2011. Oral mucosa patch test: A new tool to recognize and study the adverse effects of dietary nickel exposure. *Biological Trace Element Research*, 139(2), pp.151-159.

Pietz, R.I. *et al*., 1984. Metal concentrations in earthworms from sewage sludge-amended soils at a strip mine reclamation site. *Journal of Environment Quality*, 13, pp.651-654.
Pilgrim, W. & B. Schroeder, 1997. Multi-media concentrations of heavy metals and major ions from urban and rural sites in New Brunswick, Canada. *Environmental Monitoring and Assessment*, 47(1), pp.89-108.
Pizzutelli, S., 2011. Systemic nickel hypersensitivity and diet: Myth or reality? *European Annals of Allergy and Clinical Immunology*, 43(1), pp.5-18.
Poggio, L. *et al.*, 2009. Metals pollution and human bioaccessibility of topsoils in Grugliasco (Italy). *Environmental Pollution*, 157(2), pp.680-689.
Poirier, L.A. *et al*., 1984. Inhibition by magnesium and calcium acetates of lead subacetate- and nickel acetate-induced lung tumors in strain A mice. *Cancer Research*, 44(4), pp.1520-1522.
Ponizovsky, A.A. *et al*., 2008. Nickel partitioning in acid soils at low moisture content. *Geoderma*, 145(1-2), pp.69-76.
Pott, F. *et al*., 1987. Carcinogenicity studies on fibres, metal compounds, and some other dusts in rats. *Experimental Pathology*, 32(3), pp.129-152, in IARC (2011).
Pott, U. & D.H. Turpin, 1998. Assessment of atmospheric heavy metals by moss monitoring with *Isothecium stoloniferum Brid*. In the Fraser Valley, B.C., Canada. *Water Air Soil Pollut.*, 101(1-4), pp.25-44.
Poulik, Z., 1997. The danger of accumulation of nickel in cereals on contaminated soil. *Agri. Ecosystems Environ.*, 63(1), pp.25-29.
Pyle, G.G., J.W. Rajotte & P. Couture, 2005. Effects of industrial metals on wild fish populations along a metal contamination gradient. *Ecotoxicology and Environmental Safety*, 61(3), pp.287-312.
Qian, J. *et al*., 1996. Distribution and plant availability of heavy metals in different particle-size fractions of soil. *Science of the Total Environment*, 187, pp.131-141.
Rahil-Khazen, R. *et al*., 2002. Multi-element analysis of trace element levels in human autopsy tissues by using inductively coupled atomic emission spectrometry technique (ICP-AES). *Journal of Trace Elements in Medicine and Biology*, 16(1), pp.15-25.
Raithel, H.J. *et al*., 1982. Untersuchungen zur Ausscheidungskinetik von Nickel bei Beschaftigten in der Glas- und galvanischen Industrie. In T.M. Fliedner, ed. *Verhandlungen der deutschen Gesellschaft fur Arbeitsmedizin*. Stuttgart: Gentner Verlag, pp. 223-28, in Roels *et al*. (1993).
Raithel, H.J. *et al*., 1988. Investigations on the quantitative determination of nickel and chromium in human lung tissue. Industrial medical, toxicological, and occupational medical expertise aspects. *International Archives of Occupational and Environmental Health*, 60(1), pp.55-66.
Raithel, H.J. *et al*., 1993. Biomonitoring of nickel and chromium in human pulmonary tissue. *International Archives of Occupational and Environmental Health*, 65(1 Supp.), p.S197-S200.
Rasmussen, P.E., 2004. Can metal concentrations in indoor dust be predicted from soil geochemistry? *Canadian Journal of Analytical Sciences and Spectroscopy*, 49(3), pp.166-174.
Rasmussen, P.E. *et al*., 2006. Challenges in quantifying airborne metal concentrations in residential environments. *Canadian Journal of Analytical Sciences and Spectroscopy*, 51(1), pp.1-8.
Rasmussen, P.E. *et al*., 2007. Monitoring personal, indoor, and outdoor exposures to metals in airborne particulate matter: Risk of contamination during sampling, handling and analysis. *Atmosp. Environ.*, 41, pp.5897-5907.
Rasmussen, P.E. *et al*., 2008. Influence of matrix composition on the bioaccessibility of copper, zinc, and nickel in urban residential dust and soil. *Human and Ecological Risk Assessment*, 14(2), pp.351-371.
Rasmussen, P.E., K.S. Subramanian & B.J. Jessiman, 2001. A multi-element profile of house dust in relation to exterior dust and soils in the city of Ottawa, Canada. *Science of the Total Environment*, 267(1-3), pp.125-140.
Rauser, W.E., 1978. Early effects of phytotoxic burdens of cadmium, cobalt, nickel and zinc in white beans. *Can. J. Bot.*, 56, pp.1744-1749.

Rehab, F.I. & A. Wallace, 1978. Excess trace metal effects on cotton: Nickel and cadmium in Yolo loam soil. *Comm. Soil Sci. Plant Analysis*, 9, pp.779-784.
Rencz, A.N., 1980. Nickel in soils and vegetation of glaciated terrains. In J.O. Nriagu, ed. *Nickel in the Environment*. New York, NY: John Wiley and Sons, pp. 189-202.
Rencz, A.N., R.G. Garrett & S.W. Adcock, 2006. Geochemical Background in Soil and Till. Geological Survey of Canada Open File 5084. Available at: http://geoscan.nrcan.gc.ca/starweb/geoscan/servlet.starweb?path=geoscan/downloade.web&search1=R=222148.
Rendall, R.E.G., J.I. Phillips & K.A. Renton, 1994. Death following exposure to fine particulate nickel from a metal arc process. *Annals of Occupational Hygiene*, 38(6), pp.921-930.
Rezuke, W.N., J.A. Knight & F.W. Sunderman Jr, 1987. Reference values for nickel concentrations in human tissues and bile. *American Journal of Industrial Medicine*, 11(4), pp.419-426.
Richardson, G.M., 1997. Compendium of Canadian Human Exposure Factors for Risk Assessment.
Richardson, G.M. *et al.*, 2001. Critical review on natural global and regional emissions of six trace metals to the atmosphere.
Richter, O.R., 1980. Nickel speciation in a soil/water system. In J.O. Nriagu, ed. *Nickel in the Environment*. New York, NY: Wiley and Sons, pp. 189-202.
Rickert, W.S., 1991. An Evaluation of Changes in Pb, Cd, Hg and Ni Contents of Whole Tobacco, Mainstream Condensate and Sidestream Condensate from Canadian Cigarettes During the Period 1968-1988 Labstat Incorporated.
Robert, C., 2007. Ministère de Développement Durable, de l'Environnement et des Parcs du Québec Email to J. Aldridge of Health Canada.
Roberts, B.A., 1980. Some chemical and physical properties of serpentine soils from western Newfoundland. *Canadian Journal of Soil Science*, 60(2), pp.231-240.
Roduner, J., E. Haudenschild-Falb & E. Kunz, 1987. Oral nickel challenge in non-pompholyx and pompholyx-type nickel eczema. *Perorale Nickelprovokation bei Nichtdyshidrosiformem und Dyshidrosiformem Nickelekzem*, 38(5), pp.262-266.
Roels, H. *et al*., 1993. Relationship between atmospheric and urinary nickel in workers manufacturing electrical resistances using nickel oxide: Role of the bioavailability of nickel. *Occupational Medicine*, 43(2), pp.95-104.
Rogers, J.E. & S.W. Li, 1985. Effect of metals and other inorganic ions on soil microbial activity: Soil dehydrogenase assay as a simple toxicity test. *Bulletin of Environmental Contamination and Toxicology*, 34, pp.858-865.
Rom, W.N. *et al*., 1984. Pneumoconiosis and exposures of dental laboratory technicians. *American journal of public health*, 74(11), pp.1252-7.
Rooney, C.P., F.J. Zhao & S.P. McGrath, 2007. Phytotoxicity of nickel in a range of European soils: Influence of soil properties, Ni solubility and speciation. *Environmental Pollution*, 145(2), pp.596-605.
Rose, G.A. & G.H. Parker. 1983. Metal contents of body tissues, diet items, and dung of ruffed grouse near Sudbury, Ontario, Canada. *Can. J. Zool*. 61: 505-511.
Roshon, R.D., 1988. *Genecological studies on two populations of Betula pumila var. glandulifera, with special reference to their ecology and metal tolerance*. Sudbury, ON: Laurentian University.
Rossman, R. & J. Barnes, 1988. Trace element concentrations in near-surface waters of the Great Lakes, and methods of collection, storage and analysis. *Journal of Great Lakes Research*, 14, pp.188-204.
Ryan, C.A. *et al*., 2002. Examination of a vehicle for use with water soluble materials in the murine local lymph node assay. *Food and Chemical Toxicology*, 40(11), pp.1719-1725.
Rystedt, I. & T. Fischer, 1983. Relationship between nickel and cobalt sensitization in hard metal workers. *Contact Dermatitis*, 9(3), pp.195-200.
Räsänen, L., U. Mattila & K. Kalimo, 1999. Patch testing with nickel sulfate versus nickel chloride. *Contact Dermatitis*, 40(5), pp.287-288.

Sadiq, M., 1985. Uptake of cadmium, lead, and nickel by corn grown in contaminated soils. *Water Air Soil Pollut.*, 26, pp.185-190.
Saikat, S., B. Barnes & D. Westwood, 2007. A review of laboratory results for bioaccessibility values of arsenic, lead and nickel in contaminated UK soils. *Journal of Environmental Science and Health - Part A Toxic/Hazardous Substances and Environmental Engineering*, 42(9), pp.1213-1221.
Salnikow, K. *et al*., 1999. Nickel-induced transformation shifts the balance between HIF-1 and p53 transcription factors. *Carcinogenesis*, 20(9), pp.1819-1823.
Salnikow, K. & A. Zhitkovich, 2008. Genetic and epigenetic mechanisms in metal carcinogenesis and cocarcinogenesis: Nickel, arsenic, and chromium. *Chemical Research in Toxicology*, 21(1), pp.28-44.
Salt, D.E., R.C. Prince & I.J. Pickering, 2002. Chemical speciation of accumulated metals in plants: evidence from X-ray absorption spectroscopy. *Microchemical Journal*, 71(2-3), pp.255-259. Available at: http://www.sciencedirect.com/science/article/pii/S0026265X02000176.
Sanei, H., F. Goodarzi & S. Hilts, 2007. Site-specific natural background concentrations of metals in topsoil from the Trail region, BC, Canada. *Geochemistry: Exploration, Environment, Analysis*, 7(1), pp.41-48.
SARA, 2001. Sudbury Area Risk Assessment Volume I: Background, Study Organization and 2001 Soils Survey Chapter 7. The 2001 Soil Survey. Available at: http://www.sudburysoilsstudy.com.
SARA, 2008. Sudbury Area Risk Assessment Volume II: Human Health Risk Assessment- Final Report. Available at: http://www.sudburysoilsstudy.com.
Saviozzi, A., R. Levi-Minzi & R. Cardelli, 1997. The influence of heavy metals on carbon dioxide evolution from a typic xerochrept soil. *Water, Air, and Soil Pollution*, 93, pp.409-417.
Scanlon, P.F., 1987. Heavy metals in small mammals in roadside environments: implications for food chains. *Science of the Total Environment*, 59, pp.317-323.
Schmidt, J.A. & A.W. Andren, 1980. The atmospheric chemistry of nickel. In J.O. Nriagu, ed. *Nickel in the Environment*. New York, NY: John Wiley and Sons, pp. 93-135.
Schnabel, E. *et al*., 2010. Sensitization to contact allergens and bronchial hyper-responsiveness. *Contact Dermatitis*, 63(3), pp.157-163.
Schroeder, H.A. & M. Mitchener, 1975. Toxic effects of mercury, methyl mercury and nine other trace metals on mice. *Journal of Nutrition*, 105, pp.452-458.
Schroeder, H.A., M. Mitchener & A.P. Nason, 1974. Life-term effects of nickel in rats: survival, tumors, interactions with trace elements and tissue levels. *Journal of Nutrition*, 104(2), pp.239-243. Available at: http://jn.nutrition.org/content/104/2/239.long
Scott, D.E., W.A. Dick & M.A. Tabatabai, 1985. Inhibition of pyrophosphatase activity in soils by trace elements. *Soil Sci.* , 139, pp.112-117.
Scott-Fordsmand, J.J., P.H. Krogh & S.P. Hopkin, 1999. Toxicity of nickel to a soil-dwelling springtail, *Folsomia fimetaria* (*Collembola: Isotomidae*). *Ecotoxicology and Environmental Safety*, 43(1), pp.57-61.
Scott-Fordsmand, J.J., J.M. Weeks & S.P. Hopkin, 1998. Toxicity of nickel to the earthworm and the applicability of the neutral red retention assay. *Ecotoxicology*, 7(5), pp.291-295.
Seemann, J. *et al*., 1985. Analytical measurements of Cd, Pb, Zn, Cr and Ni in human tissues. *Lab Med* , 9, pp.294-299, in Rezuke *et al*. (1987).
Semkin, R.G., 1975. *A Limnogeochemical Study of Sudbury Area Lakes*. Hamilton, ON: McMaster University.
SENES, 2002. Port Radium Site Assessment - Summary Report on Site Conditions and Decommissioning Considerations. Draft Report. .
Serita, F., H. Kyono & Y. Seki, 1999. Pulmonary clearance and lesions in rats after a single inhalation of ultrafine metallic nickel at dose levels comparable to the threshold limit value. *Industrial Health*, 37(4), pp.353-363. Available at: http://www.ncbi.nlm.nih.gov/pubmed/10547950.

Sertoli, A., P. Lombardi & S. Francalanci, 1985. Effects of hapten oral administration in subjects with allergic contact dermatitis. II. Personal contribution. *Effetto della Somministrazione Orale di Apteni in Soggetti Sensibilizzati Affetti da Eczema Allergico da Contatto. II. Contributo personale*, 120(3), pp.213-218.
Severa, J. *et al*., 1995. Distribution of nickel in body fluids and organs of rats chronically exposed to nickel sulphate. *Human and Experimental Toxicology*, 14(12), pp.955-958.
Shah, M., F.M. Lewis & D.J. Gawkrodger, 1998. Nickel as an occupational allergen: A survey of 368 nickel-sensitive subjects. *Archives of Dermatology*, 134(10), pp.1231-1236.
Sharpe, D.R. & P.E. Rasmussen, 1996. Soil Geochemical Survey of Southern Ontario Geological Survey of Canada Terrain Sciences Division.
Sheppard, M.I., S.C. Sheppard & C.A. Grant, 2007. Solid/liquid partition coefficients to model trace element critical loads for agricultural soils in Canada. *Canadian Journal of Soil Science*, 87(2 Spec. iss.), pp.189-201.
Shier, W.T., 1994. Metals as toxins in plants. *J. Toxicol.-Toxin Reviews*, 13, pp.205-216.
Shirakawa, T. *et al*., 1990. Hard metal asthma: Cross immunological and respiratory reactivity between cobalt and nickel? *Thorax*, 45(4), pp.267-271.
Shirali, P. *et al*., 1991. Ni_3S_2 uptake by lung cells and its interaction with plasma membranes. *Journal of Applied Toxicology*, 11(4), pp.279-288.
Shuhaimi-Othman, M., D. Pascoe & U. Borgmann, 2006. Reduced metals concentrations of water, sediment and *Hyalella azteca* from lakes in the vicinity of the Sudbury metal smelters, Ontario, Canada. *Environ. Monitor. Assess.*, 117(1-3), pp.27-44.
Silvestri, D.L. & S. Barmettler, 2011. Pruritus ani as a manifestation of systemic contact dermatitis: Resolution with dietary nickel restriction. *Dermatitis*, 22(1), pp.50-55.
Singh, B.R., & A.S. Jeng. 1993. Uptake of zinc, cadmium, mercury, lead, chromium and nickel by ryegrass grown in a sandy soil. *Norw. J .Agric. Sci.*, 7(2), pp.147-157.
Sinigaglia, F., 1994. The molecular basis of metal recognition by T cells. *Journal of Investigative Dermatology*, 102(4), pp.398-401.
Sivulka, D.J., 2005. Assessment of respiratory carcinogenicity associated with exposure to metallic nickel: A review. *Regulatory Toxicology and Pharmacology*, 43(2), pp.117-133.
SK Environment and Resource Management, 1997. Simple sample report SK. Environmental Resource Management.
Skraba, D., 1989. *Effects of Surface Liming of Soils on Streamflow Chemistry in a Denuded, Acid, Metal-contaminated Watershed Near Sudbury, Ontario*. Sudbury, ON: Laurentian University.
SLI, 2000a. A one-generation reproduction range-finding study in rats with nickel suofate hexahydrate. Final report. Springborn Laboratory, Inc. Study No. 3472.3. Prepared for Nickel Producers Encironmenatl Research Association, (NiPERA) Inc.), Durham, NC.
SLI, 2000b. An oral (gavage) two-generation reproduction toxicity study in Sprague-Dawley rats with nickel sulphate hexahydrate. Prepared by Springborn Laboratories Inc., Spencerville, OH for Nickel Producers Environmental Research Association, Durham, NC.
Smith, J.C. & B. Hackley, 1968. Distribution and excretion of nickel-63 administered intravenously to rats. *Journal of Nutrition*, 95(4), pp.541-546.
Smith, M.K. *et al*., 1993. Perinatal toxicity associated with nickel chloride exposure. *Environmental Research*, 61(2), pp.200-211.
Snodgrass, W.J., 1980. Distribution and behaviour of nickel in the aquatic environment. In J.O. Nriagu, ed. *Nickel in the environment*. New York, NY: Wiley and Sons, pp. 203-274.
Solomons, N.W. *et al.*, 1982. Bioavailability of nickel in man: Effects of foods and chemically-defined dietary constituents on the absorption of inorganic nickel. *Journal of Nutrition*, 112(1), pp.39-50.
Sommer, H.C., U. Hass & P. Thyregod, 2002. Generalized linear model with overdispersion - a case study of the toxicological effect of nickel sulphate hexahydrate on mortality rate of rat

reproducibility. In *17th International Workshop on Statistical Modelling*. Chania, Crete, pp. 603-607.
Soon, Y.K. & S. Abboud, 1990. Trace elements in agricultural soils of northwest Alberta. *Can. J. Soil. Sci.* 70, pp.277-288.
Spears, J.W., 1984. Nickel as a "newer trace element" in the nutrition of domestic animals. *Journal of Animal Science*, 59(3), pp.823-835.
Spears, J.W., R.W. Harvey & L.J. Samsell, 1986. Effects of dietary nickel and protein on growth, nitrogen metabolism and tissue concentrations of nickel, iron, zinc, manganese and copper in calves. *Journal of Nutrition*, 116(10), pp.1873-1882.
Spears, J.W. & E.E. Hatfield, 1985. Interaction between nickel and copper in the rat. *Biological Trace Element Research*, 7(3), pp.181-193.
Spiegelberg, T., W. Koerdel & D. Hochrainer, 1984. Effect of NiO inhalation on alveolar macrophages and the humoral immune system of rats. *Ecotoxicol. Environ. Safety*, 8, pp.516-525.
Spinelli, V. *et al*., 2005. Asthma induced by nickel. *L'asthme au nickel*, 45(2), pp.103-107.
Stangl, G.I. & M. Kirchgessner, 1996. Nickel deficiency alters liver lipid metabolism in rats. *Journal of Nutrition*, 126(10), pp.2466-2473. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8857506.
Statistics Canada, 2005. Population urban and rural by province and territory Statistics Canada, Censuses of Population, 1851-2001. Available at: http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/demo62a-eng.htm.
Stedman, D.H. & D.A. Hikade, 1980. Nickel toxicology. In S.S. Brown, ed. *Proc. of the 2nd International Conference on Nickel Toxicology*, Swansea, Wales, Sept. 1980. London, UK: Academic Press, pp. 183-186.
Steinman, R.M. *et al*., 1983. Endocytosis and the recycling of plasma membrane. *Journal of Cell Biology*, 96(1), pp.1-27.
Stelting, H.J. & T. Platzek, 2005. Allergy to printer's ink. The underestimated danger. *Tonerallergie. Die unterschätzte gefahr*, 45(2), pp.457-461.
Stofan, J.R. *et al*., 2007. Daily fluid turnover during preseason training in U.S. college football. *International Journal of Sport Nutrition and Exercise Metabolism*, 17(4), pp.340-351.
Stoner, G.D., M.B. Shimkin & M.C. Troxell, 1976. Test for carcinogenicity of metallic compounds by the pulmonary tumor response in strain A mice. *Cancer Research*, 36(5), pp.1744-1747.
Stranger, M., S.S. Potgieter-Vermaak & R. Van Grieken, 2009. Particulate matter and gaseous pollutants in residences in Antwerp, Belgium. *Science of the Total Environment*, 407(3), pp.1182-1192.
Sunderman, F.W. *et al*., 1957. Nickel poisoning. IV. Chronic exposure of rats to nickel carbonyl; a report after one year of observation. *A. M. A. archives of industrial health*, 16(6), pp.480-485.
Sunderman, F.W. *et al.*, 1959. Nickel poisoning. IX. Carcinogenesis in rats exposed to nickel carbonyl. *A. M. A. archives of industrial health*, 20(1), pp.36-41.
Sunderman F.W., Jr. *et al*., 1986. Biological monitoring of nickel. *Toxicol. Industr. Health*, 2(1), pp.17-78.
Sunderman, F.W., S. Nomoto & M. Nechay, 1971. Nickel metabolism in myocardial infarction: Measurements of nickel in human tissues. In D.D. Hemphill, ed. *Trace Substances in Environmental Health* . Columbia: University of Missouri Press, pp. 352-356, in Rezuke *et al*. (1982).
Sunderman F.W., Jr. & E. Horak, 1981. Biochemical indices of nephrotoxicity, exemplified by studies of nickel nephropathy. In S.S. Brown & D.S. Davies, eds. *Organ-Directed Toxicity*. Oxford, UK: Pergamon Press , pp. 55-67.
Sunderman, F.W. *et al*., 1988. Acute nickel toxicity in electroplating workers who accidently ingested a solution of nickel sulfate and nickel chloride. *American Journal of Industrial Medicine*, 14(3), pp.257-266.
Sunderman, F.W. Jr., 1984. Carcinogenicity of nickel compounds in animals. In F.W. Sunderman Jr., A. Aitio, & A. Berlin, eds. *Nickel in the Human Environment*. Lyon, Fr.: Oxford University Press for the International Agency for Research on Cancer (IARC), pp. 127-142.

