Screening Assessment for the Challenge

Cobalt
(Elemental cobalt)
Chemical Abstracts Service Registry Number
7440-48-4

Cobalt chloride
Chemical Abstracts Service Registry Number
7646-79-9

Sulfuric acid, cobalt (2+) salt (1:1)
(Cobalt sulfate)
Chemical Abstracts Service Registry Number
10124-43-3

Sulfuric acid, cobalt salt
(Cobalt sulfate)
Chemical Abstracts Service Registry Number
10393-49-4

Environment Canada
Health Canada

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Synopsis

Pursuant to section 74 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999), the Ministers of the Environment and of Health have conducted a screening assessment of elemental cobalt, Chemical Abstracts Service Registry Number (CAS RN) 7440-48-4, cobalt chloride, CAS RN 7646-79-9, and cobalt sulfate, CAS RN 10124-43-3 and CAS RN 10393-49-4. The substances elemental cobalt, cobalt chloride and cobalt sulfate (CAS RN 10124-43-3) were identified in the categorization of the Domestic Substances List as high priorities for action under the Challenge. Elemental cobalt and cobalt sulfate (CAS RN 10124-43-3) were considered to pose greatest potential for exposure of individuals in Canada whereas cobalt chloride was considered to pose intermediate potential for exposure. All of these substances are classified by other agencies on the basis of carcinogenicity. These substances all met the ecological categorization criteria for persistence; cobalt chloride and cobalt sulfate also met the categorization criteria for inherent toxicity to aquatic organisms. Therefore this assessment considers both human health and ecological risks.

The substances were assessed together as they generate a common moiety of concern, Co^{2+}, under physiological and environmental conditions, and are thus considered to be toxicologically equivalent. Additionally, measurements of cobalt in environmental media and foods are not able to distinguish between forms of cobalt. However, this assessment does not consider other cobalt substances, which may also contribute to this moiety. To the extent possible, only releases of cobalt related to the three cobalt substances were considered for the ecological assessment. Other anthropogenic sources of the cobalt moiety to the environment were not systematically included.

In 2006, according to domestic information reported under section 71 of CEPA 1999, between 1 000 000 and 10 000 000 kg of elemental cobalt were manufactured,and between 100 000 and 1 000 000 kg of elemental cobalt were imported and used. In 2006, Canadian companies reported the manufacture of between 100 000 and 1 000 000 kg and the import and use of between 10 000 and 100 000 kg of cobalt chloride. Additionally in 2006, submissions for cobalt sulfate reported: (1) the manufacture of between 1 000 000 and 10 000 000 kg for CAS RN 10124-43-3 and 64 400 kg for CAS RN 10393-49-4; (2) the import of between 100 000 and 1 000 000 kg (CAS RN 10124-43-3) and 1 449 700 kg (CAS RN 10393-49-4); (3) the use of between 1 000 000 and 10 000 000 kg (10124-43-3) and 1 462 600 kg (10393-49-4). In 2008, in Canada, the majority of cobalt from cobalt-containing commercial substances was recycled (70%) or was disposed (27%). In Canada, elemental cobalt, cobalt chloride, and cobalt sulfate are primarily used as industrial raw materials; in particular elemental cobalt is commonly used in the production of alloys and carbides with high temperature and wear resistance.

Anthropogenic releases of elemental cobalt, cobalt chloride and cobalt sulfate to the environment are almost entirely due to various industrial activities including base metal production and alloys/superalloys manufacturing. Following release from these sources, the above cobalt substances may enter the aquatic ecosystem. Elemental cobalt, in the form of powders, has a limited capacity for dissolution in water, whereas cobalt chloride

and cobalt sulfate have high water solubility. Therefore these substances will dissolve in contact with moisture once in the aquatic media and will yield a variety of dissolved cobalt species of varying proportions depending on the environmental conditions. Dissolved cobalt has been demonstrated to have a relatively high potential to cause harm to aquatic organisms.

Site-specific exposure scenarios were developed for the major industrial sources of elemental cobalt, cobalt chloride and cobalt sulfate to the environment. Exposure concentrations were predicted near seven industrial facilities that include five nickel/copper/cobalt smelters and refineries, one cobalt alloy manufacturer and one manufacturer of a battery component. Based on a risk quotient analysis, there is likelihood of harm to aquatic organisms resulting from exposure to the total cobalt moiety. However, the specific contribution of the three substances to the total exposure to the dissolved cobalt moiety remains uncertain. It is therefore concluded, at this time, that the three substances are not individually entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends. Elemental cobalt, cobalt chloride and cobalt sulfate meet the criteria for persistence but do not meet the criteria for bioaccumulation potential as set out in the *Persistence and Bioaccumulation Regulations*.

Based on available information on concentrations of total cobalt in environmental media (soil, drinking water, ambient air) and food, as well as results from surveys conducted under section 71 of CEPA 1999, the general population is expected to be exposed primarily to cobalt through diet. The dietary intake of total cobalt by Canadians was found to be similar to that of other developed nations. Adult Canadians are also potentially exposed to cobalt through the use of personal care products reported to contain cobalt chloride.

Based principally on the weight of evidence-based assessments of international or other national agencies, a critical effect for characterization of risk to human health for elemental cobalt, cobalt chloride, and cobalt sulfate is carcinogenicity. Increased incidences of lung tumours were observed in male mice and rats exposed by inhalation to the highest concentration of cobalt sulfate tested, and in female mice and rats at the two highest concentrations of cobalt sulfate tested in a 2-year bioassay. No evidence was available to suggest carcinogenicity via the oral route. *In vitro* and *in vivo* genotoxicity data indicate that elemental cobalt, cobalt choride and cobalt sulfate have the potential to cause DNA and chromosome damage. However, these effects are likely mediated by indirect mechanisms including the generation of reactive oxygen species, increased oxidative stress, and inhibition of DNA repair enzymes. As the tumours observed in experimental animals are unlikely to have resulted from direct interaction with genetic material, a margin of exposure approach is used to assess risk to human health.

The critical effect level for non-cancer effects by the oral route is a conservatively estimated LOAEL of 0.04 mg Co/kg-bw per day based on lethal cardiomyopathy in subjects who consumed large quantities of beer containing cobalt sulfate. The affected

population may have been more sensitive due to dietary insufficiencies and prior cardiac damage from excessive alcohol consumption. As cobalt is known to stimulate red blood cell production, cobalt salts have been used in humans to treat anaemia at doses up to 0.32 mg Co/kg-bw per day for periods of several weeks to several months. There is some evidence for reproductive and developmental toxicity of soluble cobalt (II) salts in rodents, but only at dose levels more than 100 times higher than the lowest effect levels in humans.

The critical effect level for non-cancer effects by inhalation is a LOAEC of 0.0151 mg Co/m^3 in workers exposed to cobalt dust, based on a significantly higher prevalence of eye, nose and throat irritation and cough, and reduced lung function, relative to controls (unexposed workers). These effects were not observed in workers exposed to cobalt dust at 0.0053 mg Co/m^3. The critical effect level in humans is 25 times lower than the lowest concentration at which tumours were observed in rodent bioassays.

The margins between upper-bounding estimates of exposure to cobalt from environmental media, food and consumer products and levels associated with effects are considered adequate to address uncertainties in the health effects and exposure databases. On the basis of the adequacy of the margins between conservative estimates of exposure to cobalt and critical effect levels in humans, it is concluded that cobalt, cobalt chloride and cobalt sulfate are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Based on the information available, it is concluded that elemental cobalt, cobalt chloride and cobalt sulfate do not individually meet any of the criteria set out in section 64 of the *Canadian Environmental Protection Act*, 1999.