Sunderman F.W. Jr, *et al*., 1989. Nickel absorption and kinetics in human volunteers. *Proceedings of the Society for Experimental Biology and Medicine*, 191(1), pp.5-11.
Sunderman F.W. Jr., & A. Oskarsson, 1988. Nickel. In E. Merian, ed. *Metals and Their Compounds in the Environment*. Weinhem, FRG: VCH Verlagsgescellschaft, pp. 1-9, in Environment Canada and Health Canada.
Sunderman F.W. Jr, & C.E. Selin, 1968. The metabolism of nickel-63 carbonyl. *Toxicology and Applied Pharmacology*, 12(2), pp.207-218.
Sunderman F.W. Jr., M.I. Decsy & M.D. McNeely, 1972. Nickel metabolism in health and disease. *Annals of the New York Academy of Sciences*, 199, pp.300-312.
Swain, L.G. & D.G. Walton, 1994. 1993 Survey of sediments and tissues from Boundary Bay and Roberts Bank. Fraser River Estuary Monitoring Ministry of Environment Lands and Parks, Water Quality Branch.
Szakmáry, E. *et al*., 1995. Haemodynamic effect of nickel chloride in pregnant rats. *Acta Physiologica Hungarica*, 83(1), pp.3-12.
Tabatabai, M.A., 1977. Effects of trace elements on urease activity in soils. *Soil Biology and Biochemistry*, 9, pp.9-13.
Tallkvist, J. *et al*., 1998. Transport and subcellular distribution of nickel in the olfactory system of pikes and rats. *Toxicological Sciences*, 43(2), pp.196-203.
Tallkvist, J. & H. Tjälve, 1997. Effect of dietary iron-deficiency on the disposition of nickel in rats. *Toxicology Letters*, 92(2), pp.131-138.
Tallkvist, J. & H. Tjälve, 1998. Transport of nickel across monolayers of human intestinal Caco-2 cells. *Toxicology and Applied Pharmacology*, 151(1), pp.117-122.
Tanaka, I. *et al*., 1986. Retention of nickel oxide (green) aerosol in rat lungs by long-term inhalation. *Biological Trace Element Research*, 9(3), pp.187-195.
Tanaka, I. *et al*., 1988. Biological half-time in rats exposed to nickel monosulfide (amorphous) aerosol by inhalation. *Biological Trace Element Research*, 17, pp.237-246.
Tanaka, I., S. Ishimatsu & K. Matsuno, 1985. Biological half time of deposited nickel oxide aerosol in rat lung by inhalation. *Biological Trace Element Research*, 8(3), pp.203-210.
Tarnawska, M.P. W. Migula, J. Przybylowicz, M.A. Mesjasz-Przybylowicz, 2007. Nickel toxicity in the hepatopancreas of an isopod *Porcellio scaber* (*Oniscidea*). *Nuclear Insturments and Methods in Physics Research Section B: Beam Interactions with Materials and Atoms*, 260(1), pp.213-217. Available at: http://dx.doi.org/10.1016/j.nimb.2007.02.082.
TCEQ. 2011. Nickel and Inorganic Nickel Compounds. Development Support Document. Final. Texas Commission on Environmental quality. June 1, 2011. Available at: http://www.tceq.state.tx.us/assets/public/implementation/tox/dsd/final/june11/nickel_&_compounds.pdf.
Tedeschi, R.E. & F.W. Sunderman, 1957. Nickel poisoning. V. The metabolism of nickel under normal conditions and after exposure to nickel carbonyl. *A. M. A. Archives of Industrial Health*, 16(6), pp.486-488.
Temple, P.J. & S. Bisessar, 1981. Uptake and toxicity of nickel and other metals in crops grown on soil contaminated by a nickel refinery. *J. Plant. Nutr.*, 3, pp.473-482.
Templeton, D.M., F.W. Sunderman Jr. & R.F.M., Herber, 1994. Tentative reference values for nickel concentrations in human serum, plasma, blood, and urine: Evaluation according to the TRACY protocol. *Science of the Total Environment*, 148(2-3), pp.243-251.
Tennstedt, D., 2011. A nickel-free regimen has its place in the treatment of eczemas and dyshidrosis: Contra. *Le régime sans nickel a sa place dans les eczémas et la dysidrose: contre*, 51(3), pp.347-349.
TERA, 1999. International Toxicity Estimates for Risk (ITER) Database. Available at: http://www.tera.org/iter/

Thayer, J.S., 2002. Biological methylation of less-studied elements. *Applied Organometallic Chemistry*, 16(12), pp.677-691.
Thyssen, J.P., 2010. Children toys as a cause of nickel allergy should be explored. *Dermatitis*, 21(3), p.182.
Thyssen, J.P. *et al*., 2007. The epidemiology of contact allergy in the general population - Prevalence and main findings. *Contact Dermatitis*, 57(5), pp.287-299.
Thyssen, J.P. *et al*., 2009. Contact dermatitis caused by nickel release from hair clasps purchased in a country covered by the EU Nickel Directive. *Contact Dermatitis*, 60(3), pp.180-181.
Thyssen, J.P. *et al.*, 2011. Assessment of nickel and cobalt release from 200 unused hand-held work tools for sale in Denmark - Sources of occupational metal contact dermatitis? *Science of the Total Environment*, 409(22), pp.4663-4666.
Thyssen, J.P., T. Menné & J.D. Johansen, 2010. Identification of metallic items that caused nickel dermatitis in Danish patients. *Contact Dermatitis*, 63(3), pp.151-156.
Toman R, P. Massányi, M. Adamkovicova, N. Lukac, M. Cabaj & M. Martiniakova, 2012. Quantitative histological analysis of the mouse testis after the long-term administration of nickel in feed. J Environ Sci Health A Tox Hazard Subst Environ Eng. 47(9):1272-9.
Torjussen, W. & I. Andersen, 1979. Nickel concentrations in nasal mucosa, plasma, and urine in active and retired nickel workers. *Annals of Clinical Laboratory Science*, 9(4), pp.289-298. Available at: http://www.ncbi.nlm.nih.gov/pubmed/485092.
Torres, K.C. & M.L. Johnson, 2001a. Bioaccumulation of metals in plants, arthropods, and mice at a seasonal wetland. *Environmental Toxicology and Chemistry*, 20(11), pp.2617-2626.
Torres, K.C. & M.L. Johnson, 2001b. Testing of metal bioaccumulation models with measured body burdens in mice. *Environmental Toxicology and Chemistry*, 20(11), pp.2627-2638.
Tossavainen, A. *et al*., 1980. Application of mathematical modelling for assessing the biological half-times of chromium and nickel in field studies. *British Journal of Industrial Medicine*, 37(3), pp.285-291.
Traynor, M.F. & B.D. Knezek, 1973. Effects of nickel and cadmium contaminated soils on nutrient composition of corn plants. *Trace Subst. Environ. Health*, 7, pp.83-87.
Trivedi, T., 2004. pers. comm. Unpublished monitoring data on metal concentrations in walleye from inland waters collected for the National Contaminants Information System (NCIS). Fisheries and Oceans Canada, Burlington, ON.
Turi, M.C. *et al*., 2008. Systemic Nickel Allergy Syndrome: An update. *Italian Journal of Allergy and Clinical Immunology*, 18(3), pp.98-102.
Turkall, R.M., G.A. Skowronski & M.S. Abdel-Rahman, 2008. Effects of soil and aging on the dermal bioavailability of hydrocarbons and metals in soil. *International Journal of Soil, Sediment and Water:* 1(1), pp.1-13. Available at: http://scholarworks.umass.edu/intljssw/vol1/iss1/3.
Turkall, R.M., M.S.Abdel-Rahman & G.A. Skowronski, 2010. Effects of Soil Matrix and Aging on The Dermal Bioavailability of Hydrocarbons and Metals in the Soil: Dermal Bioavailability of Soil Contaminants. Proceedings of the Annual International Conference on Soils, Sediments, Water and Energy. V13, Article 29. Available at: http://scholarworks.umass.edu/cgi/viewcontent.cgi?article=1026&context=soilsproceedings.
Turkoglu, O. *et al*., 2004. Monitoring copper, nickel, cobalt, lead, cadmium, manganese and chromium levels in house dust samples from Kayseri, Turkey. *Trace Elements and Electrolytes*, 21(1), pp.4-9, as cited in Health Canada (2011).
Turner, A. & K.H. Ip, 2007. Bioaccessibility of metals in dust from the indoor environment: Application of a physiologically based extraction test. *Environmental Science and Technology*, 41(22), pp.7851-7856.
Turner, A. & L. Simmonds, 2006. Elemental concentrations and metal bioaccessibility in UK household dust. *Science of the Total Environment*, 371(1-3), pp.74-81.

Tyler, G., 1981. Heavy metals in soil biology and biochemistry. In E.A. Paul & J.N. Ladd, eds. *Soil Biochemistry*. New York: Dekker Inc., pp. 371-404.
USEPA, 1994. Methods for the derivation of inhalation reference concentrations and application of inhalation dosimetry USEPA. Available at: http://www.epa.gov/raf/publications/pdfs/RFCMETHODOLOGY.PDF.
USEPA, 1996. Integrated Risk Information System (IRIS) Database USEPA. Available at: http://www.epa.gov/ncea/iris/subst/0271.htm.
USEPA, 2003. SW-846 On-Line: Test Methods for Evaluating Solid Wastes; Physical/Chemical Methods, USEPA. Available at: http://www.epa.gov/epawaste/hazard/testmethods/sw846/index.htm.
USEPA, 2009. Human exposure database system (HEDS): HEDS studies USEPA. Available at: http://www.epa.gov/heds/.
USGS, 2011. Mineral Commodity Summaries. January 2011. Available at: http://minerals.usgs.gov/minerals/pubs/commodity/nickel/.
Uthus, E.O., 1997. Dietary nickel and folic acid interact to affect folate and methionine metabolism in the rat. *Biological Trace Element Research*, 58(1-2), pp.25-33.
Uthus, E.O., 1999. Compartmental model of nickel metabolism in rats based on orally administered ^{63}Ni. *Proc ND Acad Sci*, 53, pp.92-96.
Uthus, E.O. & C.D. Seaborn, 1996. Deliberations and evaluations of the approaches, endpoints and paradigms for dietary recommendations of the other trace elements. *Journal of Nutrition*, 126(9 Supp.), p.2452S-2459S.
Valentine, R. & G.L. Fisher, 1984. Pulmonary clearance of intratracheally administered $^{63}Ni_3S_2$ in strain A/J mice. *Environmental Research*, 34(2), pp.328-334.
Van Nostrand, J.D. *et al*., 2005. Effect of pH on the toxicity of nickel and other divalent metals to *Burkholderia cepacia* PR1(301). *Environmental Toxicology and Chemistry*, 24(11), pp.2742-2750.
Van Winkle, M.R. & P.A. Scheff, 2001. Volatile organic compounds, polycyclic aromatic hydrocarbons and elements in the air of ten urban homes. *Indoor Air*, 11(1), pp.49-64.
Vasiluk, L., M.D. Dutton & B. Hale, 2011. In vitro estimates of bioaccessible nickel in field-contaminated soils, and comparison with in vivo measurement of bioavailability and identification of mineralogy. *Science of the Total Environment*, 409(14), pp.2700-2706.
Veien, N.K., 2011. Systemic contact dermatitis. *International Journal of Dermatology*, 50(12), pp.1445-1456.
Veien, N.K., T.O. Hattel Justesen & A. Norholm, 1983. Oral challenge with metal salts. (II). Various types of eczema. *Contact Dermatitis*, 9(5), pp.407-410.
Veien, N.K., T. Hattel & G. Laurberg, 1993. Low nickel diet: An open, prospective trial. *Journal of the American Academy of Dermatology*, 29(6), pp.1002-1007.
Veien, N.K. & K. Kaaber, 1979. Nickel, cobalt and chromium sensitivity in patients with pompholyx (dyshidrotic eczema). *Contact Dermatitis*, 5(6), pp.371-374.
Vergnano, O. & J.G. Hunter, 1952. Nickel and cobalt toxicities in oat plants. *Annals of Botany*, 17, pp.317-328.
Verkleij, J.A.C., 1990. Mechanisms of metal tolerance in higher plants. In A.J. Shaw, ed. *Heavy Metal Tolerance in Plants: Evolutionary Aspects*. Boca Raton, FL: CRC Press, pp. 179-193.
Vermeire, T.G. *et al*., 1991. Voorstel voor de human-toxicologische onderbouwing van C-toetsingswaarden. National Institute of Public Health and the Environment, RIVM-report no. 725201005, February 1991; Bilthoven, The Netherlands. In: Baars, A.J., R.M.C. Theelan, P.J.C.M. Hanssen, J.
Vesper, S.J. & T.C. Weidensaul, 1978. Effects of cadmium, nickel, copper, and zinc on nitrogen fixation by soybeans. *Water Air Soil Pollut.*, 9, pp.413-422.

Vyskočil, A., C. Viau & M. Čížková, 1994. Chronic Nephrotoxicity of Soluble Nickel in Rats. *Human & Experimental Toxicology*, 13(10), pp.689-693. Available at: http://het.sagepub.com/cgi/content/abstract/13/10/689.
Waalkes, M.P. *et al*., 2004. Minimal influence of metallothionein over-expression on nickel carcinogenesis in mice. *Toxicology Letters*, 153(3), pp.357-364.
Wahlberg, J.E. & E. Skog, 1971. Nickel allergy and atopy. Threshold of nickel sensitivity and immunoglobulin E determinations. *British Journal of Dermatology*, 85(2), pp.97-104.
Wall, G.J. & M. Marsh., 1988. Within-pedon variability of trace metals in southern Ontario. *Canadian Journal of Soil Science*, 68, pp.53-61.
Wall, L.M., 1980. Nickel penetration through rubber gloves. *Contact Dermatitis*, 6(7), pp.461-463.
Wallace, A. *et al*., 1977. Nickel phytotoxicity in relationship to soil pH manipulation and chelating agents. *Comm. Soil Sci. Plant Anal.*, 8, pp.757-764.
Wang, C. undated pers. comm., Agriculture Canada.
Warren, H.V. & R.E. Delavaut, 1954. Variations in the nickel content of some Canadian trees. *Transactions of the Royal Society of Canada*, XLVIII, pp.71-74.
Wase, A.W., D.M. Goss & M.J. Boyd, 1954. The metabolism of nickel. I. Spatial and temporal distribution of Ni63 in the mouse. *Archives of Biochemistry and Biophysics*, 51(1), pp.1-4.
Wataha, J.C., C.T. Hanks & R.G. Craig, 1992. Uptake of metal cations by fibroblasts in vitro. *Journal of Biomedical Materials Research*, 27(2), pp.227-232.
Webb, M., 1970. Interrelationships between the utilization of magnesium and the uptake of other bivalent cations by bacteria. *BBA - General Subjects*, 222(2), pp.428-439.
Webb, M. & S.M. Weinzierl, 1972. Uptake of $^{63}Ni^{2+}$ from its complexes with proteins and other ligands by mouse dermal fibroblasts in vitro. *British Journal of Cancer*, 26(4), pp.292-298.
Webber, M.D., H.D. Monteith & D.G.M. Corneau, 1983. Assesment of heavy metals and PCBs at sludge application sites. *Journal of the Water Pollution Control Federation*, 55(2), pp.187-195.
Weber, C.W., 1969. Nickel toxicity in young growing mice. *J. Animal Sci.*, 28, pp.620-623.
Weber, C.W. & B.L. Reid, 1968. Nickel toxicity in growing chicks. *Journal of Nutrition*, 95, pp.612-616.
Wehner, A.P. & D.K. Craig, 1972. Toxicology of inhaled NiO and CoO in Syrian golden hamsters. *American Industrial Hygiene Association Journal*, 33(3), pp.146-155. Available at: http://www.tandfonline.com/doi/abs/10.1080/0002889728506624#
Weinheimer, E.M. *et al*., 2008. The Effect of Exercise on Water Balance in Premenopausal Physically Active Women. *Journal of the American Dietetic Association*, 108(10), pp.1662-1667.
Weinzierl, S.M. & M. Webb, 1972. Interaction of carcinogenic metals with tissue and body fluids. *British Journal of Cancer*, 26(4), pp.279-291.
Weischer, C.H., W. Kordel & D. Hochrainer, 1980. Effects of $NiCl_2$ and NiO in Wistar rats after oral uptake and inhalation exposure, respectively. *Zent Bakteriol Mikrobiol Hyg (B)*, 171, pp.336-351.
Wells, G.C., 1956. Effects of nickel on the skin. *British Journal of Dermatology*, 68(7), pp.237-42, in Samitz and Katz (1976).
Welp, G., 1999. Inhibitory effects of the total and water-soluble concentrations of nine different metals on the dehydrogenase activity of a loess soil. *Biology and Fertility of Soils*, 30, pp.132-139.
Weng, L. *et al*., 2003. Phytotoxicity and bioavailability of nickel: chemical speciation and bioaccumulation. *Environmental Toxicology and Chemistry*, 22 (9), pp.2180-2187.
Weng, L.P. *et al*., 2004. Understanding the effects of soil characteristics on phytotoxicity and bioavailability of nickel using speciation models. *Environmental Science & Technology*, 38(1), pp.156-162.
Whanger, P.D., 1973. Effects of dietary nickel on enzyme activities and mineral contents in rats. *Toxicology and Applied Pharmacology*, 25(3), pp.323-331. Available at: http://www.sciencedirect.com/science/article/pii/0041008X73903062.
Whitby, L.M. & T.C. Hutchinson, 1974. Heavy-metal pollution in the Sudbury mining and smelting region of Canada, II. Soil Toxicity tests. *Environmental Conservation*, 1, pp.191-200.

WHO, 1991. Environmental Health Criteria Series #108: Nickel WHO International Program on Chemical Safety, ed. Available at: http://www.inchem.org/documents/ehc/ehc/ehc108.htm.
WHO. 2000. Air Quality Guidelines Second Edition. Copenhagen, Denmark, World Health Organization, Geneva, Switzerland.
WHO, 2005. Nickel in Drinking Water: Background document for development of WHO Guidelines for Drinking-Water Quality WHO. Available at: http://www.who.int/water_sanitation_health/gdwqrevision/nickel2005.pdf.
Willaert, G., M.Verloo, 1988. Biological effects of nickel species and their determination in plant and soil. *Plant and Soil*, 107, pp.285-292.
Wilson, R., H. Jones-Otazo, S. Petrovic, I. Mitchell, Y. Bonvalot, D. Williams, G.M.Richardson, 2012. Revisiting Dust and Soil Ingestion Rates Based on Hand-to-Mouth Transfer. *HERA*.
Wilson, R., 2009. pers. comm.
Wilson, S., J. Murray & H. Huntington, 1998. AMAP Assessment Report: Arctic Pollution Issues. Arctic Monitoring and Assessment Programme.
Winterhalder, P., 1992. Department of Biology, Laurentian University, Sudbury, ON.
Winterhalder, P., 1994. pers. comm. Department of Biology, Laurentian University, Sudbury, ON .
Wolfaardt, J.F. & E. Peters, 1992. The base metal alloy question in removable partial dentures-a review of the literature and a survey of alloys in use in Alberta. *Journal (Canadian Dental Association)*, 58(2), pp.146-151.
Yang, X.E. *et al*., 1997. Accumulation and transport of nickel in relation to organic acids in ryegrass and maize grown with different nickel levels. *Plant and Soil*, 196(2), pp.271-276.
Yee, E., 2004. Data on background concentrations of metals within various media in northern Manitoba as reported in the Lynn Lake Risk Assessment completed by Dillon Consulting. MB Conservation, Winnipeg, MB .
Ysart, G. *et al*., 2000. 1997 UK total diet study - Dietary exposures to aluminium, arsenic, cadmium, chromium, copper, lead, mercury, nickel, selenium, tin and zinc. *Food Additives and Contaminants*, 17(9), pp.775-786.
YTDOE, 2002. Environment Act. Contaminated Sites Regulation. Schedule 1. Generic Numerical Soil Standards YTDOE Environment Act Regulations and Forms. Available at: http://www.environmentyukon.gov.yk.ca/pdf/csregs.pdf.
Zachariae, C. *et al*., 2003. Effect of a moisturizer on skin susceptibility to $NiCl_2$. *Acta Dermato-Venereologica*, 83(2), pp.93-97.
Zhang, Y. *et al*., 2009. Comparative genomic analyses of nickel, cobalt and vitamin B12 utilization. *BMC Genomics*, 10(78).
Zhao, J. *et al*., 2009. Occupational toxicology of nickel and nickel compounds. *Journal of Environmental Pathology, Toxicology and Oncology*, 28(3), pp.177-208.
Zober, A., K. Kick & K.H. Schaller, 1984. “Normal values” of chromium and nickel in human lung-, kidney-, blood- and urine samples. *Untersuchungen zum Nickel- und Chrom-Gehalt Ausgewahlter Menschlicher Organe und Korperflussigkeiten*, 179(1), pp.80-95, in Rezuke *et al*. (1987).
Zober, A., D. Weltle & K.H. Schaller, 1984. Study of the kinetics of chromium and nickel in biological material during a week of arc welding work using chromium-nickel-containing filler metals. *Schweissen und Schneiden/Welding and Cutting*, 36(10), p.E162-E164, in Roels *et al*. (1993).
Zornoza, P., S. Robles & N. Martin, 1999. Alleviation of nickel toxicity by ammonium supply to sunflower plants. *Plant and Soil*, 208(2), pp.221-226.

Appendix 1. Summary tables of nickel concentrations in environmental media

Outdoor Air

Location	Year	Concentration ng/m^3	Range ng/m^3	Comments	Reference
Canada	1987-1990	-	2 - 20		(Dann 1991)
Canada	1986 – 1996	1.6	-	Only PM2.5 sampled	(Burnett *et al.* 2000)
Canada	2002	3.4	0.63 - 453.8	Extremely low and high values from Iqualuit and Québec City	(Peris 2004)
Kejimkujik	2000	1.5	-	Annual average; lowest of 14 stations	
Québec City	2001	49.9	-	Annual average; highest of 16 stations	
Québec City	2002	21.9		Annual average; highest of 13 stations	
Winnipeg	2001	1.2	-	Annual average; lowest of 16 stations	
Calgary	2002	1.1	-	Annual average; lowest of 13 stations	
Port Moody	2000	9.3	-	Annual average; highest of 14 stations	
Canada - Urban and rural areas	2003-2009	0.94 $\pm$ 2.4		NAPS PM2.5 – acid digest, ICP-MS (means reported); n=3054	(EC 2011)
Canada Rural areas:	Jan 2007 - April 2009	0.5	0.3 - 0.7	NAPS database, PM2.5 - acid digest; ICP/MS (means reported)	(Dann 2010)
Canterbury	Jan 2007-Mar 2008	0.3	0.0 - 2.4	mean concentration; n=90 (undeveloped land)	(Dann 2010)
Wallaceburg	Jan 2007 - Apri 2009	0.7	0.0 - 5.6	mean concentration; n=192 (agricultural land)	(Dann 2010)
Simcoe	Jan 2007- April 2009	0.4	0.0 - 7.5	mean concentration; n=200 (agricultural land)	(Dann 2010)
Canada Urban areas:	Jan 2007 - May 2009	0.8	0.1 - 1.4	NAPS database, PM2.5 – acid digest, ICP-MS (means reported)	(Dann 2010)
Montréal	Jan 2007 - Mar 2008	1.4	0.0 - 6.6	mean concentration; n=122 (commerical land)	(Dann 2010)
Windsor	Jan 2007 - May 2009	0.9	0.0 - 4.7	mean concentration; n=209 (residential land)	(Dann 2010)
Toronto	Jan 2007 - May 2009	0.7	0.0 - 74.1	mean concentration; n=275 (commercial land)	(Dann 2010)
Metro Van-Abbotsford	Jan 2007 - Jan 2009	0.5	0.0 - 0.7	mean concentration; n=229 (residential land)	(Dann 2010)
Metro Van- Burnaby	Jan 2007 - May 2009	1.3	0.1 - 11.1	mean concentration; n=225 (residential land)	(Dann 2010)