The relative importance of the three substances as contributors to the environmental loading and effects of total dissolved cobalt does however warrant further examination. Consequently, it is proposed that these and other substances contributing to the total loadings of the cobalt moiety in the environment be considered in a future moiety-based assessment.

The three substances will be considered for inclusion in the Domestic Substances List inventory update initiative. In addition and where relevant, research and monitoring will support verification of assumptions used during the screening assessment.

Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999) requires the Minister of the Environment and the Minister of Health to conduct screening assessments of substances that have met the categorization criteria set out in the Act to determine whether these substances present or may present a risk to the environment or to human health.

Based on the information obtained through the categorization process, the Ministers identified a number of substances as high priorities for action. These include substances that

- met all of the ecological categorization criteria, including persistence (P), bioaccumulation potential (B) and inherent toxicity to aquatic organisms (iT), and were believed to be in commerce in Canada; and/or
- met the categorization criteria for greatest potential for exposure (GPE) or presented an intermediate potential for exposure (IPE) and had been identified as posing a high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity.

The Ministers therefore published a notice of intent in the *Canada Gazette*, Part I, on December 9, 2006 (Canada 2006), that challenged industry and other interested stakeholders to submit, within specified timelines, specific information that may be used to inform risk assessment, and to develop and benchmark best practices for the risk management and product stewardship of those substances identified as high priorities.

During Categorization, elemental cobalt and cobalt sulfate (CAS RN 10124-43-3) were identified as high priorities for assessment of human health risk because they were considered to present GPE; cobalt chloride was considered to present IPE and had been classified by other agencies on the basis of carcinogenicity. While not initially listed in the Challenge, sulfuric acid, cobalt salt (CAS RN 10393-49-4) was identified as an alternate registry number for cobalt sulfate. As cobalt sulfate (CAS RN 10124-43-3) was identified as a high priority for assessment of human health risk, information on both registry numbers was requested from stakeholders. The Challenge to stakeholders for these substances was published in the Canada Gazette on June 20, 2009 (Canada 2009a, 2009b). Substance profiles were released at the same time. The substance profiles, except for CAS RN 10393-49-4, presented the technical information available prior to December 2005 that formed the basis for categorization of these substances. As a result of the Challenge, submissions of information pertaining to the substance were received (Environment Canada 2010a).

In solution, cobalt (II) salts including cobalt chloride and cobalt sulfate are considered to be toxicologically equivalent, as they generate a common moiety of concern, Co^{2+}. Elemental cobalt may also be oxidized under physiological and environmental conditions to produce Co^{2+} cations. Additionally, measurement methods of cobalt in environmental

media and foods do not usually distinguish between forms of cobalt. Therefore, these substances were considered together in this assessment. It must be noted, however, that some parts of the ecological exposure and risk characterization have not accounted for other cobalt substances that may contribute to exposure to this moiety of concern. Exposure of humans to cobalt from environmental sources was based on total cobalt, however exposure from cobalt present in consumer products only addressed the products that were notified to Health Canada as containing elemental, chloride and sulfate forms.

Although cobalt, cobalt chloride and cobalt sulfate were determined to be high priorities for assessment with respect to human health, they all met the ecological categorization criteria for persistence, and cobalt chloride and cobalt sulfate also met the categorization criteria for inherent toxicity to aquatic organisms. Therefore this assessment considers both human health and ecological risks.

Screening assessments focus on information critical to determining whether a substance meets the criteria as set out in section 64 of CEPA 1999. Screening assessments examine scientific information and develop conclusions by incorporating a weight-of-evidence approach and precaution.[1]

This final screening assessment includes consideration of information on chemical properties, hazards, uses and exposure, including the additional information submitted under the Challenge. Data relevant to the screening assessment of this substance were identified in original literature, review and assessment documents, stakeholder research reports and from recent literature searches, up to February 2010 for the ecological assessment and up to April 2010 for the human health assessment. Key studies were critically evaluated; modelling results may have been used to reach conclusions.

Evaluation of risk to human health involves consideration of data relevant to estimation of exposure (non-occupational) of the general population, as well as information on health hazards (based principally on the weight of evidence assessments of other agencies that were used for prioritization the substance). Decisions for human health are based on the nature of the critical effect and/or margins between conservative effect levels and estimates of exposure, taking into account confidence in the completeness of the identified databases on both exposure and effects, within a screening context. The final screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents a summary of the critical information upon which the conclusion is based.

[1] A determination of whether one or more of the criteria of section 64 are met is based upon an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and the use of consumer products. A conclusion under CEPA 1999 on the substances in the Chemicals Management Plan (CMP) Challenge Batches 1-12 is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the *Controlled Products Regulations*, which is part of the regulatory framework for the Workplace Hazardous Materials Information System [WHMIS] for products intended for workplace use.

This final screening assessment was prepared by staff in the Existing Substances Programs at Health Canada and Environment Canada and incorporates input from other programs within these departments. The ecological and human health portions of this assessment have undergone external written peer review/consultation. Comments on the technical portions relevant to human health were received from Dr. Bernard Gadagbui, Toxicology Excellence for Risk Assessment; Dr. Pam Williams, E Risk Sciences; and Dr. John Christopher, CA OEHA. Additionally, the draft of this screening assessment was subject to a 60-day public comment period. While external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Health Canada and Environment Canada. Approaches used in the screening assessments under the Challenge have been reviewed by an independent Challenge Advisory Panel.

The critical information and considerations upon which the final assessment is based are summarized below.

Substance Identity

Substance name

For the purposes of this document, the substances will be referred to as elemental (zero valence) cobalt, cobalt chloride and cobalt sulfate. The latter applies to both cobalt sulfate and sulfuric acid, cobalt salt because the CAS RN of the latter is an Alternate Chemical Abstracts Registry Number for the former. An alternate CAS RN is a second Registry Number generated for a second structural representation of a substance. Substances with more than one Registry Number will have a Primary RN, denoted RN, and any Alternate Registry Numbers are located in the AR field in records obtained from the Chemical Abstracts Services STN database (CAS 2010, STN 2010). The Primary RN for cobalt sulfate is CAS RN 10124-43-3 while CAS RN 10393-49-4 is an Alternate Registry Number for this substance. In this document, cobalt sulfate refers to both CAS RN 10124-43-3 and CAS RN 10393-49-4: therefore three substances rather than four are mentioned. Details on the identities of all four CAS RN are provided in Tables 1a-d.

Table 1a. Substance identity for elemental cobalt

Chemical Abstracts Service Registry Number (CAS RN)	**7440-48-4**
DSL name	**Cobalt**
National Chemical Inventories (NCI) names[1]	*Cobalt (English, French, German) (TSCA, REACH, EINECS, AICS, ECL, SWISS, PICCS, ASIA-PAC, NZIoC)* *KOBALT (German) (SWISS)*
Other names	*ACO 4, C.I. 77320, Co 0138E, Cobalt element* *Cobalt-59, N 354Di, R 401, R 401 (metal)* *UN 3178*
Chemical group (DSL Stream)	Discrete inorganics
Major chemical class or use	Cobalt-containing inorganic compounds
Major chemical sub-class	Metals (zero valence state)
Chemical formula	Co
Chemical structure	n/a
SMILES[2]	Co
Molecular mass	58.9 g/mol

[1] National Chemical Inventories (NCI). 2007: AICS (Australian Inventory of Chemical Substances); ASIA-PAC (Asia-Pacific Substances Lists); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Commercial Chemical Substances); ELINCS (European List of Notified Chemical Substances); ENCS (Japanese Existing and New Chemical Substances); PICCS (Philippine Inventory of Chemicals and Chemical Substances); and TSCA (Toxic Substances Control Act Chemical Substance Inventory).

[2] Simplified Molecular Input Line Entry System

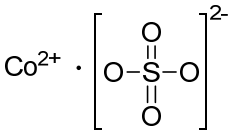
Table 1b. Substance identity for cobalt chloride

Chemical Abstracts Service Registry Number (CAS RN)	**7646-79-9**
DSL name	**Cobalt chloride**
National Chemical Inventories (NCI) names[1]	*Cobalt chloride (CoCl2)* (TSCA, AICS, SWISS, PICCS, ASIA-PAC, NZIoC) *cobalt dichloride* (REACH, EINECS, ECL) *Cobalt chloride* (ENCS, PICCS) *KOBALT(II)-CHLORID (German) (SWISS)* *COBALTOUS CHLORIDE* (PICCS) *COBALT (II) CHLORIDE* (PICCS)
Other names	*Cobalt dichloride (CoCl2), Cobalt(2+) chloride* *Cobalt(II) chloride, Cobaltous dichloride* *Dichlorocobalt, NSC 51149*
Chemical group (DSL Stream)	Discrete inorganics
Major chemical class or use	Cobalt-containing inorganic compounds
Major chemical sub-class	Chlorides
Chemical formula	$CoCl_2$
Chemical structure	Co^{2+} $[Cl^-]_2$
SMILES[2]	Cl[Co]Cl
Molecular mass	129.8 g/mol

[1] National Chemical Inventories (NCI). 2007: AICS (Australian Inventory of Chemical Substances); ASIA-PAC (Asia-Pacific Substances Lists); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Commercial Chemical Substances); ELINCS (European List of Notified Chemical Substances); ENCS (Japanese Existing and New Chemical Substances); PICCS (Philippine Inventory of Chemicals and Chemical Substances); and TSCA (Toxic Substances Control Act Chemical Substance Inventory).

[2] Simplified Molecular Input Line Entry System

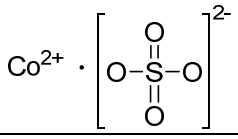
Table 1c. Substance identity for cobalt sulfate

Chemical Abstracts Service Registry Number (CAS RN)	**10124-43-3**
DSL name	**Cobalt sulfate**
National Chemical Inventories (NCI) names[1]	*Sulfuric acid, cobalt(2+) salt (1:1)* (TSCA, AICS, PICCS, ASIA-PAC, NZIoC) *cobalt sulfate* (REACH, EINECS) *Cobalt sulfate* (ENCS, ECL, PICCS) *COBALT (II) SULFATE* (PICCS) *COBALTOUS SULFATE* (PICCS)
Other names	*Cobalt monosulfate* *Cobalt sulfate (1:1)* *Cobalt sulfate (CoSO4)* *Cobalt(2+) sulfate* *Cobalt(II) sulfate* *Sulfuric acid, cobalt (2+) salt*
Chemical group (DSL Stream)	Discrete inorganics
Major chemical class or use	Cobalt-containing inorganic compounds
Major chemical sub-class	Sulfates
Chemical formula	$CoSO_4$
Chemical structure	
SMILES[2]	O1S(=O)(=O)O[Co]1
Molecular mass	155.0 g/mol

[1] National Chemical Inventories (NCI). 2007: AICS (Australian Inventory of Chemical Substances); ASIA-PAC (Asia-Pacific Substances Lists); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Commercial Chemical Substances); ELINCS (European List of Notified Chemical Substances); ENCS (Japanese Existing and New Chemical Substances); PICCS (Philippine Inventory of Chemicals and Chemical Substances); and TSCA (Toxic Substances Control Act Chemical Substance Inventory).

[2] Simplified Molecular Input Line Entry System

Table 1d. Substance identity for Sulfuric acid, cobalt salt (cobalt sulfate).

Chemical Abstracts Service Registry Number (CAS RN)	**10393-49-4**
DSL name	**Sulfuric acid, cobalt salt**
National Chemical Inventories (NCI) names[1]	*n/a*[2]
Other names	*Cobalt sulfate*
Chemical group (DSL Stream)	Discrete inorganics
Major chemical class or use	Cobalt-containing inorganic compounds
Major chemical sub-class	Sulfates
Chemical formula	Co.xH2O4S
Chemical structure	
SMILES[3]	Not applicable
Molecular mass	*n/a*

[1] National Chemical Inventories (NCI). 2007: AICS (Australian Inventory of Chemical Substances); ASIA-PAC (Asia-Pacific Substances Lists); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Commercial Chemical Substances); ELINCS (European List of Notified Chemical Substances); ENCS (Japanese Existing and New Chemical Substances); PICCS (Philippine Inventory of Chemicals and Chemical Substances); and TSCA (Toxic Substances Control Act Chemical Substance Inventory).

2- Information Not Available

[3] Simplified Molecular Input Line Entry System

Physical and Chemical Properties

Table 2 contains experimental physical and chemical properties of elemental cobalt, cobalt chloride and cobalt sulfate (CAS RN 10124-43-3) that are relevant to their environmental fate and that of the cobalt ions they release upon dissolution. Physical and chemical properties for CAS RN 10393-49-4 were not available but are expected to be comparable to the properties of cobalt sulfate CAS RN 10124-43-3. The dissociation constants (pK_a, pK_b) and the partition coefficients between octanol and water (Log K_{ow}) and between organic carbon and water (Log K_{oc}) are not relevant to the environmental fate of the substances assessed and so are not presented nor considered.

Table 2. Physical and chemical properties for elemental cobalt, cobalt chloride and cobalt sulfate (CAS RN 10124-43-3)

Substance	Type	Value	Temperature (°C)	Reference
Physical state				
Elemental cobalt	Experimental	Solid	Ambient	ATSDR 2004
Cobalt chloride	Experimental	Solid	Ambient	ATSDR 2004
Cobalt sulfate	Experimental	Solid	Ambient	ATSDR 2004
Melting point (ºC)				
Elemental cobalt	Experimental	1495	-	Lide 2009-2010
Cobalt chloride	Experimental	724-737	-	ATSDR 2004; Lide 2009-2010
Cobalt sulfate	Experimental	Decomposes at 735	-	ATSDR 2004
Boiling point (ºC)				
Elemental cobalt	Experimental	2870-2927	-	ATSDR 2004; Lide 2009-2010
Cobalt chloride	Experimental	1049	-	ATSDR 2004
Cobalt sulfate	-	Not available	-	-
Density (kg/m^3)				

Substance	Type	Value	Temperature (°C)	Reference
Elemental cobalt	Experimental	8860	20	Lide 2009-2010
Cobalt chloride	Experimental	3356	36	ATSDR 2004
Cobalt sulfate	Experimental	3710	Not available	ATSDR 2004
Vapour pressure (Pa)				
Elemental cobalt	Experimental	133.3 (1 mm Hg)	1 910	ATSDR 2004
	Extrapolated to ~20 (°C) from experimental	Likely negligible[2]	~20	-
Cobalt chloride	Experimental	10 000 (75 mm Hg)	818	Lide 2007-2008
	Extrapolated to ~20 (°C) from experimental	Likely low to negligible[2]	~20	-
Cobalt sulfate	-	Likely negligible	-	-
Henry's Law constant (Pa·m^3/mol)				
Elemental cobalt	-	Likely negligible	-	-
Cobalt chloride	-	Likely negligible	-	-
Cobalt sulfate	-	Likely negligible	-	-
Water solubility (g/L)				
Elemental cobalt	Experimental	insoluble	-	ATSDR 2004; IPCS 2006
Cobalt chloride	Experimental	450	7	ATSDR 2004
		530	20	Dean 2004
		562	25	Lide 2007-2008