Outdoor Air

Location	Year	Concentration ng/m^3	Range ng/m^3	Comments	Reference
Kelowna	Jan 2007 - Sept 2007	0.1	0.0 - 4.9	mean concentration; n=43 (commercial land)	(Dann 2010)
Arctic		<0.5	-	remote area samples	(Chan & Lusis 1988; Hoff & Barrie 1986)
Des Huron River Watershed	1993 - 1995	0.59 mg/m^2/yr	-	depositon estimates	(Gelinas & Schmit 1998)
Shawinigan	1999	10		95th percentile value	(Bisson 2004)
Shawinigan	2000	20		95th percentile value	(Bisson 2004)
Rouyn-Noranda	2002	10		95th percentile value; mining region	(Bisson 2004)
Ontario	2001	6.2		1410 PM_{10} samples from 27 stations; over half of stations reported minimum of 2.0 ng/m^3	(OMOE 2002)
Great Lakes	1995 - 1998	0.72	0.61 - 0.87	annual average, three stations	(Dryfhout-Clark 2004)
Hamilton	1999	90		mean value; n=2; 24 hr PM_{10} samples; (steel manufacturing; industrial land)	(Lamoureux 2005)
Ottawa (rural)	2004	1	0.4 - 1.8	median $PM_{2.5}$	(Rasmussen *et al*. 2006)
Ottawa (urban)	2004	0.6	0.5 - 1.3	median $PM_{2.5}$	(Rasmussen *et al*. 2006)
Port Colborne	1993	13	NS	Geometric mean	(Leece 1997)
Port Colborne	2001 - 2002	60		mean value; n=4; 24hr PM_{10} samples (previous Ni refinery; waste processing and precious metal recovery)	(Lamoureux 2003)
Sarnia	1998 - 1999	157		mean value; n=4 24 hr PM_{10} samples; (petroleum refinery, industrial land)	(Lamoureux 2003)
Sudbury	1978 - 1988	-	100 - 250	near industrial sources	(Chan & Lusis 1988)
Sudbury, Copper Cliff	2000	612		mean value; n=3 24hr PM_{10} samples (active Ni smelting and refinery, industrial land)	(Lamoureux 2005)
Sudbury, Copper Cliff	2003 - 2004	0.21		mean value; n=5 24hr PM_{10} samples (active Ni smelting and refinery, industrial land)	(Lamoureux 2005)
Toronto, Windsor (urban)	1998 - 2000	41		mean value; n=4 24 hr PM_{10} samples	(Lamoureux 2005)

Outdoor Air

Location	Year	Concentration ng/m^3	Range ng/m^3	Comments	Reference
Windsor	1991-1992	2.1	0.4 - 8.7	mean $PM_{10;}$ n=46; Phase 1 and 2 Windsor Airshed Study	(Bell *et al*. 1994)
Windsor	2004	-	1 - 10 ng/m^3	$PM_{2.5}$ range; outdoor and personal air	(Rasmussen *et al*. 2007)
Windsor	2005	1.3	<DL - 2.9	median $PM_{2.5}$ from two-week samples collected in the summer for 39 sites ICP/MS	(Niu *et al*. 2010a)
Windsor	2005	1.4 ± 0.6		mean $PM_{2.5}$ from two-week samples collected in the summer (39 sites) - analyses by ICP/MS	(Niu *et al*. 2010b)
New York State			2 - 3	n=394; range of mean $PM_{2.5}$ from two counties	(Koutrakis *et al.* 1992)
	2001	-	0.0 - 1.252	rural	(Hutzell & Luecken 2007)
	2001	-	2.93 - 3.043	suburban	(Hutzell & Luecken 2007)
	2001	-	2.863-12.97	urban	(Hutzell & Luecken 2007)

Indoor Air

Location	Year	Concentration ng/m^3	Range ng/m^3	Comments	Reference
Canada		7.21 ± 10.5	0 - 100	n=3054; based on studies listed below from Canada and other countries listed below.	(HC 2011)
Ontario - Ottawa (rural)	2004	0.7	0.2 - 1.3	median $PM_{2.5}$	(Rasmussen *et al*. 2006)
Ontario - Ottawa (urban)	2004	0.6	0.4 - 2.1	median $PM_{2.5}$	(Rasmussen *et al*. 2006)
Ontario - Ottawa (rural)	2004	1.5	0.3 - 2.4	median PM_{10}	(Rasmussen *et al*. 2006)
Ontario - Ottawa (urban)	2004	1.0	0.5 - 3.0	median PM_{10}	(Rasmussen *et al*. 2006)
Ontario - Windsor	1991 - 1992	1.3	0.3 - 9.2	median $PM_{10;}$ n=37; Windsor Air Quality Study	(Bell *et al.* 1994)
Ontario - Windsor	1991 - 1992	1.0	0.3 - 9.2	mean PM_{10};n=37; Windsor Air Quality Study	(Bell *et al*. 1994)
Alberta - High Level	May - June 1997	12.01		$PM_{2.5}$ mean; n=20	(AB Health 1998)
Illinois - Chicago	June 1994 - April 1995	1	ND - 4	$PM_{2.5}$ arithmetic mean; n=48	(Van Winkle & Scheff 2001)
Illinois - Chicago	June 1994 - April 1995	1.5	ND - 4	$PM_{2.5}$ median	(Van Winkle & Scheff 2001)
Maryland - Townson	1998	1.71		$PM_{2.5}$ median; n=10	(Graney *et al*. 2004)
Maryland - Townson	1998	0.4		$PM_{2.5}$ median; n=10	(Graney *et al*. 2004)
Minnesota - Minneapolis/St. Paul	April - November 1999	12		$PM_{2.5}$ mean; n=235	(Adgate *et al*. 2007)
Taiwan, Taipei	November 1992 - February 1993	22	13 - 39	$PM_{2.5}$ mean; n=21; (3 residences; 7 measurements)	(Li *et al.* 1993)
Singapore - Choa Chu Kang	May 2004		0.72 - 1.34	$PM_{2.5}$ arithmetic mean; n=2	(Balasubramanian & Lee 2007)
Belgium - Antwerp	-	0.7	0.2 - 1.25	$PM_{2.5}$ mean; n=15	(Stranger *et al*. 2009)
Sweden - Götenborg	April 2 - June 7; Sept 26 - Nov 6 2002; March 27 - June 12; Oct 30 2003	4.6	0.67 - 63	$PM_{2.5}$ mean; n=30	(Molnár *et al.* 2006)
Sweden - Götenborg	April 2 - June 7; Sept 26-Nov 6 2002; March 27 - June 12; Oct 30 2003	1.4	0.67 - 63	$PM_{2.5}$ median; n=30	(Molnár *et al*. 2006)

Indoor Dust

Location	Year	Concentration ng/m^3	Range ng/m^3	Comments	Reference
Canada	**-**	48.1 ± 41	0 - 336	mean; n=679; estimated typical Canadian concentration based on data from Canada, the USA, the UK, Poland, Turkey, Australia and Bahrain	(HC 2011)
Ontario - Ottawa	1993	62.9	16.0 - 243.3	arithmetic mean and range	(Rasmussen *et al*. 2001)
Ontario - Ottawa	1993	53.6	16.0 - 243.3	geometric mean and range	(Rasmussen *et al*. 2001)
Ontario - Ottawa	1993	51.5	16.0 - 243.3	median	(Rasmussen *et al*. 2001)
Ontario - Ottawa	2001 - 2002	48 ± 32	15 - 84	arithmetic mean and range	(Rasmussen *et al*. 2001)
Ontario - Ottawa	2001 - 2002	41		median and geometric mean	(Rasmussen *et al*. 2001)
New Jersey - Jersey City	-	89 + 25	NS - 341	PM10 n=61; concentrations converted from mass to mg/g	(Adgate *et al*. 1998)
New Jersey - Jersey City	-		NS - 260	PM <60 mg/g; n=64; concentrations converted from mass to mg/g	(Adgate *et al*. 1998)
Arizona	1995 1997	37.6 ± 17.31	<14 - 142.7	arithmetic mean; n=117	US EPA NHEXAS cited in HC 2011
Arizona	1995 1997	34.3	<14 - 142.7	geometric mean; n=117	US EPA NHEXAS cited in HC 2011
United Kingdom	October and November 2005	56.5 + 20	27.2 - 97.1	arithmetic mean; n=32	(Turner & Simmonds 2006)
United Kingdom	October and November 2005	53.1	27.2 - 97.1	geometric mean; n=32	(Turner & Simmonds 2006)
Poland - Warsaw	May - July 1997	39 ± 24	14 - 107	houses and apartments; (63-125 μm)	(Lisiewicz *et al.* 2000)
Poland - Warsaw	May - July 1997	54 ± 68	20 400	houses and apartments; (32-63 μm)	(Lisiewicz *et al.* 2000)
Poland - Warsaw	May - July 1997	74 ± 74	23 - 357	houses and apartments; (0-32 μm)	(Lisiewicz *et al.* 2000)
Turkey - Kayseri	April and June 2002	64.6 ± 25.3	-	n=27	(Turkoglu *et al*. 2004)
Australia - Sydney	1997 and 1999	49 + 25	34 - 80	n=10; residential ceiling dust; <500 m from industrial building	(Davis & Gulson 2005)
Australia - Sydney	1997 and 1999	52 + 15	24 - 83	n=19; residential celing dust; 500-1500 m from industrial buidling	(Davis & Gulson 2005)
Australia - Sydney	1997 and 1999	28 + 10	10 - 50	n=9; residential ceiling dust; >1500 m from industrial building	(Davis & Gulson 2005)
Australia - Sydney	August 1999	27.2	4.8 - 549	n=82; geometric mean = 15.6	(Chattopadhyay *et al*. 2003)
Bahrain	-	10 ± 6.6	2 - 43	n=76	(Madany *et al*. 1994)
Worldwide	-	40	-	median; house dust	(Fergusson & Kim 1991)

Soil

Location	Year	Soil type	Sample Depth	Concentration mg/kg	Range mg/kg	Comments	Reference
overall	-			-	5 - 50	remote areas	(McKeague & Wolynetz 1980)
Appalachians				18	-	remote areas	(McKeague & Wolynetz 1980)
Canadian Shield				12	-	remote areas	(McKeague & Wolynetz 1980)
St. Lawrence				18	-	remote areas	(McKeague & Wolynetz 1980)
Lowlands				18	-	remote areas	(McKeague & Wolynetz 1980)
Interior Plains				40	-	remote areas	(McKeague & Wolynetz 1980)
Cordilleran				20	-	remote areas	(McKeague & Wolynetz 1980)
Canada		-		24	2.5-69	background	(Sheppard *et al*. 2007)
Canada		till <0.63 µm	-	26.8 ± 42.8	0.5 - 210	mean and provisional range	(Rencz *et al*. 2006; Grunsky 2010)
				16 ± 13.3		median	(Rencz *et al*. 2006; Grunsky 2010)
				400		local upper limit (ultramafic bedrock)	(Rencz *et al*. 2006; Grunsky 2010)
Great Bear Lake				19.5		unimpacted area	(SENES 2002)
Great Bear Lake				93.6		impacted area	(SENES 2002)
New Brunswick-western		ultramafic		3.46		neutral soils (pH 6.8 - 7.3)	(Roberts 1980)
East St. John		surface		18	-	urban garden soils	(Pilgrim & Schroeder 1997)
West St. John		surface		16	-	urban garden soils	(Pilgrim & Schroeder 1997)
Fredericton		surface		46	-	urban garden soils	(Pilgrim & Schroeder 1997)
Québec	-	agricultural		21.8	2.1 - 54		(Giroux *et al.* 1992)
St. Lawrence Lowlands				50		background estimates	(MEF 1998)
Appalachians				55		background estimates	(MEF 1998)
Grenville				30		background estimates	(MEF 1998)
Superior and Rae				50		background estimates	(MEF 1998)
Labrador Trough				100		background estimates	(MEF 1998)
Island of Montréal	1997	surface	0 - 15 cm	-	25.6 - 243	urban soils	(Ge *et al*. 2000)
Montréal	1997	surface	0 - 15 cm	75.3	-	contaminated urban soil	(Murray & Hendershot 2000)
Rouyn-Noranda		organic	FH horizon	22		uncontaminated area	(Johnson & Hale 2004)
Rouyn-Noranda		organic	FH horizon	19		contaminated area	(Johnson & Hale 2004)
Ontario	-			15	<5 - 35	urban parklands	(OMEE 1994)
Ontario				13.5	<5 - 56	rural parklands; mean; n=101	(OMEE 1994)

Soil

Location	Year	Soil type	Sample Depth	Concentration mg/kg	Range mg/kg	Comments	Reference
				32	<5 - 56	rural parklands (98th percentile)	(OMEE 1994)
	-	all land uses		43	-	background estimate	(OMEE 1994)
Ontario - central and southern	-	agricultural	A horizon	24.98	3 - 500	mean and range	(Sharpe & Rasmussen 1996)
		agricultural	A horizon	18.00	3 - 500	median and range	(Sharpe & Rasmussen 1996)
		agricultural	C horizon	22.34	4 - 87	mean and range	(Sharpe & Rasmussen 1996)
		agricultural	C horizon	22.43	4 - 87	median and range	(Sharpe & Rasmussen 1996)
Ontario - central and southern	-	shales	surface	-	87 - 225	mean background in shale deposits	(McIlveen 1998)
Ontario - central and southern		soil	surface	-	48 - 101	soil concentrations immediately above shale deposits	(McIlveen 1998)
Ontario - Essex county	-			23	19 - 27	rural soils	(Gizyn 1994)
Ontario	2000			-	NS - 17 000	adjacent to Ni refinery	(Birmingham & McLaughlin 2006)
Ottawa	-	clay loam	0 - 20 cm	36	26 - 46	farm field (n=19)	(Wang n.d.)
Ottawa	-	clay loam	50 - 65 cm	72	54 - 87	n=20	(Wang n.d.)
Ottawa	1993	Residential	urban garden soil	16.3 ±3.78	10.5 - 27.9		(Rasmussen *et al*. 2001)
Ottawa	2001-2002	urban garden soil	garden soil	14 ± 5	5 - 30	mean	(Rasmussen *et al*. 2008)
Ottawa	2001-2002	urban garden soil	garden soil	13	5 - 30	median	(Rasmussen *et al*. 2008)
Port Colborne	1991	soils and dust	0 - 5 cm		36 -9800	n=37; near INCO refinery	(Leece 1997)
Port Colborne	1991	soils and dust	0 - 5 cm	67	<100	low concentration range	(Leece 1997)
Port Colborne	1991	soils and dust	0 - 5 cm	398	100 - 1000	medium concentration range	(Leece 1997)
Port Colborne	1991	soils and dust	0 - 5 cm	4290	>1000	high concentration range	(Leece 1997)
Port Colborne	2002		0 - 15 cm	-	63.7 - 22 444	contaminated area	(Everhart *et al*. 2006)
Sault Ste. Marie & southward	1995	<2 mm	0 - 25 cm	25	3 - 500	mean and range	(Garrett 2004)
Sault Ste. Marie & southward	1995	<2 mm	0 - 25 cm	18	3 - 500	median and range	(Garrett 2004)
Southwest Ontario		topsoil		20.2 ± 7.6		watersheds	(Mills & Zwarich 1975)
Sudbury	1970s	surface		2000		within several km of smelters and refineries	(Hutchinson *et al*. 1981; Freedman & Hutchinson 1980; Temple & Bisessar 1981)

Soil

Location	Year	Soil type	Sample Depth	Concentration mg/kg	Range mg/kg	Comments	Reference
Sudbury	mid 1980s - early 1990s				100 - 725	within 5 km of Sudbury smelters	(Winterhalder 1994; 1992; Skraba 1989; Roshon 1988; Archambault 1991)
Sudbury	1995		5 - 15 cm	-	12 - 841		(Gratton *et al.* 2000)
Sudbury	-	organic	FH horizon	670	-	contaminated	(Johnson & Hale 2004)
Sudbury	-	organic	FH horizon	90	-	uncontaminated	(Johnson & Hale 2004)
Sudbury	-	topsoil	10 - 20 cm	-	0.37 - 37.33		(Nkongolo *et al.* 2008)
Sudbury	2001	urban, rural and undisturbed soils	0 - 20 cm	264	7 - 3700	mean and range	(SARA 2001)
Sudbury	2001	urban, rural and undisturbed soils	0 - 20 cm	95	7 - 3700	median and range	(SARA 2001)
Sudbury and Rouyn-Noranda	2001			-	14 - 435		(Feisthauer *et al*. 2006)
Windsor area	-	urban soils		21	14 - 24		(Gizyn 1994)
Prairies - Manitoba, Saskatchewan and Alberta	1992	agricultural		20	3 - 46	mean and range; dpeosits of parent material (moraine/till)	(Garrett 2004)
Prairies - Manitoba, Saskatchewan and Alberta	1992	agricultural		19	3 - 46	median and range; dpeosits of parent material (moraine/till)	(Garrett 2004)
Manitoba - north		rural	-	-	17.7 - 140.5	background	(Yee 2004)
Manitoba - north	-	organic	0 - 5 cm	14			(Jones Geoff (via Edwin Yee) 2004)
Manitoba - north		clay/silt	5 - 10 cm	11	-		(Jones Geoff (via Edwin Yee) 2004)
Manitoba - north		clay/silt	10 - 15 cm	9	-		(Jones Geoff (via Edwin Yee) 2004)
Manitoba - north		clay/silt	15 - 30 cm	28	-		(Jones Geoff (via Edwin Yee) 2004)
Manitoba - central		organic	0 - 12 cm	8	-		(Jones Geoff (via Edwin Yee) 2004)
Manitoba - central		clay/silt	12 -25 cm	10	-		(Jones Geoff (via Edwin Yee) 2004)
Manitoba - south		organic	0 - 2 cm	21	-		(Jones Geoff (via Edwin Yee) 2004)
Manitoba - south		clay/silt/sand	2 - 15 cm	16	-		(Jones Geoff (via Edwin Yee) 2004)
Manitoba - south		sand	17 - 22 cm	8	-		(Jones Geoff (via Edwin Yee) 2004)

Soil

Location	Year	Soil type	Sample Depth	Concentration mg/kg	Range mg/kg	Comments	Reference
Alberta – northwestern		agricultural	surface, organic	27	<5 - 78		(Soon & Abboud 1990)
Alberta		agricultural	surface, inorganic	15	<5 - 32		(Soon & Abboud 1990)
Alberta		agricultural	subsurface	24	11 - 38		(Soon & Abboud 1990)
Alberta		agricultural	0 - 15 cm	20	-		(Lutwick 1994)
Alberta		agricultural	15 - 30 cm	22	-		(Lutwick 1994)
Alberta		agricultural	30 - 60 cm	25	-		(Lutwick 1994)
Alberta		agricultural	60 - 100 cm	27	-		(Lutwick 1994)
Alberta		agricultural	0 - 15 cm	19.7	2 - 211		(Dinwoodie 2004)
Alberta		transportation	0 - 5 cm	21.1	6 - 42		(Nason 2004)
Alberta - southern half		transportation	5 - 15 cm	21.5	6 - 39		(Nason 2004)
Alberta - southern half		new urban parkland	0 - 5 cm	19.3	10 - 33		(Nason 2004)
Alberta - southern half		new urban parkland	5 - 15 cm	19.1	8 - 30		(Nason 2004)
Alberta - southern half		old urban parkland	0 - 5 cm	18.8	11 - 28		(Nason 2004)
Alberta - southern half		old urban parklland	5 - 15 cm	18.1	11 - 25		(Nason 2004)
Alberta - southern half		rural parkland	0 - 5 cm	14.4	10 - 18		(Nason 2004)
Alberta - southern half		rural parkland	5 - 15 cm	15.0	9 - 21		(Nason 2004)
Alberta - southern half		commercial	0 - 5 cm	17.4	11 - 29		(Nason 2004)
Alberta - southern half		commercial	5 - 15 cm	16.9	11 - 29		(Nason 2004)
British Columbia			surface		50 - 150	Regional background estimates represented by 95th percentiles	(BCMOE 1999)
Vancouver Island			surface	55	-	Regional background estimates represented by 95th percentiles	(BCMOE 1999)
Southern Interior			surface	75	-	Regional background estimates represented by 95th percentiles	(BCMOE 1999)
Kootenay			surface	50	-	Regional background estimates represented by 95th percentiles	(BCMOE 1999)
Cariboo			surface	150	-	Regional background estimates represented by 95th percentiles	(BCMOE 1999)

Soil

Location	Year	Soil type	Sample Depth	Concentration mg/kg	Range mg/kg	Comments	Reference
Skeena			surface	50	-	Regional background estimates represented by 95th percentiles	(BCMOE 1999)
Omineca Peace			surface	60	-	Regional background estimates represented by 95th percentiles	(BCMOE 1999)
Lower Mainland (excluding Greater Vancouver)			surface	80	-	Regional background estimates represented by 95th percentiles	(BCMOE 1999)
Lower Mainland (excluding Greater Vancouver)			0 - 60 cm	27	1.0 - 146	Mean and range; n=408 nitric perchloric digestion	(Harris 2004)
Lower Mainland (excluding Greater Vancouver)			0 - 60 cm	36	1.5 - 192	mean and range; n=140; aqua regia digestion	(Harris 2004)
Lower Mainland (excluding Greater Vancouver)			0 - 60 cm	90	1.5 - 192	95th percentile; n=140	(Harris 2004)
Greater Vancouver		residential and agricultural	0 - 10 cm	16.81	2.21 - 46.07	Prior to and after start-up of solid waste incinerator	(SLI 2000)
Greater Vancouver		residential and agricultural	10 - 20 cm	15.53	1.02 - 43.37	Prior to and after start-up of solid waste incinerator	(SLI 2000)
Greater Vancouver		residential and agricultural	20 - 30 cm	14.93	0.21 - 51.3	Prior to and after start-up of solid waste incinerator	(SLI 2000)
Greater Vancouver		residential and agricultural				Prior to and after start-up of solid waste incinerator	(SLI 2000)
Greater Vancouver			surface	75	-	Regional background estimates represented by 95th percentiles	(BCMOE 1999)
Mt. Robson Provincial Park	2002		0 - 25 cm		9.5 - 72.1	disturbed	(Arocena *et al*. 2006)
Mt. Robson Provincial Park	2002		0 - 25 cm		27.6 - 67.1	undisturbed	(Arocena *et al*. 2006)
Trail	1989	sandbox		16.4 $\pm$ 5.3	7 - 38	Arithmetic mean	(Kelly *et al*. 1991)
Trail	1989	sandbox		15.7	7 - 38	Geometric mean	(Kelly *et al*. 1991)
Trail	1989	park		16.9 $\pm$ 4.0	13 - 35	Arithmetic mean	(Kelly *et al*. 1991)
Trail	1989	park		16.5	13 - 35	Geometric mean	(Kelly *et al*. 1991)
Trail	1989	residential		18.1 $\pm$ 4.3	12 - 43	Arithmetic mean	(Kelly *et al*. 1991)
Trail	1989	residential		17.7	12 - 43	Geometric mean	(Kelly *et al*. 1991)
Trail	-			21.8	-	background	(Sanei *et al*. 2007)
Worldwide	-			20 - 40	0.2 - 450	mean values	(He *et al*. 2005; Adriano 2001)
Worldwide					19 - 22	mean values	(Kabata-Pendias & Mukherjee 2007)

Sediment

Location	Year	Concentration mg/kg dw	Range mg/kg dw	Comments	Reference
Canada	-	-	<10 - >4000	lake samples	(Bradley & J. R. Morris 1986; Bodo 1989)
Canada	-	-	2 - 50	background freshwater	(Bodo 1989; Arafat & Nriagu 1986; M. B. Jackson 1988; Moore & Ramamoorthy 1984)
Canada	-	15	5 - 50	70 000 lake sediment samples, mainly from Shield and Appalachian regions	(Friske *et al*. 1993)
Canada	2004	20	4 - 60	77 891 stream sedimen; median values and range of individual ecozones	(Garrett 2010)
Bay of Fundy	1997 - 2002	26	15-36		(Hung 2007)
New Brunswick - lakes	-	8.7			(Painter *et al*. 1994)
New Brunswick - streams	-	13.5			(Painter *et al*. 1994)
Northern Labrador	-	45.2			(Painter *et al*. 1994)
Northern Labrador	-	60.7			(Marvin *et al*. 2007)
Québec	-	15		lake and stream sediment	(Painter *et al*. 1994)
Québec - Montréal	2004 - 2005	-	11 - 75	St. Lawrence lakes	(Desrosiers *et al.* 2008)
Québec	2001	66 (median)	17 - 345	Lakes Chibougamau and aux Dorés	(Laliberté & Trembaly 2002)
Québec	2002	35 (mean)	9 - 140	Lakes Chibougamau, aux Dorés, Waconichi and Obatogamau	(Laliberté 2004)
Québec	2002	29 (median)	9 - 140	Lakes Chibougamau, aux Dorés, Waconichi and Obatogamau	(Laliberté 2004)
Québec	2002		20 - 140	Lake Chibougamau (n =6)	(Laliberté 2004)
Québec	2002		28 - 63	Lake Aux Dorés (n=5)	(Laliberté 2004)
Québec	2002		10 - 13	Lake Waconichi (n=5)	(Laliberté 2004)
Québec	2002		9 - 40	Lake Obatogamau (n=10)	(Laliberté 2004)
Québec	2002		12 - 48	Nemenjiche river (n=5) - river goes through mine site.	(Laliberté 2004)
Hamilton Harbour	-	-	62 - 74 nM		(Brassard *et al*. 1997)
Great Lakes - Lake Ontario	-	43	-		(Murdoch *et al*. 1988)
Great Lakes - Lake Erie	-	36.3	-		(Murdoch *et al*. 1988)