Substance	Type	Value	Temperature (°C)	Reference
Cobalt sulfate	Experimental	362	20	IPCS 2006
		383	25	Lide 2007-2008
Capacity for dissolution after 7 days generated using the Transformation Dissolution protocol (mg/L)[3]				
Elemental cobalt (powdered form - SSA[4]= 0.127m^2/g)	Experimental	0.3 (1 mg/L loading)	**20-25**	**CDI 2010a**
		2.44 (10 mg/L loading)		
		10.96 (100 mg/L loading)		
Elemental cobalt (powdered form - SSA[4]= 0.36m^2/g)	Experimental	0.55 (1 mg/L loading)	**20-25**	
		2.4 (10 mg/L loading)		
		10.67 (100 mg/L loading)		
Elemental cobalt (powdered form - SSA[4]= 0.65m^2/g)	Experimental	0.71 (1 mg/L loading)	**20-25**	
		3.29 (10 mg/L loading)		
		12.78 (100 mg/L loading)		
Log K_{sw}(Partition coefficient soil-water)[1] (L/kg)				

Substance	Type	Value	Temperature (°C)	Reference
Dissolved forms of cobalt	Experimental	0.41–3.49 Median = 2.99[5]	-	Allison and Allison 2005[6]; Buchter et al 1989[7]; Harvey et al 2007; Sheppard et al 2007 ; Thibeault et al 1990[8]; Watmough et al. 2005[9], Yasuda et al. 1995[10]
Log K_{sdw} (Partition coefficient sediment-water)[1] (L/kg)				
Dissolved forms of cobalt	Experimental	2.92-3.48 Median = 3.20[11]	-	Allison and Allison 2005[12]; Davis et al. 1996[13]
Log K_{spw} (Partition coefficient suspended particles-water)[1] (L/kg)				
Dissolved forms of cobalt	Experimental	4.18-5.83 Median = 5.33[14]	-	Allison and Allison 2005[15]; Chiffoleau et al. 1994[16] Gobeil et al. 2005[17]; Lofts and Tipping 2000[18]; Nguyen et al. 2005[19]; Rondeau et al 2005[20]

[1] Partition coefficients measured for dissolved cobalt (Co–containing species).
[2] Professional judgment was used to extrapolate a vapour pressure from the elevated temperature experimental value, based on the tendency of vapour pressure to decrease with a temperature decrease.
[3] As measured by the Transformation Dissolution Protocol, method (OECD 29) (OECD 2001) which is a measure of potential for reactivity of the metal-containing substance to attain a limiting concentration under a set of standard laboratory conditions representative of those generally occurring in the aquatic environment.
[4] Specific Surface Area
[5] Log K_{sw} is the median of the geometric mean of the various K_{sw} coefficients reported in each reference.
[6] Log K_{sw} (2.1) calculated using the average of 11 partitioning coefficient values from a literature search (Allison and Allison 2005).
[7] Retention study conducted on 15 elements for 11 U.S soils of various horizon and taxonomic classifications to determine the effects of element and soil properties on Log K_{sw}. Soils of variable pH (3.9-8.5), % TOC (0.21-11.6), sum of cations exchange capacity (0.8-30.2 cmol/kg), sand % (5.9-90.2 %), silt % (6.0-89.4%) and clay % (0.5-54.7%) (Buchter et al. 1989).
[8] Study not obtained.

[9] The linear regression of cobalt:Log K_{sw} in soils against soil pH (Log K_{sw}Co = 0.54±0.05pH + 0.69±0.29) based on 46 forest soil samples (pH = 3.9 – 8.1) collected at the border the Precambrien Shield in central Ontario was used to calculate a representative Co logK_{sw} in forest soils (Watmough et al. 2005). Using a representative pH for forest ecosystem typical of Canadian forests (geometric mean pH = 4.58, n=37, Mead and Comforth 1995) yields a Log K_{sw} for Co of 3.16.

[10] Log K_{sw} determined for five radionuclide (^{54}Mn, ^{60}Co, ^{65}Zn, ^{85}Sr, ^{137}Cd) using a batch technique for 36 agricultural soils samples (paddy and upland soils) collected in Japan. Soils samples had different pH (2.98-7.43), CEC (14-390 mmol/kg), total Ca (14-714 mmol/kg), total K (19-545 mmol/kg), Fe (281-2006 mmol/kg), Al (2405-4418 mmol/kg), NH_4-pr (0.39-9.44 L/kg), C (0.7-102.1 g/kg), N (0.1-7.2 g/kg) (Yasuda et al 1995).

[11] Log K_{sdw} equals to the median of 2.924 (Davis et al 1996) and 3.48 (Allison and Allison 2005).

[12] This value represents the mean of the soil-Kd linear regression equation (lognormal assumed).

[13] Log K_{sdw} calculated by dividing cobalt concentration (4.2 mg/L) from bulk sediment core samples with dissolved cobalt concentration (<0.012 mg/L) from a filtered surface water sample collected within 1m of the sediment (Davis et al 1996). Samples collected at the Industriplex Superfund Site in the Aberjona watershed (U.S.). The surface water cobalt concentration value of 0.012 mg/L was used as a worst-case scenario.

[14] This value is the median of Log K_{sw} coefficient reported in each reference

[15] This Log K_{spw} (4.8) represents the average of 20 partitioning coefficient values from a literature search (Allison and Allison 2005).

[16] Partition coefficient (Log K_{spw} = 4.18) calculated using the average particulate matter cobalt concentrations with dissolved cobalt concentrations measured in freshwaters of the Seine estuary (France) (Chiffoleau et al 1994).

[17] Log K_{spw} calculated by dividing the mean of cobalt concentration (17.8 mg/kg) measured in particulate matter from water samples (n=6) by dissolved cobalt concentration (6.2 x 10^{-5} mg/L) from filtered surface water samples (n=6) collected in the St-Lawrence river (Levy, QC) (Gobeil et al. 2005).

[18] Log K_{spw} were calculated from surface water samples collected at four tributaries from the Humber river catchment, namely the Upper Swale river (log Kspw 3.64-4.76; n=26), the Nidd river (Log K_{spw} 4.28-5.22; n=12), the Swale river (Log K_{spw} 4.50-5.68; n=7) and the Trent River (Log K_{spw} 3.83-4.99; n=29) (Lofts and Tipping 2000).

[19] Log K_{spw} calculated from surface water samples collected at 19 sampling stations located in Lake Balaton (Hungary) during two main expeditions in June 2000 (Log K_{spw} = 4.9-5.5) and September 2001 (K_{spw} = 4.5-5.5) (Nguyen et al. 2005).

[20] Log K_{spw} calculated from surface water samples collected in the upper St. Lawrence (Cornwall, log K_{spw} =5.12), the north-shore tributaries (Ottawa, Log K_{spw} = 5.60; and St.Maurice, Log K_{spw}=5.22) and the south-shore tributaries (Richelieu, Log K_{spw}=5.35; St Francois, log K_{spw}=5.24; Yamaska, Log K_{spw} =5.04; and Nicolet, Log K_{spw}=5.27) using the mean dissolved cobalt concentration and the mean of particulate cobalt concentration for each site (Rondeau et al. 2005).

Sources

Natural Sources

Cobalt is a naturally occurring element in the terrestrial crust. Cobalt concentrations in the upper continental crust have been determined to average about 25 ppm and to range between 0.1 and 110 ppm (Reimann and de Caritat 1998). Cobalt is not known to naturally exist in its elemental (metallic) form; naturally occurring cobalt is comprised of various mineral, oxide and salt forms; sources include wind blown continental dusts, weathering of rocks, seawater spray, forest fires and volcanoes (IPCS 2006).

Natural emissions to the atmosphere have been estimated to range between 690 and 11 000 tonnes of cobalt per year globally (Nriagu 1989). Atmospheric fall-out and introduction of cobalt into surface water and soil as a result of natural weathering and erosion processes are reflected in the geochemical background levels in these media. These background levels are considered as needed when estimating the exposure of ecological receptors to cobalt substances in the characterization of ecological risk section of this assessment.

Anthropogenic Sources

Anthropogenic sources of cobalt include burning of fossil fuels (primarily oxides), wastewater biosolids, phosphate fertilizers, mining and smelting of cobalt containing ores and industrial processes that use cobalt compounds (Hodge and Dominey 2001, IPCS 2006).

Table 3 presents information on the quantities of elemental cobalt, cobalt chloride and cobalt sulfate that are used, imported or manufactured in Canada, based on the survey submissions received in response to the notice published under section 71 of CEPA 1999 (Canada 2009b). It should be noted that the term “manufacture” as defined in the section 71 notice includes the incidental production of a substance at any level of concentration as a result of the manufacturing, processing or use of other substances, mixtures, or products.

Table 3. Quantities of cobalt, cobalt chloride and cobalt sulfate manufactured, imported and used in Canada for the year 2006, according to the section 71 survey under CEPA 1999 (Environment Canada 2010a)

Substance	CAS RN	Quantity reported for 2006 (kg)		
		Manufactured	Imported	Used
Elemental Cobalt	7440-48-4	1 000 000 - 10 000 000	100 000 - 1 000 000	100 000 - 1 000 000
Cobalt chloride	7646-79-9	100 000 - 1 000 000	10 000 - 100 000	10 000 – 100 000
Cobalt sulfate	10124-43-3	1 000 000 - 10 000 000	100 000 - 1 000 000	1 000 000 - 10 000 000
	10393-49-4	64 400	1 449 700	1 462 600

It should be noted that products containing cobalt, cobalt chloride or cobalt sulfate may enter Canada even if they are not identified as such in the section 71 survey because they may be imported unknowingly in manufactured items, or in quantities below the 100 kg reporting threshold for the survey. Although there was information received in response to the section 71 survey indicating that these substances were imported in 2006 as components of manufactured items, available information is currently not sufficient to derive a quantitative estimate of the importance of this source. It is recognized that cobalt, cobalt chloride or cobalt sulfate contained in manufactured items that are disposed of in landfill may have a potential to leach out into groundwater, surface water and/or soil, depending on the presence at the landfill of a liner, a leachate collection system and/or a leachate treatment system (on-site or off-site).

Historically, based on DSL nomination information (Environment Canada 1988), the total quantity of elemental cobalt and cobalt sulfate reported to be manufactured, imported or in commerce in Canada during 1986 was greater than 10 000 000 kg for each substance whereas the cobalt chloride quantity was reported to be between 100 000 and 1 000 000 kg.

Cobalt Production (Mining and Recycling)

Cobalt is rarely the exclusive metal isolated from a mine but rather it is an additional product of either copper or nickel mining (BGS 2009). Canada became a major producer of cobalt from 1952 – 1955 after the introduction of a method to isolate cobalt from nickel ores in 1940 by the International Nickel Company. A total of 2899 tonnes of cobalt was mined in Canada in 2006. 341 tonnes were extracted from Québec, 1368 tonnes from Ontario, 721 tonnes from Newfoundland and Labrador and 469 tonnes from Manitoba (Statistics Canada 2008). Cobalt is generally found with nickel and copper deposits. Mining areas include the Sudbury district, Northern Quebec (100 km South of

Deception Bay) and Thompson, Manitoba (Natural Resources Canada and Statistics Canada 2003). Canada has produced cobalt since 1905 and contributes approximately 20% of total world production (Nagpal 2004).

In Canada, cobalt is refined from sulfide ores (Natural Resources Canada and Statistics Canada 2003). The refining process includes milling, separation by flotation and roasting to form oxide or sulfate forms. Water is then added to the matte and the metal is precipitated with a basic solution and then dissolved in sulfuric acid. The resulting cobalt sulfate is more concentrated and only needs electrolysis to form elemental cobalt (ATSDR 2004; Hatch 2000).

Two important steps are required to produce elemental cobalt. The cobalt separation step divides cobalt ore minerals from nickel and copper compounds. Next, the conversion or reduction step transforms cobalt compounds into elemental cobalt. Those two steps do not always take place in the same facility.

Cobalt chloride and cobalt sulfate are prepared by the reaction of hydrochloric acid and sulfuric acid, respectively with elemental cobalt, cobalt hydroxide, carbonate and various oxides; very high purity chloride and sulfate salts are prepared electrolytically (Richardson 2003).

Cobalt is also obtained from recycled scrap metal in Canada (Environment Canada 2010a). It can also be obtained from recycled batteries (Environment Canada 2010b).

Many section 71 submissions indicated that unintentional "manufacture" of elemental cobalt, cobalt chloride and/or cobalt sulfate occurs. For example, some pulp and paper mills are feeding furnaces with wood residues. Bark and wood pulp waste include cobalt traces that are released when wood residues are burned for energy recovery (USEPA 1998). They reported releases of elemental cobalt from air stacks (Environment Canada 2009), although, when considering combustion conditions, cobalt oxide, cobalt hydroxide and cobalt sulfate releases are possible (Pavageau 2004). Zinc smelters also reported releases of cobalt but in a waste mixture. The composition and the proportions of the cobalt species in this mixture are unknown. Because they cannot be specifically linked to the cobalt substances that are the subject of this assessment, these types of unintentional production will not be further considered in this assessment.

Uses

There are a few applications of elemental cobalt; it is predominantly used as a component in alloys and carbides for applications requiring high strength and temperature resistance (Donaldson and Beyersmann 2005). The alloys and carbides produced have their own CAS RN, therefore elemental cobalt as CAS RN 7440-48-4, primarily used in industrial processes associated with these manufacture activities, will not be found in the resulting consumer products. Anhydrous cobalt chloride is commonly used as an indicator in desiccants (Richardson 2003). Cobalt sulfate is the most inexpensive form of ionic cobalt and is used in the electroplating industry and agriculturally as a feed supplement and

fertilizer (Natural Resources Canada and Statistics Canada 2003; Richardson 2003). Cobalt chloride or sulfate may also be used as the cobalt source in storage batteries, porcelain pigments, glazes and ink driers (Richardson 2003). While the chloride and sulfate salts may be the source of cobalt for applications such as pigments, glazes, and batteries generally the salt is thermally decomposed or calcined (CDI 2010b); therefore cobalt sulfate and chloride will not be present in the final product.