Sediment

Location	Year	Concentration mg/kg dw	Range mg/kg dw	Comments	Reference
Great Lakes - Lake Huron	-	30-51	-		(Murdoch *et al*. 1988)
Great Lakes - Lake Michigan	-	20	-		(Murdoch *et al*. 1988)
Great Lakes - Lake Superior	-	24-70	-		(Murdoch *et al*. 1988)
Great Lakes - Lake Erie	-	36.3	-	typical background	(Marvin *et al*. 2004)
Great Lakes - Lake Erie/Ontario	2001	-	21.7 - 96.2		(Marvin *et al*. 2007)
Ontario - Killarney Park	-	<100	-	remote area	(Belzile *et al*. 2004)
Ontario - 12 lakes	1998	-	41.74 - 610.4	near shore sediment	(Shuhaimi-Othman *et al*. 2006)
Ontario lakes and rivers	1994 - 2003	31.7	<0.5 - 850		(Boyd 2004)
Great Lakes	2001 - 2002	22.3 - 51	<1 - 287		(Gewurtz *et al*. 2008)
Ontario - storm water management facilities	-	-	11 - 43		(Marsalek *et al*. 2006)
Ontario - Sudbury	-		NS - 4000		(Bradley & Morris 1986; Arafat & Nriagu 1986)
Ontario - Sudbury	2001	21.9 - 4744.8			(Pyle *et al*. 2005)
Northern Manitoba	-	-	14.3 - 28.4	freshwater sediment; 5 samples	(Yee 2004)
British Columbia - lakes	-	17.3			(Painter *et al*. 1994)
British Columbia - streams	-	12.3			(Painter *et al*. 1994)
British Columbia - various rivers and bays	-		23.9 - 51.3	Extreme low and high values from Boundary Bay and Serpentine River, respectively	(Swain & Walton 1994)
Fraser River Basin	-	42 - 91	NS - 134	background (pre-1900)	(Gallagher & Macdonald 2004)
Yukon		22		stream sediments 30 954 samples from 8 geological provinces	(Heon 2003)
Cassiar Platform		19			(Heon 2003)
Insular		36			(Heon 2003)
Intermontane		18			(Heon 2003)
North-American Shelf		21			(Heon 2003)
Northern Shelf		23			(Heon 2003)
Selwyn Basin		28			(Heon 2003)
Triass-Cretac		215			(Heon 2003)

Sediment

Location	Year	Concentration mg/kg dw	Range mg/kg dw	Comments	Reference
Tanana Terrane		18			(Heon 2003)
Yukon streams	2004		16.31 - 111.1	range of mean T-Ni concentrations from 20 ecoregions	(Garrett 2010)
Yukon streams	2004		8 - 38	range of median T-Ni concentrations from 20 ecoregions	(Garrett 2010)

Water

Location	Year	Concentration µg/L	Range µg/L	Comments	Reference
Canada - agroecosystems	-	0.5	-	river samples	(He *et al*. 2005)
Canada	-	106 nM	-	tap water	(Brassard *et al.* 1997)
Canada	-	-	0.228 - 0.693	marine water	(Bruland *et al.* 1979)
Canada	-	2	1 - 10	surface water	(Leger 1991; Moore & Ramamoorthy 1984; NRCC 1981)
Canada	-	<2.0 (median)	<2.0 - 69	Survey of raw, treated and distributed drinking water	(Méranger *et al.* 1981)
Canada - Ontario, Alberta, Atlantic	-	2	-	drinking water	(Moon *et al*. 1988; Jones-White 1992; EC 1989b)
Canada	-	106 nM	-	tap water	(Brassard *et al.* 1997)
Canada	1995 - 1996	0.96	0.73 - 3.3	tap water	(Dabeka *et al*. 2002)
Canada - (Ottawa, St. John's, Vancouver and Montréal)	2000 - 2003	2.37	1.43 - 3.10	Total Diet Study; kitchen tap water	(Dabeka 2009)
Canada - (Ottawa, St. John's, Vancouver and Montréal)	2000 - 2003	2.37	<0.07 - 0.80	Total Diet Study; area tap water	(Dabeka 2009)
Canada (Ontario, Saskatchewan, Newfoundland and Labrador)	1999 - 2009	2.85 ± 4.06	0 - 38.5	n=12 251; mean ± SD	(HC 2011)
Newfoundland and Labrador	2000 - 2009	1.47 ± 5.94		n=3801	Government of Newfoundland and Labrador cited in HC 2011
New Brunswick, southeastern (Moncton area)	1991 -1 993	18.4 (mean)	<13 - 289	n=1002, total Ni from residential kitchen taps	(Boyle *et al.* 1994)
New Brunswick, southeastern (Moncton area)	1991 - 1993	6.0 (median)	<13 - 289	n=1002, total Ni from residential kitchen taps	(Boyle *et al.* 1994)
New Brunswick, central (Fredericton)	1993 - 1995	16.4 (mean)	<7 - 97	n=465; total Ni from residential kitchen taps	(Boyle *et al.* 1994)
New Brunswick, central (Fredericton)	1993 - 1995	6.5 (median)	<7 - 97	n=465; total Ni from residential kitchen taps	(Boyle *et al.* 1994)
Québec - Appalachians		1.7 (geometric mean)	<1 - 500	groundwater; n=15 552	(Choinière & Beaumier 1997)
Québec - St. Lawrence Lowlands		1.4 (geometric mean)	<1 - 1080	groundwater; n=6745	(Choinière & Beaumier 1997)
Québec - Grenville		1.3 (geometric mean)	<1 - 140	groundwater; n=1890	(Choinière & Beaumier 1997)
Québec - Superior and Rae		2.8 (geometric mean)	<1 - 140	groundwater; n=1890	(Choinière & Beaumier 1997)

Water

Location	Year	Concentration µg/L	Range µg/L	Comments	Reference
Québec	1994 - 2006	2.7 (mean)	1 - 9	Drinking water database; n=21; 14 samples <MDL; range doesn't include <MDL (0.05 & 1 mg/L)samples	(Robert 2007)
Ontario	1998 - 2007	3.49 ± 2.59		n=8378	Drinking Water Surveillance Program (Ontario MOE) cited in HC 2011
Lake Ontario	1997 - 1998	-	NS - 24.36	Lake Ontario tributaries	(OMOE 1999)
Ontario - 12 lakes	1998	-	4 - 94.3	12 lakes; surface water	(Shuhaimi-Othman *et al*. 2006)
Ontario	1998 - 2003	1	<1 - 4	Surface water; 19 samples from 6 reference sites	(Boyd 2004)
Ontario	1990 - 2002	1.12 (mean)		Groundwater; drinking water distribution (48 supplies; n=996)	(Cheung 2004)
Ontario	1990 - 2002	3.33 (mean)		Lakes; drinking water distribution (84 treatment plants; n=2878)	(Cheung 2004)
Ontario	1990 - 2002	1.02 (mean)		Lakes; drinking water distribution; lakes (47 treatment plants; n=2222)	(Cheung 2004)
Ontario – excluding Sudbury	1993 - 1994	-	<0.2 - 7.8	Drinking water survey	(Graham 1995)
Ontario - Port Colborne	1990 - 1994	1.2	NS	Treated water from Port Colborne treatment plant	(Leece 1997)
Ontario - Port Colborne	1990 - 1994	-	<2 - 46.2	Residential wells (n=6)	(Leece 1997)
Ontario - Sudbury		131	NS - 2000	Contaminated lakes	(Dixit *et al.* 1991)
Ontario - Sudbury	1972 - 1992	-	26 - 300	Drinking water	(Jenkins 1992; Hopfer *et al*. 1989; Flora & Nieboer 1980)
Ontario - Sudbury	1983 - 1995	5	1.9 - 33.5	Lake samples	(Mallory *et al*. 1998)
Ontario - Sudbury	1999	-	0.6 - 7.3 µM	Lake samples	(Mandal *et al.* 2002)
Ontario - Sudbury	2001		1 - 338.2	Lake samples	(Pyle *et al*. 2005)
Manitoba rural northern sites	-	-	<2	Surface water; 5 samples	(Yee 2004)
Saskatchewan	2000 - 2009	1.47 ± 3.48		n=72	SK Environment & Dept of Environment & Conservation cited in HC 2011

Water

Location	Year	Concentration µg/L	Range µg/L	Comments	Reference
North Saskatchewan River	1991 - 1996	3.25			(SK Environment and Resource Management 1997)
Qu'Appelle River	1991 - 1996	3.02			(SK Environment and Resource Management 1997)
South Saskatchewan River	1991 - 1996	2.58			(SK Environment and Resource Management 1997)
Saskatchewan - Rivers/streams	1998 - 2001	<1 in 90% of samples	-	63 samples	(Hase 2004)
Tobin Lake	1991 - 1996	1.75			(SK Environment and Resource Management 1997)
Saskatchewan - Lakes	1998 - 2001	<1		103 samples	(Hase 2004)
McKenzie River Basin	-	-	NS - 6.7	90th percentile value	(Lumb *et al.* 2006)
Alberta	-	-	<2 - 272	groundwater; deep wells; n=101	(Holt-Oduro 2004)
Alberta	-	6	<1 - 62	groundwater; shallow wells; n=111	(Holt-Oduro 2004)
Alberta (5 rivers)	1997 - 2003	8.3	<0.5 - 905	locations unlikely to be impacted by anthropogenic metal contamination	(Anderson 2004)
Bow River	1997 - 2003	5.1	<0.5 - 26.5	locations unlikely to be impacted by anthropogenic metal contamination	(Anderson 2004)
Athabasca River	1997 - 2003	5.9	<0.5 - 83.9	locations unlikely to be impacted by anthropogenic metal contamination	(Anderson 2004)
North Saskatchewan River	1997 - 2003	7.6	<0.5 - 87.0	locations unlikely to be impacted by anthropogenic metal contamination	(Anderson 2004)
Oldman River	1997 - 2003	5.6	<0.5 - 40.8	locations unlikely to be impacted by anthropogenic metal contamination	(Anderson 2004)
Red Deer River	1997 - 2003	17	<0.5 - 905	locations unlikely to be impacted by anthropogenic metal contamination	(Anderson 2004)

Water

Location	Year	Concentration µg/L	Range µg/L	Comments	Reference
British Columbia	-	47	5.6 - 2910	groundwater; total Ni; n=97	(Evans 2004).
British Columbia		26	5.6 - 920	groundwater; dissolved Ni; n=94	(Evans 2004).
Vancouver Island - Quinsam River	1986 - 2004	-	<0.2 - 7.6	mouth of Quinsam River; total Ni in surface water	(BCMOE 2008)
Lower Mainland - Fraser River	1979 - 2004	-	<0.2 - 24.8	at Hope; total Ni in surface water	(BCMOE 2008)
Southern Interior - Bonaparte River	1980 - 1994	-	<10 - 20	near mouth; total Ni in surface water	(BCMOE 2008)
Southern Interior - Thompson River	1984 - 2004	-	<0.2 - 7.6	at Spences Bridge; total Ni in surface water	(BCMOE 2008)
Southern Interior - Similkameen River	1966 - 2000	-	<0.2 - 0.6	at Princeton; total Ni in surface water	(BCMOE 2008)
Kootenay Region - Columbia River	1983-1997	-	<0.2 - 3.9	at Birchbank; total Ni in surface water	(BCMOE 2008)
Kootenay Region - Columbia River	1979 - 2000	-	<0.2 - 4.3	at Waneta; total Ni in surface water	(BCMOE 2008)
Kootenay Region - Kootenay River	1984 - 2005	-	<0.2 - 3.9	at Fenwick; total Ni in surface water	(BCMOE 2008)
Kootenay Region - Kootenay River	1965 - 2000	-	<0.2 - 5.3	at Creston; total Ni in surface water	(BCMOE 2008)
Cariboo - Fraser River	1984 - 2004	-	<0.2 - 43	at Marguerite; total Ni in surface water	(BCMOE 2008)
Skeena - Salmon River	1981 - 2002	-	<0.2 - 45	near Hyder, Alaska; total Ni in surface water	(BCMOE 2008)
Skeena - Salmon River	1981 - 2002	-	<0.2 - 45	near Hyder, Alaska; total Ni in surface water	(BCMOE 2008)
Great Bear Lake	-	1.8	-		(SENES 2002)
Nahanni national park	-	1.6-8.9	-	surface water; historical average	(Halliwell & Catto 2003)
Smoking Hills, Cape Bathurst	1975 - 1981 (summers)		7 - 6300	dissolved Ni; 45 ponds; alkaline ponds (pH 8.5-10.5) & acidic ponds (pH 1.5-2.5) - acidic ponds associated with bituminous shales	(Havas & Hutchinson 1983)

Biota

Species, Tissue type	Location, Comments	Year	Concentration mg/kg dw	Range mg/kg dw	Reference
Hyalella azteca	12 lakes in Ontario	1998	-	13.3 - 35.9	(Shuhaimi-Othman *et al*. 2006)
Burbot liver	North West Territories, Great Slave Lake	1999 - 2002	<0.05	-	(Evans *et al.* 2005).
Burbot muscle,	North West Territories, Great Slave Lake	1999 - 2002	<0.05	-	(Evans *et al.* 2005).
Flounder, Starry - muscle	British Columbia - Boundary Bay and Roberts Bank	1993	< 1.0	<1.0	(Swain & Walton 1994)
Grayling liver	United States, Alaska - Desparation Lake	1991 -1993	1.07	-	(Allen-Gil *et al.* 1997)
Grayling liver	United States, Alaska - Elusive Lake	1991 -1993	0.2	-	(Allen-Gil *et al*. 1997)
Grayling liver	United States, Alaska - Feniak Lake	1991 -1993	0.59	-	(Allen-Gil *et al*. 1997)
Grayling liver	United States, Alaska - Schrader Lake	1991 -1993	0.76	-	(Allen-Gil *et al*. 1997)
Grayling muscle	United States, Alaska - Desparation Lake	1991 -1993	0.33	-	(Allen-Gil *et al*. 1997)
Grayling muscle	United States, Alaska - Elusive Lake	1991 -1993	0.12	-	(Allen-Gil *et al.* 1997)
Grayling muscle	United States, Alaska - Feniak Lake	1991 -1993	0.28	-	(Allen-Gil *et al*. 1997)
Grayling muscle	United States, Alaska - Schrader Lake	1991 -1993	0.22	-	(Allen-Gil *et al*. 1997)
Unknown liver	North West Territories, Great Slave Lake	1999 - 2002	<0.05	-	(Evans *et al.* 2005).
Unknown muscle	North West Territories, Great Slave Lake	1999 - 2002	<0.05	-	(Evans *et al.* 2005).
Landlocked lake char	Canada - Arctic	1999 - 2003	0.024 - 0.425 ww	-	(Muir *et al*. 2005)
Walleye	Lake Erie, Wheatley and Port Stanley (n=15)	1996	<0.02 (80% of samples)		(Trivedi 2004)
Walleye	Lake Huron, French River (n=20)	1995 - 1996	0.052		(Trivedi 2004)
Walleye	Lake Ontario, Bay of Quinte-Lennox (n=20)	1995 - 1997	<0.02 in 55% of samples		(Trivedi 2004)
Walleye	Lake Ontario, Bay of Quinte-Lennox (n=22)	2002	<0.05 in 95% of samples		(Trivedi 2004)
Yellow perch liver	Ontario - Sudbury lakes	2001	3.8 - 22.4	-	(Pyle *et al*. 2005)
Yellow perch muscle	Ontario - Sudbury lakes	2001	1.0 - 144.5	-	(Pyle *et al*. 2005)
Arctic surfclam	Newfoundland - Banquereau Bank; n=19	1996		0.73 - 5.57	(Fancey 2004)
Crab tissue - gills, testes, viscera, muscle	Newfoundland - Inner Avalon; n=23	1996		0.52 - 18.7	(Fancey 2004)
Crab tissue - gills, testes, viscera, muscle	Newfoundland - Outer Avalon; n=36	1996		0.25 - 39.3	(Fancey 2004)
Crab tissue - gills, testes, viscera, muscle	Newfoundland - Bay St. George; n=30	1996		0.30 - 31.2	(Fancey 2004)
Crab tissue - gills, testes, viscera, muscle	Newfoundland - Bonavista; n=24	1996		0.30 - 25.6	(Fancey 2004)

Biota

Species, Tissue type	Location, Comments	Year	Concentration mg/kg dw	Range mg/kg dw	Reference
Crab tissue - gills, testes, viscera, muscle	Newfoundland - White Bay; n=24	1996		0.28 - 38.0	(Fancey 2004)
Crab tissue - gills, testes, viscera, muscle	Newfoundland - Conception Bay; n=36	1996		0.13 - 51.4	(Fancey 2004)
Crab tissue - gills, testes, viscera, muscle	Newfoundland - Shoal Patch; n=24	1996		0.35 - 34.9	(Fancey 2004)
Crab tissue - gills, testes, viscera, muscle	Newfoundland - Port au Choix; n=29	1996		0.39 - 23.8	(Fancey 2004)
Crab - Cancer magister hepatopancreas; composite	British Columbia - Boundary Bay; inshore	1993	1.4 (0.2 ww)	-	(Swain & Walton 1994)
Crab - Cancer magister hepatopancreas; composite	British Columbia - Boundary Bay; offshore	1993	2.3 (0.31 ww)	-	(Swain & Walton 1994)
Crab - Cancer magister hepatopancreas; composite of 6	British Columbia - Roberts Bank	1993	2.1 (0.38 ww)	-	(Swain & Walton 1994)
Crab - Cancer magister muscle tissue	British Columbia - Roberts Bank	1993	<1.0	<1.0	(Swain & Walton 1994)
Snails	United States, Alaska - Elusive Lake	1991 - 1993	11.8	-	(Allen-Gil *et al.* 1997)
Zebra Mussels	St. Lawrence River, Canada	1996	8.84 - 52.59	-	(de Lafontaine *et al*. 2000)
Adult Elk kidney	Ontario - Sudbury	1995 - 1997	1.23	-	(Parker 2001)
Adult Elk liver	Ontario - Sudbury	1995 - 1997	0.71	-	(Parker 2001)
Adult Elk muscle	Ontario - Sudbury	1995 - 1997	0.62	-	(Parker 2001)
Caribou	North West Territories	1995		<0.01 - 1.33	(Larter & Nagy 2000)
Muskrat kidney	Ontario - North Bay (uncontaminated area)		1.65	-	(Parker 2004)
Muskrat kidney	Ontario - Sudbury (contaminated area)		9.45	-	(Parker 2004)
Muskrat liver	Ontario - North Bay (uncontaminated area)		1.3	-	(Parker 2004)
Muskrat liver	Ontario - Sudbury (contaminated area)		4.41	-	(Parker 2004)
Black spruce needles	Ontario - Sudbury		-	3.48 - 21.08	(Nkongolo *et al.* 2008)
Moss	British Columbia - Lower Fraser Valley (rural)	1993	1.1	-	(Pott & Turpin 1998)
Moss	British Columbia - Lower Fraser Valley (urban)	1993	3	-	(Pott & Turpin 1998)
Pine	Ontario - Sudbury	1995	3.3 - 50.8	-	(Gratton *et al*. 2000)
Various plant forage species	Ontario - Sudbury	1995 - 1997	1.04 - 23.78	-	(Parker 2001)
Beet tops	New Brunswick - Saint John urban gardens (n=11)	-		1.2 - 3.1 (ww)	(Pilgrim & Schroeder 1997)
Beet root	Ontario – Sudbury (residential)	2003		<dl-1.169 (ww)	(SARA 2008)
Berries (strawberry, blueberry,	Manitoba - Northern		< 0.1		(Yee 2004)

Biota					
Species, Tissue type	**Location, Comments**	**Year**	**Concentration mg/kg dw**	**Range mg/kg dw**	**Reference**
mossberry)					
Blueberries	Ontario- Sudbury (wildland)	2003		0.264-1.034 (ww)	(SARA 2008)
Carrots	Ontario – Sudbury (residential)	2003		0.061-2.512 (ww)	(SARA 2008)
Carrots	New Brunswick - Fredericton (rural garden)		0.5 (ww)		(Pilgrim & Schroeder 1997)
Carrots	Manitoba - Northern		<0.1		(Yee 2004)
Cucumber	Ontario – Sudbury (residential)	2003		0.035-2.705 (ww)	(SARA 2008)
Cucumber	Ontario – Sudbury (commercial)	2003		<dl-0.930 (ww)	(SARA 2008)
Lettuce	Ontario – Sudbury (residential)	2003		0.088-2.960 (ww)	(SARA 2008)
Lettuce	New Brunswick - Fredericton (rural garden)		1.5 (ww)		(Pilgrim & Schroeder 1997)
Lettuce (washed)	Ontario - Sudbury		166		(Hutchinson *et al.* 1981)
Mushrooms	Ontario – Sudbury (wildland)	2003		0.103-0.255 (ww)	(SARA 2008)
Onions	Ontario – Sudbury (residential)	2003		0.116-2.364 (ww)	(SARA 2008)
Potatoes	Ontario – Sudbury (residential)	2003		<dl-2.030 (ww)	(SARA 2008)
Potatoes	Ontario – Sudbury (commercial)	2003		<dl-1.580 (ww)	(SARA 2008)
Potatoes	Manitoba - Northern		< 0.1		(Yee 2004)
Radishes	Manitoba - Northern		0.5 - 0.7 (ww)		(Yee 2004)
Strawberriew	Ontario – Sudbury (commercial)	2003		<dl-0.432 (ww)	(SARA 2008)
Tomatoes	Ontario – Sudbury (residential)	2003		<dl-1.843 (ww)	(SARA 2008)
Turnips	Manitoba - Northern		< 0.1		(Yee 2004)
Zucchini	Ontario – Sudbury (residential)	2003		0.047-1.888 (ww)	(SARA 2008)

Commercial Food					
Food Type	**Year**	**Concentration**	**Range**	**Comment**	**Reference**
Canada	1995 - 1996	3.5 mg/L	0.73 - 35	retail distilled water	(Dabeka *et al*. 2002)
Canada	1995 - 1996	1.96 mg/L	0.73 - 11	retail mineral water	(Dabeka *et al*. 2002)
Canada	1995 - 1996	1.32 mg/L	0.73 - 7	retail spring water	(Dabeka *et al*. 2002)
Total Diet Studies					
shelled seeds	2000	3.173 ng/g		Canada (Ottawa -TDS)	(Dabeka 2004)
white sugar	2000	2.600 ng/g		Canada - Ottawa -TDS	(Dabeka 2004)
herbs and spices	2000	2.122 ng/g		Canada - Ottawa - TDS	(Dabeka 2004)
nuts	2000	1.960 ng/g		Canada - Ottawa - TDS	(Dabeka 2004)
infant formula; ready-to-use	-	24.9 and 7.6 ng/g	2.7 - 171 ng/g	mean and median	(Dabeka 1989)
infant formula; milk based with added iron		7.5 and 7.4 ng/L		mean and median; n=27	(Dabeka 1989)
infant formula; milk based with added iron		5.7 and 5.5 ng/L		mean and median; n=6	(Dabeka 1989)
infant formula; soy-based		63.7 and 31.2 ng/g		mean and median; n=16	(Dabeka 1989)
Canada - human milk for breast fed infants					
Newfoundland and Labrador		19.3 µg/L	3 - 28 µg/L	samples collected 1/wk for 8 weeks and 3 months	(Friel *et al*. 1999)
United States		1.16 ± 0.41 ng/mL	0.52 - 2.04 ng/mL	up to 35 days post=partum (immature milk); n=46; 13 women	(Casey & Neville 1987)
Worldwide		13.3 µg/L	11 - 16 µg/L	6 countries; 3 months post-partum	(Parr *et al*. 1991)
Portugal		5.8 and 5.3 µg/L	3.7 - 10.7 µg/L	mean and median;	(Almeida *et al*. 2008)
Canadian food intake rates (µg/kg bw/day)					
infant	2000-2007	12.53 ± 2.31	5.59 - 19.48		(HC 2010)
toddler	2000-2007	11.14 ± 4.28	0 - 23.98		(HC 2010)
child	2000-2007	8.15 ± 3.20	0 - 17.74		(HC 2010)
teen	2000-2007	4.96 ± 1.90	0 -10.67		(HC 2010)
adult	2000-2007	3.94 ± 1.46	0 - 8.32		(HC 2010)

Human and biological Tissues					
Tissue	**Year**	**Concentration**	**Range**	**Comment**	**Reference**
Lungs	1980s	173 µg/kg dw	71-371 µg/kg dw	N=10 at autopsy	(Rezuke *et al*. 1987)
			<1-242 µg/kg dw	Data compiled from earlier studies	(Rezuke *et al*. 1987)
		330±380 µg/g dw		Workers exposed to poorly-soluble Ni	
		34±48 µg/g dw		Workers exposed to soluble Ni	(Andersen and Svenes 1989)
		0.76±0.39 µg/g dw		Unexposed controls	
Kidneys	1980s	62 µg/kg dw	19-171 µg/kg dw	N=10 at autopsy	(Rezuke *et al*. 1987)
			<1-165 µg/kg dw	Data compiled from earlier studies	(Rezuke *et al*. 1987)
Thyroid	1980s	141 µg/kg dw	41-240 µg/kg dw	N=10 at autopsy	(Rezuke *et al*. 1987)
Adrenal	1980s	132 µg/kg dw	53-241 µg/kg dw	N=10 at autopsy	(Rezuke *et al*. 1987)
Liver	1980s	50 µg/kg dw	11-102 µg/kg dw	N=10 at autopsy	(Rezuke *et al*. 1987)
			8-21 µg/kg dw	Data compiled from earlier studies	(Rezuke *et al*. 1987)
Heart	1980s	54 µg/kg dw	10- 110 µg/kg dw	N=10 at autopsy	(Rezuke *et al*. 1987)
			1-14 µg/kg dw	Data compiled from earlier studies	(Rezuke *et al*. 1987)
Spleen	1980s	37 µg/kg dw	9-95 µg/kg dw	N=10 at autopsy	(Rezuke *et al*. 1987)
			1-15 µg/kg dw	Data compiled from earlier studies	(Rezuke *et al*. 1987)
Brain	1980s	44 µg/kg dw	20-65 µg/kg dw	N=10 at autopsy	(Rezuke *et al*. 1987)
Pancreas	1980s	34 µg/kg dw	7-71 µg/kg dw	N=10 at autopsy	(Rezuke *et al*. 1987)
Lymph nodes		282 µg/kg dw	84-486 µg/kg dw		(Rezuke *et al*. 1987)
Testes		148 µg/kg dw	9-417 µg/kg dw		(Rezuke *et al*. 1987)
Ovaries		102 µg/kg dw	41-163 µg/kg dw		(Rezuke *et al*. 1987)
Spinal cord/pituitary		38/33 µg/kg dw	8-77 µg/kg dw		(Rezuke *et al*. 1987)
Urine and blood			0.51 - 6.1 µg/L	normal levels	(WHO 1991)
Serum and plasma			<0.005 - 1.08 µg/L	normal levels	(WHO 1991)
Urine			129 µg/L	exposed workers	(Sunderman *et al*. 1986)
Plasma			11.9µ/L	exposed workers	(Sunderman *et al*. 1986)
Blood		1.39 µg/dl (geomean)	0.087 - 8.81 µg/dl	Tarragona, Spain; men (n=72); women (n=72) over 16 yrs	(Llobet *et al*. 1998)
Hair			0.38 to 23.83 µg/g	Tarragona, Spain; children (11-13yrs); n=124	(Granero *et al*. 1998)

Appendix 2. Toxicity of nickel to soil microbial processes.

Candidate data are screened according to whether they are considered "acceptable" (referred to as selected) or "unacceptable" (referred to as consulted) for deriving soil quality guidelines. Acceptable data that were actually used in SQG_{NEC} derivation are in bold and underlined and superscripts are used to identify data used for a particular land use; A/R = agricultural and residential parkland land uses, and C/I = commercial and industrial land uses.

Process	Endpoint (exposure)	Effect concentration (mg/kg)	Form of nickel	Soil pH	% OM[(a)]	CEC[(b)]	Test Substrate	Reference
SELECTED								
Carbon mineralisation (CO_2 release)	24 % reduction (2 months equilibration of spiked soil + 12 weeks of CO_2 measurements)	$^{A/R}\underline{\mathbf{1000}}^{C/I}$ (single dose level)	$NiSO_4$	6.0	2.2 (OC)		"Bagshot sand" (5.5% clay, 12% silt, 6 ppm nickel background)	(Bhuiya 1972)
Microbial respiration (CO_2 produced)	NOEC (14% decrease) (43 weeks) LOEC (37% decrease) (43 weeks) *IC25 (43 weeks)	400 1000 $^{A/R}\underline{\mathbf{582}}^{C/I}$	$NiCl_2$	6.0	5.7	10-12	Sandy loam (clay 9%, silt 26%. Sand 65%, 6 mg/kg nickel background)	(Doelman & Haanstra 1984)
Carbon mineralisation (CO_2 release)	18% decrease (2 weeks) 6% decrease (8 weeks) 28% decrease (8 weeks)	10 10 $^{A/R}\underline{\mathbf{100}}^{C/I}$	$NiSO_4$	4.9	2.1 (OC)		Loamy sand (82% sand, 9.9% silt, 5.2% clay, 3.1 mg/kg nickel background)	(Cornfield 1977)
Nitrobacter Nitrification	62% decrease (10 days) 64% decrease (10 days) 67% decrease (10 days)	294 (single dose level) 294 (single dose level) 294 (single dose level)	$NiCl_2$ $NiCl_2$ $NiCl_2$	7.4 7.8 5.8	5.45 (OC) 3.74 (OC) 2.58 (OC)		Okoboji (16% sand, 50% silt, 34% clay) Harps (26% sand, 44% silt, 30% clay) Webster (38% sand, 39% silt, 23% clay)	(Liang & Tabatabai 1978)
Nitrobacter Nitrogen mineralisation	17% reduction (20 days) 17% reduction (20 days)	$^{A/R}\underline{\mathbf{294}}^{C/I}$ (single dose level) $^{A/R}\underline{\mathbf{294}}^{C/I}$ (single dose level)	$NiCl_2$ $NiCl_2$	5.8 7.8	2.58 (OC) 3.74 (OC)		Webster (38% sand, 39% silt, 23% clay) Harps (26% sand, 44% silt, 30% clay)	(Liang & Tabatabai 1978)
Microbial respiration (CO_2 produced)	34% reduction (45 days) 34% reduction (45 days) 34% reduction (45 days) 34% reduction (45 days)	$\underline{\mathbf{294}}^{C/I}$ $\underline{\mathbf{294}}^{C/I}$ $\underline{\mathbf{294}}^{C/I}$ $\underline{\mathbf{294}}^{C/I}$	$NiSO_4$ $NiSO_4$ $NiSO_4$ $NiSO_4$	7.2 8.2 6.7 7.0	1.7 4.7 3.1 5.5	18.4 20.0 14.0 25.1	Walla Walla (21% sand, 57% silt, 21% clay) Sharpsburg (61% sand, 28% silt, 11% clay) Crider (10% sand, 63% silt, 27% clay) Toledo (19% sand, 30% silt, 51% clay)	(Lighthart *et al*. 1983)

Process	Endpoint (exposure)	Effect concentration (mg/kg)	Form of nickel	Soil pH	% OM[(a)]	CEC[(b)]	Test Substrate	Reference
Carbon mineralisation (CO_2 release)	26% reduction (6 weeks) 34% reduction (6 weeks)	$^{A/R}\underline{100}^{C/I}$ 1000	$NiSO_4$	5.9	2.1 (OC)		Sandy soil (82% sand, 9.8% silt, 5.2% clay, 8.1 ppm nickel background)	(Giashuddin & Cornfield 1978)
Nitrogen mineralisation Nitrogen nitrification	28% reduction (6 weeks) 36% reduction (6 weeks) 26% reduction (6 weeks) 52% reduction (6 weeks)	$^{A/R}\underline{100}^{C/I}$ 1000 $^{A/R}\underline{10}^{C/I}$ 100						
microbial respiration (CO_2 release)	ED50 (3hr) ED50 (12 days) ED50 (40 days)	561.8 982.4 $\underline{308.7}^{C/I}$	$NiSO_4$	8.6	0.9 (TOC)		semi-arid soil (11.3% sand, 35.1% silt, 53.6% clay, 5.0 mg/kg nickel background)	(Moreno *et al.* 2003)
microbial respiration (CO_2 release)	EC25 (28 days)	$^{A/R}\underline{250}^{C/I}$	$NiCl_2$	5.2	1.4 (C)	13.1	Typic Xerochrept (72% sand, 20% silt, 8% clay)	(Saviozzi *et al.* 1997)
Nitrification	EC50 (28 days)	$\underline{502}^{C/I}$	$NiCl_2$	6.4	4.4 (OC)	23.4	Grassland (60% sand, 19% silt, 21% clay, 47 mg/kg nickel background)	(Fait *et al.* 2006)
Nitrification	EC50 (4d-28d)	555	$NiCl_2$	4.1	33.05 (OC)	52.8	Histosol from Zegveld (34% clay, 26 mg/kg nickel)	(Oorts *et al.* 2006)
Nitrification Glucose respiration	EC50 (4d-28d) EC50 (24 hour)	$\underline{72}^{C/I}$ 421	$NiCl_2$	4.1	0.25 (OC)	8.4	Chromic Cambisol from Montpellier (25% clay, 16 mg/kg nickel background)	
Nitrification Maize mineralisation	EC50 (4d-28d) EC20 (28 days)	$\underline{235}^{C/I}$ 1126	$NiCl_2$	4.2	12.52 (OC)	11.9	Histosol from Rhydtalog (13% clay, 3 mg/kg nickel background)	
Nitrification Glucose respiration Maize mineralisation	EC50 (4d-28d) EC50 (24 hour) EC20 (28 day)	27 44 28	$NiCl_2$	4.5	1.32 (OC)	1.8	Mollic Cambisol from Jyndevad (1% clay, 1 mg/kg nickel background)	
Nitrification Glucose respiration Maize mineralisation	EC50 (4d-28d) EC50 (24 hour) EC20 (28 day)	$\underline{106}^{C/I}$ 177 560	$NiCl_2$	5.1	2.47 (OC)	4.3	Dystric Regosol from Kovlinge (4% clay, 2 mg/kg nickel background)	
Nitrification Glucose respiration	EC50 (4d-28d) EC50 (24 hour)	$\underline{183}^{C/I}$ 966	$NiCl_2$	5.6	0.99 (OC)	19.3	Vertic Cambisol from Aluminusa (47% clay, 19 mg/kg nickel background)	
Glucose respiration Maize mineralisation	EC50 (24 hour) EC20 (28 day)	88 166	$NiCl_2$	5.6	1.33 (OC)	4.9	Cambisol from Borris (4%clay, 3 mg/kg nickel background)	
Nitrification Glucose respiration Maize mineralisation	EC50 (4d-28d) EC50 (24 hour) EC20 (28 day)	298 1135 591	$NiCl_2$	6.1	4.3 (OC)	28.9	Dystric Cambisol from Woburn (35% clay, 39 mg/kg nickel background)	
Nitrification Glucose respiration Maize mineralisation	EC50 (4d-28d) EC50 (24 hour) EC20 (28 day)	$\underline{193}^{C/I}$ 205 108	$NiCl_2$	6.7	1.09 (OC)	7.8	Haplic Luvisol from Leuven (10% clay, 11 mg/kg nickel background)	

Process	Endpoint (exposure)	Effect concentration (mg/kg)	Form of nickel	Soil pH	% OM[(a)]	CEC[(b)]	Test Substrate	Reference
Nitrification Glucose respiration	EC50 (4d-28d) EC50 (24 hour)	454 735	$NiCl_2$	7	0.45 (OC)	12.9	Chromic Luvisol from Souli (33% clay, 81 mg/kg nickel background)	
Nitrification Glucose respiration Maize mineralisation	EC50 (4d-28d) EC50 (24 hour) EC20 (28 day)	**224**[C/I] 293 94	$NiCl_2$	7.6	1.14 (OC)	19.4	Calcaric Fluvisol from Marknesse (20% caly, 19 mg/kg nickel background)	
Nitrification Glucose respiration Maize mineralisation	EC50 (4d-28d) EC50 (24 hour) EC20 (28 day)	792 868 635	$NiCl_2$	7.5	1.37 (OC)	23.6	Calcaric Cambisol from Brecy (49% clay, 113 mg/kg nickel background)	
Nitrification Glucose respiration Maize mineralisation	EC50 (4d-28d) EC50 (24 hour) EC20 (28 day)	398 703 785	$NiCl_2$	7.6	0.49 (OC)	35.3	Inceptisol from Cordoba II (55% clay, 24 mg/kg nickel background)	
Nitrification Glucose respiration Maize mineralisation	EC50 (4d-28d) EC50 (24 hour) EC20 (28 day)	**172**[C/I] 360 154	$NiCl_2$	7.6	0.53 (OC)	13.3	Luvisol from Cordoba I (20% clay, 18 mg/kg nickel background background)	
Nitrification Glucose respiration Maize mineralisation	EC50 (4d-28d) EC50 (24 hour) EC20 (28 day)	**183**[C/I] 232 591	$NiCl_2$	7.7	0.31 (OC)	13.3	Calcic Cambisol from Guadalajara (17% clay, 11 mg/kg nickel background)	
Nitrification	EC50 (1-2 wk preincub. + 4 d – 28 d for expt.) freshly spiked Leached aged 5 months outdoors aged 10 months outdoors aged 15 months outdoors	 27 41 35 52 **116**[C/I]	$NiCl_2$	4.5	1.3 (OC)	1.8	Mollic Cambisol from Jyndevad (acid and sandy;1 % clay; 1 mg/kg nickel background)	(Oorts *et al*. 2007)
Glucose induced respiration	EC50 (1-2 wk preincub.) freshly spiked aged 5 months outdoors aged 10 months outdoors aged 15 months outdoors	 52 101 84 56						
	NOEC (1-2 wk preincub.) leached	 >251						
Maize residue mineralisation	EC20 (1-2 wk preincub.) freshly spiked aged 5 months outdoors aged 10 months outdoors	 151 221 285						
	NOEC (1-2 wk preincub.) leached aged 15 months outdoors	 >246 >519						

Process	Endpoint (exposure)	Effect concentration (mg/kg)	Form of nickel	Soil pH	% OM[(a)]	CEC[(b)]	Test Substrate	Reference
Nitrification	EC50 (1-2 wk preincub. + 4 d - 28 d for expt.)		$NiCl_2$	6.1	4.3 (OC)	28.9	Dystric Cambisol (35% clay, 39 mg/kg Ni background)	
	freshly spiked	313						
	Leached	313						
	aged 5 months outdoors	271						
	aged 10 months outdoors	621						
	aged 15 months outdoors	**3086**[C/I]						
Glucose induced respiration	EC50 (1-2 wk preincub.)							
	freshly spiked	1124						
	NOEC (1-2 wk preincub.)							
	Leached	>2385						
	aged 5 months outdoors	>4582						
	aged 10 months outdoors	>3822						
	aged 15 months outdoors	>3755						
Maize residue mineralisation	EC20 (1-2 wk preincub.)							
	freshly spiked	579						
	Leached	557						
	aged 10 months outdoors	1066						
	aged 15 months outdoors	784						
	NOEC (1-2 wk preincub.)							
	aged 5 months outdoors	>4630						
Nitrification	EC50 (1-2 wk preincub. + 4 d – 28 d for expt.)		$NiCl_2$	7.6	0.5 (OC)	35.3	Inceptisol from Cordoba II (55% clay; 24 mg/kg nickel background)	
	freshly spiked	213						
	leached	945						
	aged 5 months outdoors	**1982**[C/I]						
	NOEC (1-2 wk preincub. + 4 d - 28 d for expt.)							
	aged 10 months outdoors	>4342						
	aged 15 months outdoors	>4341						
Glucose induced respiration	EC50 (1-2 wk preincub.)							
	freshly spiked	253						
	Leached	484						
	aged 5 months outdoors	289						
	aged 10 months outdoors	3124						
	aged 15 months outdoors	2021						

Process	Endpoint (exposure)	Effect concentration (mg/kg)	Form of nickel	Soil pH	% OM[(a)]	CEC[(b)]	Test Substrate	Reference
Maize residue mineralisation	EC20 (1-2 wk preincub.) freshly spiked NOEC (1-2 wk preincub.) Leached aged 5 months outdoors aged 10 months outdoors aged 15 months outdoors	 297 >2339 >4615 >4423 >4423						
CONSULTED								
Aspergillus clavatus Growth	LOEC (3 days)	50	$NiCl_2$	4.8			Sandy soil	(Babich & Stotzky 1982)
Penicilium vermicalatum Growth	LOEC (3 days)	250	$NiCl_2$	4.8			Sandy soil	
Aspergillus flavus Growth	LOEC (3 days)	250	$NiCl_2$	4.7			Sandy soil	
Gliocladium sp. Growth	LOEC (3 days)	250	$NiCl_2$	4.7			Sandy soil	
Rhizopus stolonifer Growth	LOEC (3 days)	500	$NiCl_2$	4.6			Sandy soil	
Aspergillus flavipes Growth	LOEC (3 days)	500	$NiCl_2$	4.6			Sandy soil	
Aspergillus niger Growth	LOEC (3 days)	500	$NiCl_2$	4.6			Sandy soil	
Trichoderma vivide Growth	LOEC (3 days)	750	$NiCl_2$	4.5			Sandy soil	
Phosphatase activity	EC_{50} (6 weeks)	1109 5688 4232 6516	$NiCl_2$	7.0 6.0 7.7 7.5			Sand Sandy loam Silty loam Clay	(Doelman & Haanstra 1989)
Phosphatase activity	EC_{50} (18 months)	2530 8042 2131		7.0 6.0 7.7			Sand Sandy loam Silty loam	
Phosphatase activity (<5% inhibition)	EC_5 (3 hours)	587	$NiCl_2$	4.3-6.3			Organic-rich soil	(Tyler 1981)
Dehydrogenase activity	EC_{50} (24 hours)	77	$NiSO_4$	NA			Agricultural soil enriched with alfalfa	(Rogers & Li 1985)
Urease activity	EC_{50} (6 weeks)	100 2040 1650 3380	$NiCl_2$	7.0 6.0 7.7 7.5			Sand Sandy loam Silty loam Clay	(Doelman & Haanstra 1986)
		3030		4.4			Sandy peat	

Process	Endpoint (exposure)	Effect concentration (mg/kg)	Form of nickel	Soil pH	% OM[(a)]	CEC[(b)]	Test Substrate	Reference
	EC_{50} (18 months)	410 2790 1740 370 2320		7.0 6.0 7.7 7.5 4.4			Sand Sandy loam Silty loam Clay Sandy peat	
Urease activity	EC_{33} (2 hours)	294	$NiCl_2$	5.1- 7.8			Agricultural soil	(Tabatabai 1977)
Arylsulphate activity	NOEC (30 minutes) EC_{26} (30 minutes)	146.8 1468	$NiCl_2$	6.2- 7.6			Four different agricultural soils	(Al-Khafaji & Tabatabai 1979)
Pyrophosphatase	EC_2 (5 hours) EC_5 (5 hours) EC_2 (5 hours)	293.5 1468 1468	$NiCl_2$	4.6 7.0	1.99 (OC) 5.32 (OC)		Fine loamy Montmorillonitic soil	(Scott *et al.* 1985)
Carbon mineralisation	EC_{55}	6.6		NA			Sandy loam	(Brookes & McGrath 1984)
Microbial respiration (CO_2 produced)	EC_{10} (9 days)	29.4	$NiSO_4$	6.2	64	12.5	Rifle series	(Lighthart *et al*. 1983)
Microbial respiration (CO_2 produced)	24% inhibition to 30 % above control - no dose-response observed (70 wks)	150- 8000	$NiCl_2$	7.0	1.6	1-2	Sand	(Dolovich *et al.* 1984)
Microbial respiration (CO_2 produced) Community structure (PCA analysis) Phospholipid fatty acid analysis (PLFA total)	ED_{10} (64 days) LOEC (42% reduction) (64 days) LOEC (64 days) NOEC (64 days)	279 1230 180 1230	$NiCl_2$				humus (upper half of O_f layer)	(Åkerblom *et al.* 2007)
Soil dehydrogenase activity Soil ATP content Soil microbial biomass C	ED50 (3 hr) ED50 (12 days) ED50 (40 days) ED50 (3 hr) ED50 (12 days) ED50 (40 days) ED50 (3 hr) ED50 (12 days) ED50 (40 days)	2885.1 5978.5 9127.5 2240.1 4668.4 16694.3 386.6 795.8 7243.1	$NiSO_4$	8.6	0.9 (TOC)		semi-arid soil (11.3% sand, 35.1% silt, 53.6% clay, 5.0 mg/kg nickel)	(Moreno *et al.* 2003)
Dehydrogenase	ED10 (24 hours) ED25 (24 hours) ED50 (24 hours)	7.9 24.3 100	$NiCl_2$	7.02	1.12 (OC)	12.4	haplic fluvisol (9.7% sand, 75.1% silt, 15.2% clay, 19.4 mg/kg nickel)	(Welp 1999)

Process	Endpoint (exposure)	Effect concentration (mg/kg)	Form of nickel	Soil pH	% OM[(a)]	CEC[(b)]	Test Substrate	Reference
Urease activity Phosphatase activity protease-BAA activity	ED50 (40 days) ED50 (40 days) ED50 (40 days)	2852 5890 8197	$NiSO_4$	8.6	0.9 (TOC)		semi-arid soil (11.3% sand, 35.1% silt, 53.6% clay, 5.0 mg/kg nickel)	(Moreno *et al.* 2003)
Nitrogen fixation	NOEC (18 months)	>54	$NiSO_4$	6.5-6.77			Sandy loam (51% sand, 9% clay, 17 mg/kg nickel)	(Chaudri & McGrath 1992)
Glucose respiration Maize mineralisation Nitrification	EC50 (24 hour) EC20 (28 day) EC50 (4d-28d)	71 110 162	$NiCl_2$ $NiCl_2$	3.6 5.6	17.3 (OC) 1.33 (OC)	1.8 4.9	Haplic Podzol from Houthalen (1% clay, 1 mg/kg nickel) Cambisol from Borris (4%clay, 3 mg/kg nickel)	(Oorts *et al.* 2006)
Nitrification Nitrogen mineralisation	NOEC (6 weeks) LOEC -significant increase in (NO_3^-+NH_4^+)-N (6 weeks)	500 500	$NiSO_4$	3.4-3.9	47-53	NR	Sandy Orthic Humo-Ferric Podzols (experiment conducted on mineral layer only)	(deCatanzaro & Hutchinson 1985)
Respirtaion: delay (hours) to maximum respiration rate of glutamic acid	NOEC (18 months) LOEC 42% increase (18 months) NOEC (18 months) LOEC 66% increase (18 months)	55 400 55 400	$NiCl_2$	4.4 7.0	12.8 1.6	50-55 1-2	Sandy peat (82% sand, 13% silt, 5% clay, 4 mg/kg nickel) Sand (93% sand, 5% silt, 2% clay, 8 mg/kg nickel)	(Haanstra & Doelman 1984)
Carbon mineralisation (CO_2 release)	No Effect Level IC20 IC50 (results pooled from experiments performed at 1, 31 and 63 d)	27 90 500	$NiSO_4$	5.7	0.72 (C)	11.3	Acid sandy loam	(Gupta *et al*. 1987)

NA = not available

[a]Studies reported organic matter (OM) unless otherwise indicated, e.g., C (carbon), OC (organic carbon), or TOC (total organic carbon)

[b]Units of Cation Exchange Capacity (CEC) are either meq(+) / 100g or cmol(+) / kg.