Elemental cobalt uses reported under the section 71 survey of CEPA 1999 include colourant/pigment/stain/dye/ink, paint and coating, chemical and alloy production, metallurgy, manufactured automotive parts, formulation component, water/waste treatment chemical, and copper refining (Environment Canada 2010a). According to the same source, cobalt may be present as a trace in raw materials used for the production of cement.

Table 4 shows an estimate of the uses of the three cobalt substances of interest in this assessment by industrial sector as reported by the Cobalt Development Institute for 2008.

Table 4. World-wide cobalt uses estimated by the Cobalt Development Institute for 2008 (CDI 2009a) for elemental cobalt, cobalt chloride and cobalt sulfate.

Use	Estimated % of the world market	Cobalt substances used for manufacture			
		Elemental	Chloride	Sulfate	Other cobalt compounds
Batteries	27	x	x	-	x
Super alloys	19	x	-	-	x
Hard Material Tools	14	x	-	-	x
Colours – Glass, enamels, plastics, ceramics, artists colours, fabrics	10	-	-	x	x
Catalysts	9	-	x	x	x
Magnets	7	x	-	-	x
Tire Adhesives, Soaps, Driers for paint and dyes	6	-	-	-	x
Other Alloys	4	x	-	-	x
Feedstuffs and others uses	4	-	-	x	-

Use in the Production of Superalloys, Alloys and Magnets

Elemental cobalt in superalloys brings magnetism and resistance to abrasive and corrosive wear (ATSDR 2004). Magnetic superalloys are made with cobalt, nickel and iron. Magnets are produced by heating cobalt alloys at high temperatures. Elemental cobalt keeps its magnetic properties up to 1131˚C (Curie point) whereas elemental nickel or iron lose theirs at lower temperatures (CRC 1965). Alloys containing cobalt, chromium and tungsten are generally used for high performance cutting tools (IPCS

2006). Automobile manufacturers use cobalt alloys for certain motor parts and as a component of electric vehicle batteries. There is a high probability that the latter use will increase in importance in the future (CDI 2006a).

Use in Battery Manufacturing

Cobalt is used in three types of batteries. In the UK, cobalt is known to be used in nickel/cadmium (Ni/Cd) batteries where it enhances performance when added to the formulation in amounts between 1 and 5% w/w (CDI 2006a). Nickel-metal hydride (Ni/MH) batteries are composed of up to 15% cobalt w/w. Cobalt oxide and hydroxide are used in both Ni/Cd and Ni/MH batteries, and the manufacture of these cobalt compounds may originate from elemental cobalt (CDI 2006a). New Ni/Cd batteries and Ni/MH batteries may be used for electric cars. Lithium-ion batteries contain cathodes that are made of up to 50% cobalt by weight (CDI 2006a). They are made of $LiCoO_2$ which is formulated from different forms of cobalt (CDI 2006a). The lithium-ion batteries are the most advanced of the three and their sales are increasing given their use in electronic devices such as cellular phones and laptops. Between 1999 and 2009, the rechargeable battery (mostly lithium-ion) market value doubled (CDI 2008a).

Desiccant/Catalyst

According to information submitted under the section 71 survey, cobalt chloride is generally used in silica gel desiccants as a colour indicator. Cobalt chloride and cobalt sulfate are used as oxygen scavengers in industrial water systems to prevent corrosion (Environment Canada 2010a).

Magnetic tapes

An important use of elemental cobalt was in magnetic recording tape a few years ago (Environment Canada 1988), but this use is now negligible in Canada. Music sales in cassette tape format totalled $231 378 000 in 1993 but decreased to $93 000 in 2007 (Statistics Canada 2000, Statistics Canada 2007).

Food-related Uses

Cobalt chloride and cobalt sulfate were previously permitted food additives for use as an antigushing and foam stabilizing agent in malt liquors under the Food and Drug Regulations. In 1966, they were delisted as approved food additives and therefore are no longer permitted for use as food additives in foods offered for sale in Canada. (2010 email from Food Directorate, Health Canada to Risk Management Bureau, Health Canada, unreferenced) Cobalt, cobalt chloride and cobalt sulfate were not identified for use in food packaging applications. According to information submitted under the section 71 survey, cobalt sulfate is also used industrially as a corrosion inhibitor in boiler water (Environment Canada 2010a). The uses of cobalt chloride, sulfate and their hydrates as catalysts in boiler water additives to eliminate free reactive oxygen in boiler water systems do not present a source of exposure to the general population, since these

substances have high boiling points, there will be no transfer to steam and therefore no contact with food (2009 and 2010 emails from Food Directorate, Health Canada to Risk Management Bureau, Health Canada, unreferenced).

Cobalt sulfate monohydrate and heptahydrate are added to most agricultural feeds at low levels, typically 0.1 – 10 ppm, most commonly at the lower end of this range (2010 email from Canadian Food Inspection Agency to Risk Management Bureau, unreferenced). Cobalt is added to feed because it is an essential nutrient for ruminants; cobalt deficiency in ruminants creates symptoms similar to general malnutrition (Greiner et al. 2003). General population exposure to cobalt via these agricultural uses is captured in the estimation of daily intake from food.

Medical and Personal Care Uses

Cobalt is listed as a medicinal ingredient in the Natural Health Products Ingredients Database (NHPID), and classified as a NHP under schedule 1, item 7 (a mineral) of the Natural Health Products Regulations (NHPID 2010). Cobalt is a component of Vitamin B12 (Health Canada 2007; NHPID 2010). Because the cobalt in Vitamin B12 does not exchange with free cobalt, releases of elemental cobalt, cobalt chloride or cobalt sulfate are considered negligible. Cobalt is listed in the Licensed Natural Health Products Database (LNHPD) in products used for oligotherapy and homeopathy applications (LNHPD 2010). Because of limited information on the use patterns of these products, quantitative estimates of exposure were not derived. Cobalt chloride and cobalt sulfate are not listed in the NHPID nor the LNHPD as medicinal ingredients or non-medicinal ingredients permitted in natural health products (LNHPD 2010; NHPID 2010).

Cobalt chloride is listed in the Drug Products Database (DPD) as a medicinal ingredient in an allergy patch test for humans (DPD 2009; 2010 email from Therapeutic Products Directorate, Health Canada to Risk Management Bureau, unreferenced). Since allergy tests are conducted infrequently and the amount of cobalt chloride per patch is only 16 micrograms, the allergy patch is not considered a significant source of exposure to the general population (2010 email from Therapeutic Products Directorate, Health Canada to Risk Management Bureau, Health Canada, unreferenced). Cobalt chloride is also listed in the DPD as a medicinal ingredient in veterinary products. Cobalt sulfate is listed in the DPD as a medicinal ingredient present in veterinary products, but not for drugs used in humans (DPD 2009). The hydrates of cobalt chloride and cobalt sulfate are not listed in the DPD or the Therapeutic Product Directorate's internal Non-Medicinal Ingredients Database as medicinal ingredients or non-medicinal ingredients present in pharmaceutical drugs or veterinary products (DPD 2009).

Cobalt alloys, used in medical and dental implants, which are subject to pre-market review as per the Food and Drugs Act and the Medical Devices Regulations (Canada 2009c,d), are not assessed in this document.

Elemental cobalt is listed as an ingredient in one antiwrinkle mask and one temporary tattoo product; cobalt chloride is listed as an ingredient in 9 products used for skin

moisturizing and cleansing, hair grooming and waving preparations (CNS 2009). Elemental cobalt, cobalt chloride and cobalt sulfate are not listed on Health Canada's Cosmetic Ingredient Hotlist (Health Canada 2009a).