* Recalculated by Environment Canada using log-logistic model.

Appendix 3. Toxicity of nickel to terrestrial plants.

Candidate data are screened according to whether they are considered "acceptable" (referred to as selected) or "unacceptable" (referred to as consulted) for deriving soil quality guidelines. Acceptable data that were actually used in SQG_{SC} derivation are in bold and underlined in the "Selected" section of this appendix

Organism	Effect (exposure period)	Endpoint	Effect magnitude (%)	Effect concentration (mg/kg)	Form of nickel	Soil pH	%OM (a)	CEC (b)	Test Substrate	Reference
SELECTED										
Corn (*Zea mays L*.)	Growth (g/shoot) (14 days)	NOEC LOEC *IC25 NOEC LOEC NOEC LOEC *IC25	 -72 -81 -47 	100 250 161 100 250 100 250 182	$NiSO_4$	4.2 5.6 7.5 			Yolo loam soil	(Wallace *et al*. 1977)
Soybean (*Glycine max L*.)	Mortality (12 days) Leaf yield (mg/plant) (12 days) Stem yield (mg/plant) (12 days)	LC100 LOEC LOEC	 -32 -28	1000 (one test conc.) 1000 (one test conc.) 1000 (one test conc.)	$NiSO_4$	6.2 7.2 7.2			Yolo loam soil	
Bush bean (*Phaseolus vulgaris* L. C.V. Improved Tendergreen)	Leaf yield (mg/plant) (16 days) Leaf yield (mg/plant) (28 days) Stem yield (mg/plant) (28 days)	LOEC NOEC LOEC NOEC NOEC LOEC NOEC LOEC	-64 -36 -45 +35	100 100 250 250 25 100 25 100	$NiSO_4$	5.8 7.5 8.2 5.6-5.8 5.6-5.8 			Yolo loam soil	
Barley (*Hordeum vulgare* L. C.V. Atlas 57)	Growth (28 days)	LOEC	-70 to -75	50	$NiSO_4$	5.6-5.8			Yolo loam soil	
Rye grass (*Lolium perenne*)	Growth rate (shoot yield) (4 weeks)	NOEC LOEC *IC25	 -14 	30 90 **109**	$NiSO_4$	4.7			Loam soil	(Khalid & Tinsley 1980)
Red oak (*Quercus rubra*)	Total leaf area (16 weeks) Total dry weight (16 weeks)	NOEC LOEC *IC25		20 50 **42**	$NiCl_2$	6.0	1.5		Sandy loam soil	(Dixon 1988)

Organism	Effect (exposure period)	Endpoint	Effect magnitude (%)	Effect concentration (mg/kg)	Form of nickel	Soil pH	%OM (a)	CEC (b)	Test Substrate	Reference
Onion (*Allium cepa*)	Total dry weight (8 weeks) Mortality (8 weeks)	LOEC *IC25 LC100	-20	50 **70** 400	$NiSO_4$	8.3	0.28 (OC)	12.6	Clay-loam soil (sand 40%; silt 35%; clay 24%)	(Dang *et al*. 1990)
Fenugreek (*Trigonella poenumgraceum*)	Total dry weight (8 weeks) Mortality (8 weeks)	LOEC *IC25 LC100	-21	50 **122** 400						(Biró *et al*. 1998)
Cotton plant (*Gossypium hirsutum* L.)	Leaf growth (5 weeks)	LOEC *IC50	-44	100 110	$NiSO_4$	6.8	2.2		Loam soil	(Rehab & Wallace 1978)
	Stem growth (5 weeks)	LOEC	-59	100						
Cotton plant (Gossypium hirsutum L. cv. Giaz 45)	Leaf growth (5 weeks) Leaf growth (5 weeks)	LOEC *IC50 *IC25 LOEC	-46 -28	100 107 **96** 100						
Alfalfa (*Medicago sativa* L.)	Growth (2 months)	NOEC	-23	86	$NiSO_4$	7.0	3 humus		calcareous loamy chernozem (25% clay)	(Biró *et al*. 1998)
Alfalfa (*Medicago sativa* Fabaceae)	Mortality Emergence Total dry weight/plant	EC20 EC20 EC25		319.7 201.1 **33.9**	$NiCl_2$	5.01	5 peat		modified ASTM soil (sand 85%; clay 10%)	(Kapustka *et al*. 2006)
	Mortality Emergence Total dry weight/plant	EC20 EC20 EC25		176.5 124.6 **29.8**	$NiCl_2$	6.32	0.1		Camas soil (sand 88.8%; silt 8.0%; clay 3.2%)	
barley (*Hordeum vulgare*, Gramineae)	Mortality Emergence Total dry weight/plant	EC20 EC20 EC25		593.6 256.2 **20.2**	$NiCl_2$	5.01	5 peat		modified ASTM soil (sand 85%; clay 10%)	
	Mortality Emergence Total dry weight/plant	EC20 EC20 EC25		760.7 179.8 **88.8**	$NiCl_2$	6.32	0.1		Camas soil (sand 88.8%; silt 8.0%; clay 3.2%)	
Brassica (*Brassica rapa*, Brassicaeae)	Mortality Emergence Total dry weight/plant	EC20 EC20 EC25		>5000 43.2 **26.2**	$NiCl_2$	5.01	5 peat		modified ASTM soil (sand 85%; clay 10%)	
	Mortality Emergence Total dry weight/plant	EC20 EC20 EC20		4001.9 63 39.4	$NiCl_2$	6.32	0.1		Camas soil (sand 88.8%; silt 8.0%; clay 3.2%)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		11 13 18	$NiCl_2$	4.5	1.32 (OC)	1.84	Jyndevad (sand 95.0%; silt 3.5%; clay 1.5%; 1 mg/kg Ni background)	(Rooney *et al*. 2007)

Organism	Effect (exposure period)	Endpoint	Effect magnitude (%)	Effect concentration (mg/kg)	Form of nickel	Soil pH	%OM [(a)]	CEC [(b)]	Test Substrate	Reference
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		126 135 148	$NiCl_2$	6.7	1.09 (OC)	7.80	Ter Munck (sand 11.0%; silt 79.4%; clay 9.6%; 11 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		131 152 206	$NiCl_2$	4.2	12.52 (OC)	11.91	Rhydtalog (sand 36.8%; silt 50.5%; clay 12.7%; 3 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		162 175 205	$NiCl_2$	7.6	0.53 (OC)	13.35	Cordoba 1 (sand 46.3%; silt 33.9%; clay 19.8%; 18 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		192 215 273	$NiCl_2$	6.1	4.3 (OC)	28.87	Woburn (sand 40.7%; silt 24.0%; clay 35.3%; 39 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		32 35 43	$NiCl_2$	4.1	0.25 (OC)	8.39	Montpellier (sand 63.3%; silt 11.4%; clay 25.3%; 16 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		221 239 275	$NiCl_2$	7.6	1.14 (OC)	19.44	Marknesse (Sand 12.3%; Silt 67.7%; clay 19.9%; 19 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		22 23 26	$NiCl_2$	3.6	1.73 (OC)	1.84	Houthalen (Sand 94.9%; silt 4.8%; clay 0.4%; 1 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		252 284 367	$NiCl_2$	7.6	0.49 (OC)	35.26	Cordoba 2 (sand 23.0%; silt 21.6%; clay 55.4%; 24 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		330 358 415	$NiCl_2$	7.0	0.45 (OC)	12.85	Souli (sand 52.4%; silt 14.4%; clay 33.2%; 81 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		47 59 92	$NiCl_2$	5.6	0.99 (OC)	19.26	Aluminusa (sand 29.3%; silt 23.7%; clay 46.9%; 19 mg/kg Ni background)	

Organism	Effect (exposure period)	Endpoint	Effect magnitude (%)	Effect concentration (mg/kg)	Form of nickel	Soil pH	%OM (a)	CEC (b)	Test Substrate	Reference
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		45 49 59	$NiCl_2$	5.1	2.47 (OC)	4.31	Kövlinge II (sand 82.6%; silt 13.4%; clay 3.9%; 2 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		629 673 777	$NiCl_2$	7.5	1.37 (OC)	23.57	Brécy (sand 11.4%; silt 39.4%; clay 49.2%; 113 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		56 62 77	$NiCl_2$	5.6	1.33 (OC)	4.91	Borris (sand 78.6%; Silt 17.1%; clay 4.3%; 3 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		637 727 961	$NiCl_2$	4.1	33.05 (OC)	52.75	Zegveld (sand 47.8%; silt 18.2%; clay 34%; 26 mg/kg Ni background)	
Tomato	Shoot growth (21 d)	EC10 **EC20 EC50		199 260 415	$NiCl_2$	7.7	0.31 (OC)	13.27	Guadalajara (sand 55.2%; silt% 27.6%; clay 17.2%; 11 mg/kg Ni background)	
Oat (var. Cascade)	Dry matter yield (Grown to maturity)	NOEC LOEC *IC25 NOEC	 -27 	63.4 139.4 **133** >96.2	$NiSO_4$ $NiSO_4$	7.5 8.3	2.3 3	14.6 34.7	Light textured (8.9% clay; 8.3 mg/kg Ni background) Heavy textured (44.6% clay; 27.2 mg/kg Ni background)	(Liang & Schoenau 1995)
Radish (var. Cherry Bell)	Dry Matter Yield (30 d)	NOEC LOEC *IC25 NOEC	 -89.3 	63.4 139.4 **78** >96.2	$NiSO_4$ $NiSO_4$	7.5 8.3	2.3 3	14.6 34.7	Light textured (8.9% clay; 8.3 mg/kg Ni background) Heavy textured (44.6% clay; 27.2 mg/kg Ni background)	
Corn (*Zea mays* L.)	Above ground yield (6 weeks)	*IC25		**49**	$NiSO_4$	6.5	2.86 (C)	20.2	Grenville loam	(MacLean & Dekker 1978)
Oat	Grain yield (110 d) Straw yield (110 d)	NOEC NOEC		>500 >500	$NiCl_2$	7.8	4.0	13 .0	Grenville sandy loam	(Halstead *et al.* 1969)
Oat	Grain yield (110 d) Straw yield (110 d)	LOEC *IC25	-38	50 **31**	$NiCl_2$	6.1	1.4	6	Uplands sand	
Oat	Grain yield (110 d) Straw yield (110 d)	MATC *IC25		224 73	$NiCl_2$	5.7	4.1	11.7	Uplands sand	

Organism	Effect (exposure period)	Endpoint	Effect magnitude (%)	Effect concentration (mg/kg)	Form of nickel	Soil pH	%OM (a)	CEC (b)	Test Substrate	Reference
Alfalfa	Tops yield (83 d)	*IC25		41	$NiCl_2$	5.7	4.1	11.7	Uplands sand	
Alfalfa	Tops yield (83 d)	LOEC	-40	32	$NiCl_2$	6.1	1.4	6	Uplands sand	
Alfalfa	Tops yield (83 d)	MATC		224	$NiCl_2$	7.8	4.0	13 .0	Grenville sandy loam	
Barley	Root elongation (5 d)				$NiCl_2$	4.93	1.51	8.45	S1-Latersol (clay	(Li *et al.* 2011)
(*Hordeum vulgare*)	unleached	EC20		18			(C)		66%)	
	leached	EC20		25						
Barley	Root elongation (5 d)				$NiCl_2$	5.31	0.87	7.47	S2-Red earth (clay	
(*Hordeum vulgare*)	unleached	EC20		30			(C)		46%)	
	leached	EC20		38						
Barley	Root elongation (5 d)				$NiCl_2$	6.56	3.03	33.6	S3-Black soil (clay	
(*Hordeum vulgare*)	unleached	EC20		913			(C)		40%)	
	leached	EC20		1729						
Barley	Root elongation (5 d)			795	$NiCl_2$	6.70	1.42	19.3	S4-Paddy siol (clay	
(*Hordeum vulgare*)	unleached	EC20		649			(C)		41%)	
	leached	EC20								
Barley	Root elongation (5 d)				$NiCl_2$	6.80	2.46	12.8	S5-Paddy soil (clay	
(*Hordeum vulgare*)	unleached	EC20		480			(C)		39%)	
	leached	EC20		903						
Barley	Root elongation (5 d)				$NiCl_2$	7.12	0.99	22.3	S6-Purplish soils	
(*Hordeum vulgare*)	unleached	EC20		238			(C)		(clay 27%)	
	leached	EC20		265						
Barley	Root elongation (5 d)				$NiCl_2$	7.27	1.47	8.30	S7-Padddy soil (clay	
(*Hordeum vulgare*)	unleached	EC20		328			(C)		25%)	
	leached	EC20		980						
Barley	Root elongation (5 d)				$NiCl_2$	7.48	4.28	22.7	S8-Brown earth (clay	
(*Hordeum vulgare*)	unleached	EC20		702			(C)		20%)	
	leached	EC20		1053						
Barley	Root elongation (5 d)				$NiCl_2$	7.66	2.66	22.7	S9-Chernozem (clay	
(*Hordeum vulgare*)	unleached	EC20		1029			(C)		37%)	
	leached	EC20		1175						
Barley	Root elongation (5 d)				$NiCl_2$	7.82	2.17	28.8	S10-Black soil (clay	
(*Hordeum vulgare*)	unleached	EC20		889			(C)		45%)	
	leached	EC20		639						
Barley	Root elongation (5 d)				$NiCl_2$	8.19	1.01	11.7	S11-Cinnamon soil	
(*Hordeum vulgare*)	unleached	EC20		688			(C)		(clay 21%)	
	leached	EC20		NC						
Barley	Root elongation (5 d)				$NiCl_2$	8.72	0.87	10.3	S12-Gray desert soil	
(*Hordeum vulgare*)	unleached	EC20		544			(C)		(clay 25%)	
	leached	EC20		≥2381						
Barley	Root elongation (5 d)				$NiCl_2$	8.83	0.62	8.46	S13-Loessial soil	
(*Hordeum vulgare*)	unleached	EC20		475			(C)		(clay 28%)	
	leached	EC20		≥2286						

Organism	Effect (exposure period)	Endpoint	Effect magnitude (%)	Effect concentration (mg/kg)	Form of nickel	Soil pH	%OM (a)	CEC (b)	Test Substrate	Reference
Barley (*Hordeum vulgare*)	Root elongation (5 d) unleached leached	 EC20 EC20		 936 1457	$NiCl_2$	8.84	0.60 (C)	6.36	S14-Fluvo-aquic soil (clay 10%)	
Barley (*Hordeum vulgare*)	Root elongation (5 d) unleached leached	 EC20 EC20		 551 NC	$NiCl_2$	8.86	1.57 (C)	8.50	S15-Fluvo-aquic soil (clay 16%)	
Barley (*Hordeum vulgare*)	Root elongation (5 d) unleached leached	 EC20 EC20		 911 NC	$NiCl_2$	8.86	1.02 (C)	8.08	S16-Irrigated desert soil (clay 20%)	
Barley (*Hordeum vulgare*)	Root elongation (5 d) unleached leached	 EC20 EC20		 256 ≥2380	$NiCl_2$	8.90	0.69 (C)	8.33	S17-Fluvo-aquic soil (clay 18%)	
CONSULTED										
Pinus banksiana *Picea glauca*	Shoot dry weight (12 weeks) Root dry weight (12 weeks) Shoot dry weight (12 weeks) Root dry weight (12 weeks)	EC_{41} EC_{17} EC_{16} EC_{18}		5 5 10 5	$NiCl_2$	6.0	1.5		Sandy loam soil	(Dixon & Bushena 1988)
Celery Lettuce	Growth (69-75 days) Growth (60-78 days)	EC_{59} EC_{19}		1180 1875	NA	5.7-6.4	70		Organic soil (70% O.M.)	(Frank *et al*. 1982)
Lettuce	Dry matter yield (63 days)		-20 -54 -13 -35 -14	46 81 348 387 503	$NiSO_4$	4.9 7.7 5.6 6.6		8 10 41 20	Acid sandy loam (Steinhof) Erlach Gänsemos Gasel	(Gupta *et al*. 1987)
Red clover (*Trifolium paratense* L.)	Growth (2 months)	NOEC	-33	22 86	$NiSO_4$	7.0	3 humus		calcareous loamy chernozem (25% clay)	(Biró *et al*. 1998)
Ryegrass	Growth (12 weeks)	NOEC		>50	$NiCl_2$	6.0	0.4 (C)		Sandy soil	(Singh & Jeng 1993)
Red clover (*Trifolium*	Dry matter yield (35 days)	NOEC		>100	$Ni(C_2H_3O_2)_2$	8.2	1	23.4	Silt loam (sand 27.6%; silt 52.6%; clay 19.8%)	(Elmosly & Abdel-Sabour 1997)

Organism	Effect (exposure period)	Endpoint	Effect magnitude (%)	Effect concentration (mg/kg)	Form of nickel	Soil pH	%OM [a]	CEC [b]	Test Substrate	Reference
paratense L.)		NOEC LOEC	+126 +152	25 50	$Ni(C_2H_3O_2)_2$	7.9	0.6		Sandy loam (sand 61.0%; silt 27.8%; clay 11.2%)	
		NOEC		>100	$Ni(C_2H_3O_2)_2$	7.6	0.05	5.9	Sandy (sand 87.3%; silt 7.2%; clay 5.5%)	
Oat (?)	Degree of necrotic symptoms (36 d)	High		218 (soluble in 2.5% acetic acid)	ambient	4.8			Pure sand quartz	(Hunter & Vergnano 1952)
Multiple crop species	Nickel toxicity symtpoms	Symptoms are described		26-61	ambient	4.5-5.3			Field study in acid peat	
Corn (*Zea mays*)	Growth (5 weeks)	NOEC		>155	$NiCl_2$	6	2.16	5.7	Rubicon sand (sand 89.38%; silt 1.18%; clay 9.44%)	(Traynor & Knezek 1973)
Mustard	Grain yield (Grown to maturity)	LOEC	-19	20	NR	8.0	0.2 (C)		Loamy sand soil (Typic ustipsamment)	(Gupta & Kala 1996)
Lentil	Grain yield (Grown to maturity)	LOEC	-14	5.0						
Chickpea	Grain yield (Grown to maturity)	LOEC	-18	7.5						
Oat	Grain yield (110 d) Straw yield (110 d)	NOEC NOEC		>500 >500		6.4	21.2	61.7	Granby sandy loam	(Halstead *et al*. 1969)
Alfalfa	Alfalfa tops yield (83 d)	MATC		224						
Lettuce (var. Slobolt)	Dry Matter Yield (40 d)	LOEC	-29 -94	32.5 139.4	$NiSO_4$	7.5	2.3	14.6	Light textured (8.9% clay; 8.3 mg/kg Ni background)	(Liang & Schoenau 1995)
Lettuce (var. Slobolt)	Dry Matter Yield (40 d)	NOEC LOEC	 -35	23.2 54.8	$NiSO_4$	8.3	3	34.7	Heavy textured (44.6% clay; 27.2 mg/kg Ni background)	
Spinach	Growth (30 days)	EC_{29}		23	$NiSO_4$	4.55	2.14 (OC)	7.4	Sandy soil (3.1 mg/kg Ni)	(Willaert 1988)
		LOEC	-35	58 (single dose)		6.05	2.09 (OC)	8.5	Sandy loam soil (8.5 mg/kg Ni)	
		EC10		220		8.1	2.33 (OC)	19.6	Heavy clay soil (20 mg/kg Ni)	

NA = Not available; NC = Not calculated

[a] Studies reported organic matter (OM) unless otherwise indicated, e.g., C (carbon) or OC (organic carbon).

[b] Units of Cation Exchange Capacity (CEC) are either meq(+)/100g or cmol(+)/kg.

* Recalculated by Environment Canada using log-logistic model.

**Provided by corresponding author, Fang-Jie Zhao, in 2012

Appendix 4. Toxicity of nickel to terrestrial invertebrates.

Candidate data are screened according to whether they are considered "acceptable" (referred to as selected) or "unacceptable" (referred to as consulted) for deriving soil quality guidelines. Acceptable data that were actually used in SQG_{SC} derivation are in bold and underlined in the "Selected" section of this appendix.

Organism	Effect (exposure period)	Endpoint	Effect magnitude (%)	Effect concentration (mg/kg)	Form of nickel	Soil pH	% OM[(a)]	CEC[(b)]	Test Substrate	Reference
SELECTED										
Earthworm (*Eisenia foetida*)	Mortality (2 weeks)	LC50		243	$Ni(NO_3)_2$	6.0	10 peat		Artificial soil (20% kaolinite clay; 69% fine sand; 1 % pulverized $CaCO_3$)	(Neuhauser *et al*. 1985)
Earthworm (*Lumbricus rubellus*)	Mortality (6 weeks) Mortality (12 weeks)	***LC20 ***LC50 ***LC20 ***LC50		1007 2240 305 821	$NiCl_2$	7.3			Sandy loam	(Ma 1982)
Earthworm (*Eisenia veneta*)	Mortality (4 weeks) Reproduction (cocoon production) (4 wks)	LC10 LC50 LC100 NOEC LOEC *IC25 EC10 EC50	 -64	247 684 1000 100 300 **<u>186</u>** 85 300	$NiSO_4$	5.5-6.0	2.3 (TOC)		Loamy sand soil (sand 82%; silt 13%; clay 5%)	(Scott-Fordsmand *et al.* 1998)
Springtail (*Folsomia fimetaria*)	Adult ♂ mort. (21 d) Adult ♀ mort. (21 d) Juvenile mort. (21 d) Reproduction (# juveniles) (21 d) Adult ♂ growth (surface area) (21 d) Adult ♀ growth (surface area) (21 d) Juvenile growth (surface area) (21 d)	LC10 LC50 LC10 LC50 LC10 LC50 EC10 EC50 NOEC LOEC MATC NOEC NOEC EC10 NOEC LOEC	 -51	645 922 427 786 701 859 173 450 300 500 387 >1000 >1000 480 700 1000	$NiCl_2$	5.5-6.0	2.3 (TOC)		Loamy sand soil (sand 82%; silt content 13%; clay 5%)	(Scott-Fordsmand *et al.* 1999)

Organism	Effect (exposure period)	Endpoint	Effect magnitude (%)	Effect concentration (mg/kg)	Form of nickel	Soil pH	% OM[(a)]	CEC[(b)]	Test Substrate	Reference
Springtail (*Folsomia candida*)	Reproduction (# juveniles) (28 d)	NOEC LOEC ****IC25 EC50	 -43 	320 560 **266** 476	$NiCl_2$	6	10 peat		OECD Guideline 207 (sand 70%; Kaolinite clay 20%)	(Lock & Janssen 2002)
Earthworm (*Eisenia fetida*)	Reproduction (# cocoons) (21 d)	NOEC LOEC *IC25 EC50	 -50 	180 320 **223** 362						
	Mortality (21 d)	NOEC		>1000						
Earthworm (*Enchytraeus albidus*)	Reproduction (# juveniles) (42 d)	NOEC LOEC ****IC25 EC50	 -68 	180 320 **168** 275						
	Mortality (21 d)	LC50		510						
Nematode (*Caenorhabditis elegans*)	Mortality (24 hr)	LC50		2493	NR	7.8	5.1	28.4	ASTM (sand 80%; silt 12%; clay 8%)	(Boyd & Williams 2003)
	Mortality (24 hr)	LC50		1188	NR	6.1	1.4	2.4	Albany (sand 98%; silt 0%; clay 2%)	
	Mortality (24 hr)	LC50		1202	NR	5.7	5.1	7.2	Cecil (sand 74%; silt 16%; clay 10%)	
Nematode (*Caenorhabditis elegans*)	Mortality (NR)	LC50		348	$NiCl_2$	~4	10 peat		ASTM loam (sand 70%; clay 20%)	(Peredney & Williams 2000a)
	Mortality (NR)	LC50 LC50		165 387	$NiCl_2$ $Ni(NO_3)_2$	~4	2.46 (C)	6.23	Cecil (sand 60.2%; clay 10.4%)	
	Mortality (NR)	LC50 LC50		44 144	$NiCl_2$ $Ni(NO_3)_2$	~4	0.67 (C)	1.58	Tifton (sand 88.6%; clay 3.6%)	
Nematode (*Caenorhabditis elegans*)	Mortality (24 hr)	LC50		797	$Ni(NO_3)_2$	4 ± 0.5	10 peat		ASTM (sand 70%; Kaolin clay 20%)	(Peredney & P. L. Williams 2000b)
Nematode (multiple species)	Abundance (1-2 weeks)	LOEC *IC25	-18 	100 **138**	$NiSO_4$	4.1	1.9 (C)	3.6	sandy loam (sand 85%; silt 11%; clay 4%; 4.1 mg/kg Ni background)	(Korthals *et al.* 1996)
CONSULTED										
Earthworm (*Eisenia foetida*)	Cocoon production (6 weeks)	EC_{40}		250	NA	NA			soil mixed with horse manure	(Neuhauser *et al*. 1984)
	Growth rate (BW) (6 weeks)	EC_{32}		500	NA	NA				
Earthworm (*Eisenia foetida*)	Growth rate (8 weeks)	EC		500	$Ni(C_2H_3O_2)_2$	NA			soil mixed with horse manure	(Malecki *et al*. 1982)

Organism	Effect (exposure period)	Endpoint	Effect magnitude (%)	Effect concentration (mg/kg)	Form of nickel	Soil pH	% OM[(a)]	CEC[(b)]	Test Substrate	Reference
		EC		500	$NiCO_3$					
Earthworm (*Eisenia foetida*)	Reproduction (20 weeks)	EC EC EC EC EC EC EC EC EC EC		200 500 40,000 500 300 2000 200 500 40 000 500	$NiCl_2$ $Ni(NO_3)_2$ NiO $NiSO_4$ $Ni(C_2H_3O_2)_2$ $NiCO_3$ $NiCl_2$ $Ni(NO_3)_2$ NiO $NiSO_4$	NA			soil mixed with horse manure	
Springtail (*Folsomia candida*)	Mortality (35 d)	LC50		246	$NiCl_2$	5.8	3.9		Sandy soil (clay 5.1%; soil treated with acetone as a negative control)	(Broerse & van Gestel 2010)

NA = Not available; NC = Not calculated

[a]Studies reported organic matter (OM) unless otherwise indicated, e.g., C (carbon) or TOC (total organic carbon).

[b]Units of Cation Exchange Capacity (CEC) are either meq(+)/100g or cmol(+)/kg.

*Recalculated by Environment Canada using log-logistic model.

***Recalculated by Environment Canada using Probit analysis (no log transformation).

****Recalculated by Environment Canada using linear regression (no log transformation)

Appendix 5. Toxicity of nickel to mammals

Organism	M/F	Effect	Endpoint	Concentration in food (mg/kg)	Form of nickel	Exposure Period	Estimated Dose (mg/kg bw per day)	Reference
Beagle dog	M/F	Mortality Growth	No effect EC_{50}	2500 2500	$NiSO_4$	2 years	83 83	(Ambrose *et al*. 1976)
Calf (Holstein)	M	Mortality Growth Feed uptake Urease activity	No effect No effect No effect No effect	5 5 5 5	$NiCl_2$	140 days	0.2 0.2 0.2 0.2	(Spears *et al*. 1986)
Calf (Holstein and Brown Swiss)	M	Growth	NOEL (4% reduction) LOEL (45% reduction)	250 1000	$NiCO_3$	56 days	6.8 13.77	(O'Dell *et al.* 1971)
Calf (Holstein)	M	Growth	NOEL(2.6% reduction) LOEL(44% reduction)	250 1000	$NiCO_3$	56 days	7* 14.6*	(O'Dell *et al.* 1971)
Mouse	M/F	Mortality	LD_{50}	--	$Ni(C_2H_3O_2)_2$	NA	420*	(Haro *et al*. 1968)
Rat	M/F	Mortality	LD_{50}	--	$Ni(C_2H_3O_2)_2$	NA	350*	(Haro *et al*. 1968)
Mouse (Webster)	M F M F	Growth Growth Feed uptake Feed uptake	EC_{24} EC_{16} EC_8 No effect	1600 1600 1100 1600	$Ni(C_2H_3O_2)_2$	4 weeks	250 293 208 293	(Weber & Reid 1968)
Rat	M/F	Mortality	LD_{50}	--	$Ni(NO_3)_2$	NA	1620*	(NAS 1975)
Rat (Sprague-Dawley)	M	Growth	NOEL (3.6% reduction) LOEL (4.2% reduction)	111.75 mg/L 223.5 mg/L	$NiSO_4$	13 weeks	11.7 23.4	(Obone *et al.* 1999)
Rat (Wistar)	M	Growth	NOEL (2.3% reduction)	104.9	$NiCl_2$	31 d	7.8	(Oosting *et al*. 1991)
Rat (Wistar)	M	Growth	LOEL (9% reduction)	100 (one test dose)	$NiCl_2$	31 d	8.2	(Oosting *et al*. 1991)

Organism	M/F	Effect	Endpoint	Concentration in food (mg/kg)	Form of nickel	Exposure Period	Estimated Dose (mg/kg bw per day)	Reference
Rat (Sprague-Dawley)	M	Growth	LOEL (10% increase) NOEL(8% reduction)	30 (one test dose) 225	$NiCl_2$	42 d	2.5 20	(Spears & Hatfield 1985)
Rat	M/F	Growth rate Growth rate	NOEL (7% reduction) LOEL (43% reduction)	100 500	$Ni(C_2H_3O_2)_2$	6 weeks	9.49 51.75	(Whanger 1973)
Rat (Wistar)	F M M/F F F F	Growth Hematologic changes Fertility Gestation Lactation	EC_{35} EC_{24} No effect No effect No effect No effect	1000 2500 1000 1000 1000 1000	$NiSO_4$	2 years	50 125 50 50 50 50	(Ambrose *et al.* 1976)
Rat (Wistar)	 F	Fetal body weight Number of live foetuses Number of fetal loss Maternal body weight	No effect No effect No effect LOEC (8 % reduction)	20 mg/L(only one test concetration)	$NiCl_2$	16 days	1 1 1 1	(Adjroud 2011)
Mice Mice	M M	Sperm cell count Sperm cell count	NOEC (3% reduction) LOEC (25% reduction) NOEC (13% reduction) LOEC (25% reduction)	 	$NiCl_2$ $NiSO_4$	35 days 35 days	1.6 3.2 2.7 5.4	(Pandey & Srivastava 2000)

M= Male
F= Female
*= as reported by author

Appendix 6. Toxicity of nickel to birds.

Organism	M/F	Effect	Endpoint	Conc. in food (mg/kg)	Form of nickel	Exposure Period	Estimated Dose (mg/kg bw per day)	Reference
Mallard ducks	M/F	mortality	No effect	800	$NiSO_4$	90 d	80	(Eastin Jr. & O'Shea 1981)
		growth rate	No effect	800			80	
		histopathological changes	No effect	800			80	
		Blood chemistry changes	No effect	800			80	
Mallard ducks	M/F	mortality	LC_{75}	1200	$NiSO_4$	60 d	120	(Cain & Pafford 1981)
	F	growth rate	EC_{23}	1200		90 d	120	
Mallard ducks	F	egg production	No effect	800	$NiSO_4$	90 d	80	(Eastin Jr. & O'Shea 1981)
		hatchability	No effect	800			80	
		normal duckling @ day 14	No effect	800			80	
Chicks	F	Growth	NOEL (16% reduction)	400	$NiCl_2$	2 weeks	51.7	(Hill 1979)
			LOEL(33% reduction)	800			111.9	
Chicks (Hubbard broiler)	M/F	growth rate	EC_{18}	500	$NiSO_4$	28 d	53	(Weber & Reid 1968)
			EC_{14}	500	$Ni(C_2H_3O_2)_2$		48	
Chicks (White Plymouth rock)	M	mortality	LC_{50}	900	$NiCl_2$	21 d	90	(Ling & Leach 1979)
		growth rate	EC_{14}	300			30	
		Anemia	EC_{23}	1100			110	
Laying hens (ISA Brown)	F	Growth	NOEC (6% reduction)	0.2 mg $NiCl_2$/ L	$NiCl_2$	28 d	0.004	(Arpasova *et al*. 2007)
			LOEC (36% reduction)	2 mg $NiCl_2$/ L			0.051	
		Egg weight	NOEC (4% increase)	0.2 mg / L			0.004	

Organism	M/F	Effect	Endpoint	Conc. in food (mg/kg)	Form of nickel	Exposure Period	Estimated Dose (mg/kg bw per day)	Reference
			LOEC (18% reduction)	2 mg / L			0.051	
		Egg quality (eggshell weitgth)	17% reduction	2 mg / L			0.051	
Brolier chick	M	Growth	NOEC (6% reduction)	123.5	$NiCl_2$	42 d	5.1	Martinez and Diaz, 1996
			LOEC (14% reduction)	247			9.5	
			26% reduction	474			19.1	
Warren hens	F	Reproduction (egg weight)	NOEC (3% reduction)	500	$NiSO_4$	60 d	40.8	Meluzzi *et al.* 1996
		Reproduction (egg shell weight)	NOEC (3% reduction)	500			40.8	

M= Male
F= Female
EC= The EC endpoints represent the effects concentration as calculated byEnvironment Canada from the data presented by the author(s)
LC_{50}= Lethal concentration to 50% of the population
* = as reported by author

Appendix 7. Terrestrial bioconcentration factors.

Pathway	Tissue type	pH	OM[a] (%)	CEC[b]	Soil type	Tissue conc. (mg/kg)	Soil conc. (mg/kg)	BCF	Reference
food-beetle (*Pterostichus oblongopunctatus*)	*whole body*							0.06 (geomean of 5 test concentrations; range 0.03-0.07)	(Bednarska & Laskowski 2008)
leaf litter - Isopod (*Porcellio scaber - hepatopancreas*)								2.4 (geomean of 3 test concentrations)	(Tarnawska *et al.* 2007)
soil - earthworm								0.1	(Neuhauser *et al.* 1985)
soil - earthworm								0.1	(Pietz *et al*. 1984)
soil - earthworm								1.6	(Gish & Christensen 1973)
soil - earthworm								0.3	(Ma 1982)
Geometric mean for invertebrates								**0.30**	
soil - corn (*Zea mays*)								0.003 (Grain) 0.01 (Roots)	(Petruzzelli *et al.* 1989)
Soil – barley (*Hordeum vulgare* L.)	Whole plant at emergence	5.6	0.8 (OC)	11.8	medium clay soil	10.12	11	0.92	(Molas & Baran 2004)
soil - corn (*Zea mays*)	Whole plant at 5 weeks	6.8	2.16	5.7	Sand	15 16 19 16 19 25	8 17 31 73 96 155	1.875 0.94 0.61 0.22 0.198 0.16 (geomean = 0.44)	(Traynor & Knezek 1973)
Soil – barley (*Hordeum vulgare* L.)	Whole plant at emergence	5.1	1.2 (OC)	12.3	medium clay soil	8.86	18.5	0.47	(Molas & Baran 2004)
Soil - fenugreek	root shoot							1.32 (geomean of 12 treatments) 0.82 (geomean of 14 treatments)	(Parida *et al.* 2003)
soil - corn plants								0.1	(Sadiq 1985)
soil - winter wheat (*Triticium aestivum* L.)								0.14	(Qian *et al.* 1996)
soil - alfalfa (*Medicago sativa* L.)								0.22	

Pathway	Tissue type	pH	OM[a] (%)	CEC[b]	Soil type	Tissue conc. (mg/kg)	Soil conc. (mg/kg)	BCF	Reference
soil - soybean plant (*Glycine max* L.)								0.4 (shoot) 5.3 (root)	(Vesper & Weidensaul 1978)
soil - ryegrass (*Lolium perenne*)								1.7	(Khalid & Tinsley 1980)
soil - ryegrass (*Lolium hybridum*)								1.0	(Allinson & Dzialo 1981)
soil - oat (*Avena sativa L.*)								0.2 (straw) 0.4 (seed)	(Allinson & Dzialo 1981)
soil - cotton plants								0.7 (leaf) 0.3 (stem)	(Rehab & Wallace 1978)
Soil -lettuce	leaves	4.9		8	Steinhof	5.6 34 80 102 128	16 29 46 60 81	0.35 1.17 1.74 1.7 1.58	(Gupta *et al.* 1987)
		5.6		41	Gänsemos	5.6 19 47.2 70.8	17 84 172 387	0.33 0.23 0.27 0.18	
		7.7		10	Erlach	5.6 42 49 76 95	26 141 199 256 348	0.33 0.30 0.25 0.30 0.27	
		6.6		20	Gasel	5.6 37 50 62	21 169 261 503	0.27 0.22 0.19 0.12 (geomean for all soils = 0.37)	
Geometric mean for plants								**0.34**	

[a]Studies reported organic matter (OM) unless otherwise indicated, e.g., C (carbon) or TOC (total organic carbon).

[b]Units of Cation Exchange Capacity (CEC) are either meq(+)/100g or cmol(+)/kg.

Appendix 8. Receptor Characteristics of the Canadian General Population[1]

	Statistic	*Breast fed Infant (0 to 6 mo.)*	*Non-breast fed Infant (0 to 6 mo.)*	*Toddler (7 mo. to 4 yr)*	*Child (5 to 11 yr)*	*Teen (12 to 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
	Std. dev.	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	1142	1262
	Mean	320	320	430	590	800	890
	Std. dev.	30	30	50	80	100	110
	Distribution	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Skin Surface Area Arms (cm^2)	Minimum	200	200	396	797	1409	1588
	Maximum	1367	1367	1882	2645	3465	3906
	Mean	550	550	890	1480	2230	2510
	Std. dev.	180	180	240	300	340	360
	Distribution	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Skin Surface Area Legs (cm^2)	Minimum	539	539	907	1604	3042	3753
	Maximum	1496	1496	3012	5655	7945	8694
	Mean	910	910	1690	3070	4970	5720
	Std. dev.	160	160	340	660	810	760
	Distribution	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Soil Loading to exposed skin[2] Hands Surfaces other than hands (kg/cm^2/event)	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 outdoors (hr/d)	Minimum	0.000	0.000	0.000	0.000	0.000	0.000
	Maximum	3	3	3	4	9.45	10.76
	Mean/Mode	1.25	1.25	1.25	2.2	1.42	1.43
	Std. dev.	N/A	N/A	N/A	N/A	1.17	1.28
	Distribution	Triangular	Triangular	Triangular	Triangular	Lognormal	Lognormal

[1]Mean receptor characteristics from Richardson (1997) and CCME (2006) unless otherwise stated.
[2]Soil loadings from (Kissel *et al*. 1998; Kissel *et al.* 1996) as referenced in CCME (2006).

Appendix 9. Typical Intake Values for Environmental Media by the Canadian General Population[1]

Intake rates[1]	*Statistic*	*Breast fed Infant (0 to 6 mo.)*	*Non-Breast fed Infant (0 to 6 mo.)*	*Toddler (7 mo. to 4 yr)*	*Child (5 to 11 yr)*	*Teen (12 to 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
	Std. dev.	0.59	0.59	2.19	3.38	4.00	4.05
	Distribution	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Water Ingestion[2] (L/d)	Minimum	N/A	0.1	0.2	0.2	0.2	0.2
	Maximum	N/A	0.7	0.9	1.1	2	2.7
	Mean	N/A	0.3	0.6	0.8	1	1.5
	Std. dev.	N/A	0.2	0.4	0.4	0.6	0.8
	Distribution	N/A	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Soil Ingestion[3] (kg/d)		2.0×10^{-5}	2.0×10^{-5}	8.0×10^{-5}	2.0×10^{-5}	2.0×10^{-5}	2.0×10^{-5}
Soil Inhalation[4] (m^3/d)		1.66×10^{-9}	1.66×10^{-9}	6.32×10^{-9}	1.10×10^{-8}	1.10×10^{-8}	1.26×10^{-8}
Indoor Settled Dust Ingestion (kg/d)	Minimum	8.0×10^{-8}	8.0×10^{-8}	0.00	0.00	0.00	0.00
	Maximum	1.77×10^{-3}	1.77×10^{-3}	9.4×10^{-4}	8.33×10^{-4}	3.39×10^{-5}	6.20×10^{-5}
	Mean	3.74×10^{-5}	3.74×10^{-5}	4.06×10^{-5}	3.17×10^{-5}	2.07×10^{-6}	2.51×10^{-6}
	Std. dev.	8.33×10^{-5}	8.33×10^{-5}	5.22×10^{-5}	4.58×10^{-5}	2.32×10^{-6}	3.06×10^{-6}
	Distribution	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal
Food[5] µg/kg-d^{-1}	Minimum	0.5	5.590	0.000	0.000	0.000	0.000
	Maximum	1	19.475	23.981	17.744	10.667	8.323
	Mean/Mode	0.7	12.533	11.142	8.148	4.956	3.945
	Std. dev.	N/A	2.314	4.280	3.199	3.945	1.459
	Distribution	Triangular	Lognormal	Lognormal	Lognormal	Lognormal	Lognormal

[1]Probability distribution function curves for receptor intake rates from HC (2011) unless otherwise stated.
[2]Breast fed infants are assumed to be exclusively breastfed for 6 months and are not given drinking water. Infants that are not breastfed are assumed to consume 0.3L of drinking water based on HC 2004.
[3]Soil ingestion rates from CCME (2006).
[4]Soil inhalation rates based on (Allan & Richardson 2008) and a PM_{10} concentration of 0.76 µg/m^3 (CCME 2006).
[5]Breastfed infants are assumed to be exclusively breastfed for 6 months; non-breastfed infants are assumed to be fed a mixture of milk, formula and table food.

Appendix 10. Estimated Total Daily Nickel Intake for the Canadian General Population[1]

Medium	Typical Nickel Levels	Daily Nickel Intake in µg/kg bw/day				
		0 to 6 mo. Infant	7 mo. - 4 yrs Toddler	5-11 yrs Child	12 -19 yrs Teenager	20 + yrs Adult
Air[2] Outdoor air Indoor air	 0.00094 µg/m^3 0.0072 µg/m^3	 0.00000476 0.00104	 0.00000900 0.00193	 0.0000117 0.00167	 0.00000400 0.000993	 0.00000353 0.000899
Drinking water[3]	2.85 µg/L	0.0525[4]	0.0462	0.0326	0.0228	0.0294
Settled indoor dust[4] Ingestion Dermal	 48.1 µg/g	 0.0726 0.0200	 0.0571 0.0143	 0.0206 0.0109	 0.000864 0.00581	 0.000853 0.00545
Soil[5] Ingestion Inhalation Dermal	 26.8 µg/g	 0.0369 0.00000015 6 0.00775	 0.0717 0.00000028 4 0.00558	 0.00896 0.00000037 7 0.00422	 0.00486 0.00000012 6 0.00226	 0.00413 0.00000011 3 0.00212
Food[6]		1.70[7] 12.1[8]	10.3	7.69	4.67	3.76
Total intake (µg/kg-bw/day)[9]		1.81 - 12.4	10.7	7.7	4.7	3.8

[1]Median estimated daily intakes for each age class were derived from probability distribution functions based on typical concentrations of air (indoor and outdoor), drinking water, settled indoor dust, soil and food listed above. Receptor characteristic distribution, or point estimates listed in Appendix 8 and intake rates listed in Appendix 9.
[2]Outdoor air $PM_{2.5}$ concentrations from NAPS 2000-2009 database for urban and rural centers in Canada (HC 2011).
[3]Based on mean nickel concentrations of drinking water from Ontario, Saskatchewan, Newfoundland and Labrador (HC 2011).
[4]Based on mean total nickel in indoor settled dust from HC (2011) and dust ingestion rates from (Willson *et al*. 2012).
[5]Based on data (7398 samples) compiled by the Geological Survey of Canada (HC 2011; Grunsky 2010; Rencz *et al*. 2006).
[6]Based on the results of the Total Diet Studies (2000-2007) conducted by Health Canada Food Directorate.
[7]Based on infants exclusively breast fed for 6 months.
[8]Based on infants fed a mixture of milk, formula and table food.
[9]Note that total median EDIs for each receptor group will not equal the sum of the median EDIs listed for the five media listed because the total EDI was derived from individual probability distribution functions.

Appendix 11. Alternative approach for calculating human health soil quality guidelines for Ni when EDI > TDI.

Overview:

This appendix clearly lays out the details of an alternative approach for calculating human health soil quality guidelines when the EDI>TDI. This approach is summarised at the end of this appendix and in Figure 2, also at the end of this appendix. It seeks to minimize human exposure to the extent possible without resulting in an SQG less than the mean background soil concentration for an uncontaminated site (which is a practical lower limit for SQGs). For the purposes of soil quality guidelines derivation, the recommended procedure when the EDI>TDI is to:

1. Ensure the mean or best estimate of the mean EDI and TDI chosen are appropriate;
2. Calculate the SQG based on the 10% EDI equation;
3. Calculate the SQG based on the 20% TDI equation;
4. Choose the lower of the 10% EDI or 20% TDI calculated value and compare it to the BSC.
5. If the lowest of the calculated value chosen from the 10% EDI or 20% TDI is greater than the BSC, use this value as the provisional SQG_{DH}. If the calculated value is less than the BSC, set the SQG_{DH} to the BSC. (See figure 2 for pictorial explanation. The blue path shows the approach recommended in this document, the yellow path illustrates the CCME soil protocol (CCME 2006) when TDI > EDI, and the green path is additional recommendations when the EDI is >90% of the TDI.)

Explanation for the removal of the soil allocation factor.

The EDI[1] terms consider the contribution of background soils and the soil allocation factor as part of its calculation. Removing the SAF is similar to setting the SAF to 1 instead of 0.2. Equation 2 (see below) incorporates the background soil and soil allocation factor in the 10% EDI term. If a soil allocation factor of <1 is used, this would decrease the allowable EDI contribution from soils to 0.1 x SAF. For example, if the default SAF of 0.2 is used, this is results in an EDI contribution from soil to be 0.02 of the total EDI. The use of a SAF of 1 results in an EDI contribution from soil of up to 0.10 of the total EDI. It seems reasonable that a 10%

---

[1] The EDI is based on the sum of estimated human exposure to a substance through contact with various media (food, drinking water, soil, air, consumer products and dust). For illustrative purposes, the soil dermal EDI can be calculated using the following equation:

$$ug/kg/d = \frac{\left[\left(C_s \times SA_H \times SL_H\right) + \left(C_s \times SA_A \times SL_A\right) + \left(C_S \times SA_L \times SL_L\right)\right] \times RAF_{derm} \times EF \times 1000 ug/mg}{BW}$$

Where:
C_s = Concentration of substance in soil (mg/kg)
SA = surface area for hands, arms and legs (cm^2)
SL = soil loading for hands, arms and legs (kg/cm^2/event)
RAF_{derm} = Relative Dermal Absorption Factor (unitless)
EF = event frequency (1 event/d)
BW = Body weight (kg)

increase in EDI is within the variability of observed data from various media. (The GSC reported a provisional range of <2 to 214 mg/kg Ni in background till concentrations - Rencz 2006).