Releases to the Environment

The releases of cobalt to the environment depend upon various losses of the substances resulting from their manufacture, industrial uses, and/or consumer/commercial uses. These losses can be grouped into seven types: (1) discharge to wastewater; (2) emission to air; (3) loss to land; (4) chemical transformation; (5) disposal to landfill; (6) disposal by recycling; and (7) disposal by incineration. They are estimated based on regulatory survey data, industry data and data published by different organizations.

The National Pollutant Release Inventory (NPRI) data are not form-specific and therefore, represent all forms of cobalt (Environment Canada 2008). Between 1995 and 2007, on-site releases decreased from approximately 20 000 kg (15%) to 12 000 kg (2%) of the total losses and transfers reported, while quantities sent to disposal increased from approximately 18 000 kg (15%) to 144 000 kg (25%). Off-site recycling was the most significant removal pathway corresponding to approximately 124 000 kg (70%) and 570 000 kg (73%) of the annual total in 1995 and 2007 respectiveley. In this assessment, NPRI data were used only when industrial processes were assumed to be releasing mainly the substances being assessed in this document. Additional information pertinent to releases from industry is presented below.

Emission estimates based on late 1970's data indicate that anthropogenic sources of cobalt accounted for 24% and 14.6% of the total input (atmospheric fallout and wastewater) to two of the Great Lakes, Lake Huron and Lake Superior, indicating that natural inputs exceeded anthropogenic ones in this area (Smith and Carson 1981). Similarly, cobalt levels measured in sediment cores from Upper St-Lawrence River estuary do not decrease with depth, suggesting that recent anthropogenic releases in the St. Lawrence basin may not be significant (Coakley 1993 in IPCS 2006). More recent studies conducted in Europe suggest that anthropogenic activities exceed natural inputs as sources of cobalt to the atmosphere (Van de Velde et al. 1999; Barbant et al. 2004). Coal and fuel combustion were identified in one of these studies as being the main anthropogenic sources of cobalt in Western Europe. Regarding the specific cobalt compounds that are the subject of this assessment, local anthropogenic contamination (i.e. releases close to point sources) may be important.

For this assessment, releases associated with the following parts of the cobalt lifecycle were considered: (i) raw cobalt production (mining and refining) (ii) use in alloy and superalloy production; and (iii) use in manufactured items. These are considered to be the most important activity sectors that release the cobalt substances being evaluated in this assessment.

Because it is expected to be essentially inert, briquetted cobalt is not considered in this analysis. Cobalt chloride and cobalt sulfate which are water soluble, and elemental cobalt powders which is deemed to be potentially soluble, were considered.

Cobalt production (Nickel/copper/cobalt Smelters)

The cobalt refining process depends on the type of mineral mined. When cobalt is extracted from sulfide ore, it is first separated by flotation with a surfactant and then roasted (Hatch 2000). This will allow cobalt sulfide transformation into cobalt sulfate by oxidation. Mines in the vicinity of Cobalt, Ontario, produce cobalt from arsenide ore. The arsenide ore process to extract cobalt is similar, except that the ore mineral is first separated by a gravity process instead of a flotation process (Barceloux 1999 in IPCS 2006). Cobalt may also be recovered from the slag of copper smelters by pyrometallurgy (Queneau and Marcuson 1996). As a second step, the cobalt salt is precipitated by chlorine or sodium hypochlorite to extract elemental cobalt (IPCS 2006).

Canadian smelters import some cobalt sulfate for processing at Fort Saskatchewan, Alberta; however, cobalt may be imported in other forms as well. Cobalt sulfate is reduced to form elemental cobalt (Hatch 2000). Releases of cobalt sulfate to surface water are possibly associated with transportation and handling prior to the smelting process.

Pavageau et al. (2004) measured metals in gaseous samples released from enriched fuel combustion. This speciation test may be used as a model for the speciation of cobalt in air emissions resulting from coal combustion with furnaces operating at over 800˚C (Perry and Green 1984), since conditions are very similar to the ones in the Pavageau et al. (2004) paper. In the Pavageau experiment, fuel was enriched with 15 metals to simulate heavy oil and measurements were made using an x-ray photoelectron spectrometer. Flame temperature was maintained at 1100˚C and 40% of oxygen excess was continually provided to the flame. Those conditions, typical of high-temperature combustion processes, resulted in the formation of CoO, $Co(OH)_2$ and/or $CoSO_4$. Of the three cobalt forms of interest in this assessment, only cobalt sulfate is identified as potentially released in the form of particles from this type of combustion. Over 75% of cobalt is found adsorbed to particles. Because smelters have similar combustion conditions, cobalt oxide, cobalt hydroxide and cobalt sulfate are expected to be released via air stacks and deposited nearby smelters.

Six Ni/Cu/Co smelter or refinery facilities reported to the NPRI total releases of 6.72 tonnes of cobalt and its compounds for the year 2008 (Environment Canada 2008). Of these, 5.76 tonnes were released to air and 0.98 tonnes to water. Amounts reported to be disposed were 1.7 tonnes on-site (lanfilled) and 4.3 tonnes off-site (mainly landfilled).

To determine an emission factor to water for smelters, three sites were identified for which information on the quantity used (of the substances being assessed) and the quantity released to water (of the substances being assessed, 2 sites, or of cobalt and its compounds, 1 site) could be determined by matching up information from the S.71

survey and the NPRI database. The average of the ratios of the quantity released over the quantity used for each of the three sites was used to establish an emission factor of 0.081%. This is significantly less than the generic smelters emission factor mentionned by the European Commission (0.2%) (European Commission 2003). However, it is believed to be more specific to the sites assessed and is thus assumed to be more representative of the releases of the Canadian facilities. This calculated emission factor of 0.081% was then applied to other smelter sites where companies had declared zero releases (without providing an acceptable justification).

Alloy and Superalloy Manufacturing

Two alloy and superalloy manufacturers responded to the survey conducted under section 71 of CEPA 1999 (Environment Canada 2010a). One of the two reported a release of cobalt to air (18 kg in 2006), while the other did not report emissions for any of the three cobalt substances. The reporting company indicated to NPRI that 6 kg of cobalt and its compounds were released to air in 2008 and 6 tonnes were transferred to a metal recycling facility (Environment Canada 2008).

Recycled metal from scrap is used for alloy manufacturing by some metallurgical industries. Because scrap metal contains variable amounts of cobalt, cobalt quantities released from raw materials are difficult to estimate. A few submissions were received in response to the section 71 survey under CEPA 1999 describing the uses of different alloys in tools and automotive parts. The physical form of elemental cobalt produced and sold may have different release potentials: powders may lead to greater releases compared to ingots (briquetted cobalt) as their capacity for dissolution is higher.When used in metal components of machinery, cobalt is considered inert and releases from these manufactured items are expected to be negligible.

Welding activities may result in significant releases of cobalt oxides and elemental cobalt dusts to air, while cleaning operations contribute to releases to water. To manufacture alloys, high temperatures are required and cobalt salts dissociate before the optimal temperatures are reached. The optimal temperatures range between 1149 and 1427˚C, depending on the alloy components (Davies 2007). Based on this information, it is likely that cobalt chloride and cobalt sulfate will not be released in large amounts to the air by alloy and superalloy manufacturers, but elemental cobalt dusts may be formed and released.

Releases to air, although they represent a large part of the releases reported to NPRI, were not examined further because cobalt releases are expected to include forms (e.g. oxides, hydroxides) which are not part of this assessment.