Justification for the use of equation #2.

Equations 1, 2 and 3 (described below) all follow the general CCME SQG equation with the (TDI-EDI) term replaced with a 0.1 EDI term. Equation 2 is the simplest of the 10% EDI equations. The BSC can be removed from the equation because the EDIs are already above the TDI in cases where this approach is considered, and the addition of the BSC will not add any more precision to the calculation. If the value derived using Equation 2 is above the BSC, the SQG is set to the BSC by default.

For Ni, the EDI (for the toddler) and TDI terms are very similar (10.6 *vs*. 11 µg/kg bw/day) and the background soil concentration is higher than both the EDI and TDI terms, but also very low. Comparing SQGs derived for Ni using the three equations, the resulting SQGs from equations 1 and 3 are identical and similar using equation 2, with the differences mainly attributed to the exclusion of the BSC from the equation.

Background:

CCME (2006) outlines a protocol that should be used in the derivation of environmental and human health soil quality guidelines (SQGs). For threshold substances, the CCME equation used to derive the human health soil quality guideline takes the general form:

$$SQG_{DH} = \frac{(TDI - EDI) \times SAF \times BW}{IR \times AF \times ET} + BSC$$

where:
SQG_{DH} = Human Health Soil Quality Guideline
TDI = Tolerable Daily Intake (µg/kg bw/day)
EDI = Estimated Daily Intake (µg/kg bw/day)
SAF = Soil Allocation Factor (unitless)
BW = Body Weight (kg)
IR = Ingestion Rate of medium of concern (kg/day)
AF = Absorption Factor for medium of concern (unitless)
ET = Exposure Term (unitless)
BSC = Background Soil Concentration
RTDI = (TDI-EDI) Residual Tolerable Daily Intake (µg/kg bw/day)

To derive the guidelines for threshold substances, it is necessary to assign an allowable proportion of the total chemical exposure to the soil medium in the equation listed above. The Tolerable Daily Intake (TDI) represents the total dose to which it is believed a human receptor can be safely exposed continuously over a lifetime without any deleterious effects. The EDI is an

estimate of the total background exposure of human receptors to the substance, based on a multi-media exposure assessment.

The CCME SQGTG considers five primary media (i.e., air, water, soil, food and consumer products) to which people are potentially exposed. The CCME SQGTG proposed that a default value of 20% (0.2) be allotted to each of the five exposure media. For the purposes of deriving soil quality guidelines, 20% the RTDI is apportioned to soils so that the Soil Allocation Factor (SAF) is arbitrarily set at 0.2 and allows for 80% of the total incremental exposure from other media (i.e., food, air, water and consumer products). However, some soil contaminants may not be normally present in one or more of the other exposure media. If it can be proven that exposure to one or more of the remaining media are not relevant for the substance, the SAF may be adjusted upward from the 0.2 default by dividing the total exposure (100%) by the number of applicable exposure media so that:

$$SAF = \frac{100\%}{\#\ of\ applicable\ media}$$

For some substances where the EDI exceeds the TDI, the equation used by CCME to derive the human health soil quality guideline would not apply, as the SQG derived would result in a negative number. In these cases, the CCME (2006) protocol states that:

When the EDI is greater than the TDI (RTDI = 0), theoretically the population cannot be safely subjected to any increased exposure. In these cases, the provisional soil quality guideline should be set at the background soil concentration or practical quantification limit for that contaminant.

Issue:

During the course of developing SQGs, some substances were found to have estimated background exposure rates greater than the toxicity benchmarks established for human health. If the EDI exceeds TDI, this implies that exposure to typical background levels of the substance exceeds a dose considered protective of human health. However, this does not necessarily mean that health effects are expected in the population at large because there is usually considerable uncertainty in the EDI and TDI values. EDIs are derived from estimates of the mean concentrations of the substance in exposure media (i.e., air, water, soil and food) and estimated mean or typical intake rates of the substance of concern via the various exposure media. Uncertainty in the mean EDI or best estimate of the mean EDI can arise from various sources such as limited availability of data for chemical concentrations in various media and the lack of or uncertainty in intake rates for food, water, air, and soil. In the case of food intakes, assumptions employed by the CCME SQGTG may not reflect more current consumption patterns (Meridian 2007).

In situations where EDI>TDI, human health SQGs have either been set at background soil concentration levels or they have not been established at all. CCME (2006) does recognize that

this may result in a fairly restrictive criterion and as a result, they suggest that any models used to develop the EDI should be checked to ensure their accuracy, and to assess any regional or site-specific factors. In cases where EDI>TDI, establishing human health soil remediation guidelines to background soil concentrations or practical quantification limits may not be pragmatic or practical and may result in high remediation costs at sites without any significant benefit to the protection of human health.

Approach:

Recognising that setting a human health SQG to background soil concentration levels or practical quantification limits may not be practical, draft supplemental guidance document that outlined a general approach that could be used in cases when EDI>TDI was prepared (Meridian 2007).

Independent to the work completed by Meridian, Wilson Scientific Consulting Inc. (Wilson 2009) also addressed this issue for two substances (nickel and zinc). The processes and equations derived independently by Meridian and Wilson Scientific were very similar. Based on this work, an alternative to the approach outlined in the CCME (2006) protocol document for establishing human health SQGs in cases where the EDI>TDI for threshold substances and where exposure to soil is a minor contributor to the EDI was proposed.

Soil quality guidelines for nickel (Ni) are used as examples of SQGs that could be derived using the options presented below for critical receptors (typically a toddler for residential and commercial exposure scenarios). If the EDI<TDI for the relevant scenario and receptor group, then the standard CCME equation applies and is used to derive the human health SQG for that scenario. For Ni, the standard CCME (2006) SQG_{DH} equation would apply for industrial sites since the adult is considered the critical receptor and in that scenario, the TDI for both of these substances is greater than the EDI for the adult receptor.

For the scenarios where the EDI>TDI, the “TDI - EDI” term, also known as the Residual TDI (RTDI), in the CCME human health SQG equation, was modified and replaced with 10% EDI. EDI estimates are subject to uncertainty and variability of the data upon which the EDI estimate is based. This includes uncertainty due to limited data on chemical concentrations in some environmental media and intake rates. In addition to uncertainty, chemical concentrations in various media and intake rates can be highly variable. Background concentrations can vary by orders of magnitude between regions in some media. For example, Rencz *et* al (2006) report a mean Ni soil concentration of 26.8 mg/kg, a median concentration of 16 mg/kg, and a provisional range of <2 to 214 mg/kg in background soil concentrations.

Most other jurisdictions apply a target hazard index of 0.2 to the TDI, which is assumed to be sufficiently protective, irrespective of background exposure and exposure through other media at the site, when setting soil quality guidelines for inorganic substances. The 20% TDI equation was included to allow comparison with the SQG calculated using 10% EDI.

Exposure through food ingestion, which can comprise the largest portion of the EDI, is affected by variability in chemical concentrations within and between food types as well as the variability in diet compositions between individuals. A cursory examination of the estimated total daily intake of nickel from food by age class from the 2000 to 2007 Canadian Total Diet Study shows that food contributes approximately 94 to 96% of the total EDI and standard deviations of mean intakes range from approximately 18% to 37%, with the highest variability in intake rates in infants and toddlers. Based on the variability seen in food data and soil data, a 10% increase in the EDI appears to be well within the variability observed in the data from various media. Sigal *et al* (2006) conducted a probabilistic evaluation of EDIs for three metals and they found that the 95th percentile EDI was more than 50% greater than the mean EDI in all cases. For most naturally occurring substances, the contribution of soil ingestion to the EDI is relatively small (i.e., <1%) compared to the contribution of exposure from food and water based on EDIs (Meridian 2006). Therefore, given the variability and uncertainty in the EDI, an incremental increase in exposure of 10% of the EDI is not expected to represent a biologically significant increase in exposure so long as the EDI represents a 'typical' exposure and is not a worst-case exposure (Meridian 2006).

Equation 1 - (Meridian 2007)

Using the existing CCME human health SQG equation specified in the protocol document, Meridian modified the equation by replacing the RTDI term (i.e., TDI - EDI) with 0.1 EDI so the SQG equation becomes:

$$SQG_{DH} = \frac{(0.1 \times EDI) \times SAF \times BW}{IR \times AF \times ET} + BSC$$

The premise of this equation is that based on a multi-media exposure assessment, a 10% incremental increase in the mean EDI due to exposure to soil concentrations in excess of background soil concentration (BSC), is not expected to result in a significant shift in the range and frequency of EDI estimates across the population as a whole. Nor is it expected to result in any deleterious effects to human health. The contribution of soil to total exposure is often small (e.g., <1% of EDI) relative to other media and a small increase in soil concentration should only result in a small (perhaps negligible) increase in the EDI, so long as the EDI represents a 'typical' exposure and not a worst case exposure. The default SAF used in the CCME process is typically set at 0.2. However, as stated in CCME (2006) the SAF can be adjusted upwards if there is rationale which shows exposure to one of the five media listed is insignificant. In the case of Ni and Zn, it is proposed that consumer products would not be a significant source of Ni or Zn exposure on contaminated sites, relative to uncontaminated sites and that if this is a reasonable assumption, exposure to media on a contaminated site can be allocated as 0.25 to drinking water, 0.25 to food and 0.5 to direct exposure via soil ingestion, dermal contact and air.

Equation 2 - Wilson Scientific equation

The equation derived by Wilson Scientific is similar to the Meridian equation above except the BSC concentration and SAF were not included in the equation, so that:

$$SQG_{DH} = \frac{(0.1 \times EDI) \times BW}{IR \times AF \times ET}$$

The EDI term considers the contribution of background soils as part of its calculation, and as such, the BSC was not included in the equation. In other words, the SAF is set to 1, and is included in the (0.1 x EDI) term. In cases where the contribution of soil to total exposure is not significant compared to the contribution relative to other media, the BSC is not expected to contribute significantly to the calculation of the SQG so that the derivation equation can be simplified by excluding the BSC and SAF terms from the equation.

Equation 3 - Modified equation

After review of the above proposed approaches, a modification was made based on the concept of using 10% of the EDI when EDI > TDI, and including the BSC term in the SQG_{DH} derivation equation. One option was to subtract the soil contribution (EDI_{soil}) from the total EDI term since the contribution from the soil exposure pathway is accounted for in the BSC term in the equation so that:

$$SQG_{DH} = \frac{[0.1 \times (EDI_{total} - EDI_{soil})] \times SAF \times BW}{IR \times AF \times ET} + BSC$$

Various SAFs (0.2, 0.5 and 1.0) were applied in the equation to look at the variability of SQGs derived for Ni, based on the contribution of EDI from soil ranging from 2% to 10%.

The SAF of 0.2 is the CCME default specified in the protocol document (CCME 2006) under normal circumstances and is included for comparative purposes. Using a SAF of 0.2 will result in a 2% EDI in the numerator of the equation (e.g., 0.1x EDI x 0.2 x BW = 0.02 EDI x BW)

The use of a SAF of 0.5 will result in a 5% EDI in the numerator of the equation (e.g., 0.1 x EDI x 0.5 x BW = 0.05 EDI x BW)

A SAF of 1 will result in a 10% EDI in the numerator of the equation (e.g., 0.1 x EDI x 1 x BW = 0.1 EDI x BW).

Equation 4 - 20% TDI

To develop soil quality guidelines for the protection of human health, most other jurisdictions apply a target hazard index of 0.2 which is assumed to be sufficiently protective irrespective of

background exposure and exposure through other media at the site. In this equation, the background soil concentration is not included. The 20% TDI equation is:

$$SQG_{DH} = \frac{(0.2 \times TDI) \times BW}{AF \times IR \times ET}$$

In any case where a proportion of the EDI is used, it is recommended that the above calculation should also be completed and that the SQG be based on the lower of the estimates.

Calculations:

For Ni, the EDI exceeds the TDI for residential and commercial exposure scenarios where the toddler is considered the critical receptor. Using the equations listed above, residential and commercial soil quality guidelines were calculated using SAFs of 0.2, 0.5 and 1.0 for comparative purposes where applicable. Nickel is considered a potential carcinogen via the inhalation pathway, so in this example the dermal absorption and oral ingestion pathways are considered together and the inhalation pathway is considered separately and not included here. The resulting values are listed in the table below:

Residential scenario **Critical receptor: Toddler**	**Ni** **RSQG**
Equation 1 using SAF = 0.2	67
Equation 1 using SAF = 0.5	130
Equation 1 using SAF = 1.0	230
Equation 2 no BSC included	**200**
Equation 3 EDI_{soil} removed; SAF = 0.2	67
Equation 3 EDI_{soil} removed; SAF = 0.5	130
Equation 3 EDI_{soil} removed; SAF = 1.0	230
Equation 4 20% TDI	420

Commercial scenario **Critical receptor: Toddler**	**Ni** **CSQG**
Equation 1 using SAF = 0.2	88
Equation 1 using SAF = 0.5	180
Equation 1 using SAF = 1.0	330
Equation 2 no BSC included	**310**
Equation 3 EDI_{soil} removed; SAF = 0.2	90
Equation 3 EDI_{soil} removed; SAF = 0.5	180
Equation 3 EDI_{soil} removed; SAF = 1.0	330
Equation 4 20% TDI	640

Bold indicates equations and calculated values recommended for consideration when EDI>TDI

Industrial scenario Critical receptor: Adult	Ni ISQG
CCME equation	5100
20% TDI	7800

Discussion:

For the example above, subtracting EDI_{soil} from the overall EDI does not affect the SQG because the contribution to the EDI from soil is not significant when compared to the exposure contribution from other media (i.e., food). This is shown by the resulting SQGs calculated using Equations 1 and 3 which are essentially the same.

For the residential and commercial scenarios using toddlers as the critical receptor, all SQGs derived using the various 10% EDI equations (Equations 1, 2 and 3) were less than the calculated SQG using the 20% TDI equation (Equation 4). Therefore, a SQG calculated using any of these 10% EDI equations would be more conservative than what is currently being done in other jurisdictions that use a 20% TDI equation to derive SQGs. If a SAF of 1 is used, the SAF term essentially drops out of Equations 1 and 3. If, as stated earlier, it is accepted that a 10% increase in the EDI is within the variability observed in the various media and does not represent a biologically significant increase in exposure, the SAF term can be eliminated from the equations, without affecting the calculated SQG value significantly.

In cases where the EDI is quite large in comparison to the TDI, exposure based on 10% of the EDI may result in exposure that exceeds the TDI, therefore, it is suggested that as a further check on the appropriateness of the 10% EDI equations, 20% of the TDI be calculated and that the lower of the two values (either calculation based on 10% of the EDI or 20% of the TDI) be used to establish the SQG. This approach is more conservative than any approach taken in other jurisdictions that establish SQGs for human health.

Recommended approach to setting Human Health Soil Quality Guidelines when mean EDI > TDI:

The CCME equation which utilises the TDI - EDI term is unique. Other jurisdictions that establish SQGs for human health typically derive SQGs based on 20% of the TDI without considering exposure from background levels. In situations where the EDI > TDI, and the background soil concentration is not expected to contribute significantly to exposure, the 10% EDI equation (Equation 2) should be considered.

For the purposes of soil quality guidelines derivation, the recommended procedure when EDI>TDI is to:

1. Ensure the mean or best estimate of the chosen mean EDI and TDI are appropriate;
2. Using Equation 2, calculate the SQG based on 10% EDI;

3. Using Equation 4, calculate the SQG based on 20% TDI;
4. Choose the lower of the 10% EDI or 20% TDI calculated value (i.e., the lower of the two values calculated from Equation 2 and 4) and compare it to the BSC.
5. If the lowest of the calculated value (from Equations 2 or 4) is greater than the BSC, use this value as the provisional SQG_{DH}. If the calculated value is less than the BSC, set the SQG_{DH} to the BSC.

Note that the discussion and recommendations outlined thus far, only apply to direct contact pathways for inorganic threshold substances. In the case of Ni, these equations can be considered for oral and dermal exposure pathways. Ni is considered carcinogenic via the inhalation exposure pathway. Therefore, inhalation exposure is considered separately from oral and dermal exposure.

Other considerations:

During EDI > TDI discussions, another issue was identified: What about when the EDI approaches the TDI but does not exceed the TDI? Specifically, when the EDI is within 90% of the TDI, the term "TDI - EDI" can become quite small and result in a much lower SQG than if the EDI exceeded the TDI.

Consequently, when EDI is estimated to be greater than 90% of the TDI, the following steps are recommended:

1. Calculate the SQG using the CCME (i.e., TDI - EDI) equation
2. Calculate the SQG using 10% EDI equation 2
3. Calculate the SQG based on the 20% TDI equation
4. Compare the SQGs derived from the CCME equation (step 1) and the 10% EDI equation (step 2) and choose the higher of the two;
5. Compare the SQG (step 4) with the SQG derived using the 20% TDI equation (step 3) and use the lower of the two as the SQG.

Due to the mathematics of the equations, it is possible to calculate a lower SQG using the "TDI - EDI" equation than if the SQG is calculated using one of the 10% EDI equations in cases where the EDI is slightly less than the TDI. However, it is difficult to justify treating a substance less stringently because the EDI is slightly lower than the TDI. Intuitively, the SQG should increase as the EDI decreases. The last step of comparing the higher of the two calculated SQGs using the CCME equation and the 10% EDI equation to the SQG calculated using the 20% TDI equation ensures that the resulting SQG chosen is less than 20% of the TDI which is used by most other jurisdictions that derive SQGs.

The recommended procedure to follow when EDI is greater than TDI is summarised in Figure 2.

Other issues for future discussion:

- The equations as described do not apply to volatile, organic or non-threshold substances, or substances with multiple relevant exposure pathways (i.e., direct contact, vapour

inhalation, drinking water). The equations would have to be modified and appropriate allocation factors would be determined and included in the equation to address relevant exposure pathways for those substances.

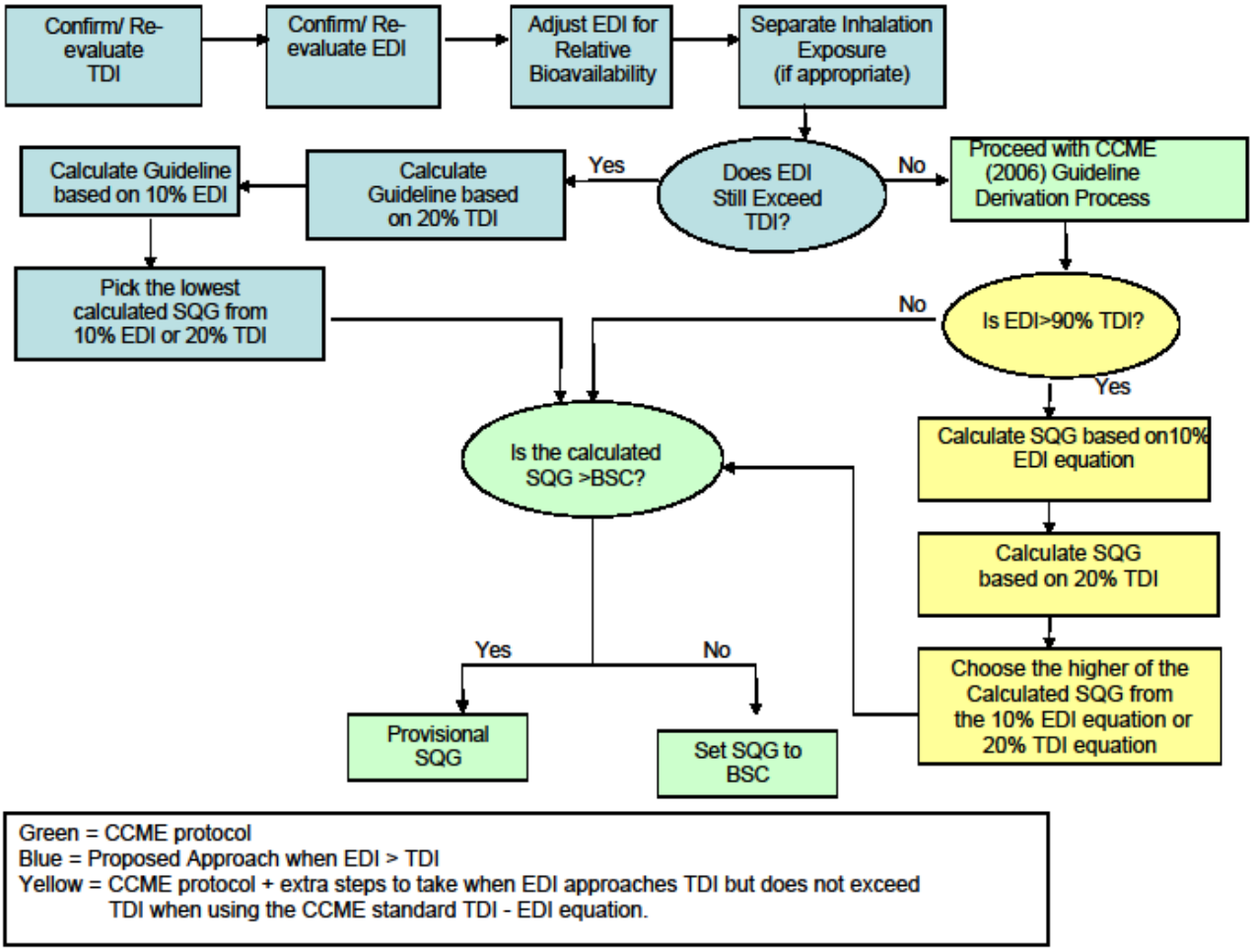

Figure 2: Approach for Deriving Human Health SQGs when EDI > TDI (for direct contact, inorganic threshold substances).

References

CCME, 2006. A Protocol for the derivation of environmental and human health soil quality guidelines. Canadian Council of Ministers of the Environment. Winnipeg, Manitoba. PN 1332

Meridian Environmental Inc. 2006. Development of an approach to deriving Human Health-based soil quality guidelines for non-carcinogenic substances where EDI exceeds TDI. Final Report. Project No 1689. Submitted to Sanya Petrovic, Environmental Health Assessment Services, Healthy Environments and Consumer Safety Branch, Health Canada. Contract No. HECS-SEP-BC/Yukon 05/06-04.

Meridian Environmental Inc. 2007. Supplemental guidance on developing human health soil quality guidelines when the estimated daily intake (EDI) exceeds the tolerable daily intake (TDI). Prepared for Contaminated Sites Division, Safe Environments Programme. Version 1.0 February 2007.

Meridian Environmental Inc. 2008. Evaluation of the effect of soil concentrations on the Estimated Daily Intake for Substances when the Estimated Daily Intake exceeds the Tolerable Daily Intake. Submitted to Mark Richardson, Contaminated Sites Division, Health Canada. Contract No. 4500173802.

Rencz, A.N, R.G. Garrett, S.W. Adcock and G.F. Bonham-Carter. (2006). Geochemical Background in Soil and Till. Geological Survey of Canada Open File 5084. 1 CD-ROM. Available at: http://geopub.nrcan.gc.ca/moreinfo_e.php?id=222148

Sigal, E.A., J.A. Archbold, G.M. Ferguson, C.M. Bacigalupo, D.R.J. Moore and G.M. Richardson. 2006. The development and application of probabilistic methods in the derivation of estimated daily intakes for typical Canadian populations. Presented at the Federal Contaminated Sites National Workshop, March 6-10 2006, Ottawa.

Wilson, R. 2009 pers. comm. Alternate methods to address SQG derivation when the EDI > TDI.