An emission factor to water of 0.1% was based mainly on professionnal assumptions along with an emission scenario document. Elemental cobalt is generally shipped to users in the form of powders. The median particle size for cobalt powders is around 30 µm (RACA journal, 2010). As an emission scenario document for this specific use was not available, the OECD emission scenario document for textiles was used and mentions an

emission factor of 0.1% for particles >40 µm and 0.3% for particles <40 µm for a likely container size used (OECD 2004). It is assumed that, contrary to textiles, cobalt is more valuable and recoverable: steel or aluminium drums are likely reused and the high density of cobalt may accelerate deposition on soil to facilitate recovery on-site. Based on these assumptions, it is expected that emissions are similar to the >40µm textile particles (0.1% emission).

Manufactured Items

Most of the cobalt produced in Canada is exported, so that in Canada a relatively small proportion of total cobalt releases are associated with the manufacture of consumer products (Natural Resources Canada and Statistics Canada 2003).

There are few applications of elemental cobalt; it is predominantly used as a component in alloys and carbides for applications requiring high strength and temperature resistance (Donaldson and Beyersmann 2005). Because the alloys and carbides produced have unique CAS registry numbers, elemental cobalt (7440-48-4) will primarily be used in industrial processes associated with these activities and not found in consumer products.

Elemental cobalt is also used as an intermediate in the production of a battery component. Even though there is no information available on the quantity of these items that are imported into Canada it is anticipated given the nature of the products available that losses of cobalt into the environment associated with consumer uses will be relatively low. Thus, it is anticipated that the proportion of the total mass of cobalt that is lost to surface water would not be significantly different from that estimated in the exposure scenarios section. It is recognized that cobalt, cobalt chloride and/or cobalt sulfate contained in manufactured items that are disposed of in landfills could have a potential to be released into groundwater, surface water and/or soil, depending on the presence at the landfill of a liner, a leachate collection system and/or a leachate treatment system (on-site or off-site). Monitoring data collected in 2008 under the Chemicals Management Plan monitoring program indicate that total cobalt concentrations in leachate from landfills range from <0.005 to 0.082 mg/L and may be a result of the presence of many possible cobalt substances, not just those assessed in this document. These data are based on a single sampling episode conducted at 10 different landfills in Canada (Conestoga-Rovers & Associates, 2008).

Environmental Fate

Partitioning

As for most of the elements of the Periodic Table, cobalt may be found under various forms in ambient air, surface water, sediments, soils and groundwater. A fate analysis based on log K_{ow}, K_{oc} and typical mass-balance fugacity modelling is not applicable to elemental cobalt, cobalt chloride and cobalt sulfate, nor to the metal ions they release upon dissolution, because, as for other non-volatile chemicals, these substances exert zero

or negligible partial pressure and fugacity in air (Diamond et al. 1992). Cobalt chloride and cobalt sulfate are highly soluble and, upon introduction in water, will dissociate and release cobalt ions (Co^{2+}). Elemental cobalt powders may also release cobalt ions in solution if discharged to surface waters. The fate of the dissolved cobalt ions, may in part be characterized by partition coefficients - namely soil-to-water (K_{sw},), suspended particle-to-water (K_{ssdw}) and sediment–to-water (K_{sdw}) partition coefficients - which are presented in Table 2. Because of the tendency of cobalt to sorb to solid particles in aquatic media (Table 2; K_{ssw}), a proportion of dissolved forms of this metal will end up in sediments (Table 2; K_{sdw}), through adsorption to settling suspended particles (Hamilton-Taylor and Willis 1984). Note that in situations where elemental cobalt is released directly, some non-dissolved elemental cobalt may be found in sediments and moist soils. When released to dry soils, elemental cobalt will mainly remain there with some of the substance dissolving and leaching locally into ground and/or surface water ecosystems (via runoff) when the soil gets soaked by rain or melting snow/ice. Elemental cobalt is not expected to be found in significant amounts in the water column, considering that its density is greater than that of water. Considering the high solubility of cobalt chloride and sulfate, they are not likely to be found in solid forms in the environment unless they are released in a very dry environment.

Air

Being a non-gaseous element with a negligible vapour pressure (Table 2), cobalt is emitted to air principally in the form of fine particulate matter (PM). Particle size distributions of atmospheric aerosols in England showed that the majority of cobalt in relatively unpolluted areas is found in the 2 to 10 µm size fraction and that concentrations are greater in urban areas than in rural sites (Eleftheriadis and Colbeck 2001). For example, cobalt oxide, cobalt hydroxide and cobalt sulfate are expected to be released via air stacks and deposited nearby smelters.

Long-Range Transport Potential (LRTP) was not quantified in this screening assessment as the assessed substances are not expected to contribute significantly to the Predicted Environmental Concentrations (PECs) presented.

Water

Solubility, dissociation and speciation

The Transformation/dissolution protocol (T/DP) (OECD Guidance document No. 29) is applied to metals, metal compounds and alloys to determine the rate and extent of release of metal ions into aqueous media. These results can then be compared with Ecotoxicity Reference Values for hazard classification purposes. Applied to the elemental cobalt powders, 7-day TD/P test results indicate that Co ions can be released into solution in the sub-milligram to 10 milligram per liter range (Table 2), depending on the loading. Maintaining a constant temperature, agitation rate and dissolved oxygen level, rate determining factors include particle surface area, mass loading, particle size, pH and agitation time (Skeaff et al. 2008).

By virtue of their high aqueous solubilities (Table 2), cobalt chloride and cobalt sulfate will dissolve and release Co^{2+} ions upon introduction in water. Under typical pH and Eh (oxidoreduction potential) conditions the (II) oxidation state is more stable than the (III) oxidation state (Cotton and Wilkinson 1988), although under conditions of high pH and Eh Co^{3+} may be more thermodynamically stable (Lee and Tebo 1994). Under conditions commonly found in oxic freshwaters (i.e., pH between 5 and 9; E_h between 0.5 and 1 V), Co^{2+}, $CoCO_3^0$, and $CoHCO_3^+$ will be the dominant species in solution (Brookins 1988; Takeno 2005).

Cobalt is expected to be more mobile under oxidizing conditions than under reducing conditions (Garrett 2005). In addition, environmental mobility will be high under acidic conditions and lower under neutral to alkaline conditions (Reimann and de Caritat 1998). Studies on inorganic complexation of cobalt in solution have demonstrated high stabilities for the complexes $CoHCO_3^+$ and $CoOH_2^0$ with thermodynamic stability constants, $\log_{10}K_f$, of 12.9 and 9.2 respectively (temperature of 25ºC, ionic strength (I) of 0 mole/L: Smith and Martell 2004). Interactions between metals and natural organic matter is a topic of interest linked particularly to the fate and bioavailability of cationic metals in aquatic systems. Over the years, a variety of physical and chemical techniques have been used for investigating complexes of cobalt with natural organic ligands in waters of different compositions. Conditional stability constants ($\log_{10}K_f$) determined by some of these studies varied between 2.45 and 11.6 depending on the nature of the organic ligand and chemical composition of water (Lee and Jonasson 1983; Ephraim et al. 1989; Pham and Garnier 1998; Kurk and Choppin 2000; Pandey et al. 2000; Hamilton-Taylor et al. 2002; Prado and Airoldi 2003; Qian et al. 1998; Alvarez-Puebla et al. 2004). Pandey et al. (2000) evaluated the affinity of many metal ions for humics in the laboratory using a humic acid extracted from soil and aqueous solutions of hydrated metal salts. Stability constants obtained at pH 3.5 and 24ºC followed the order Cu>Fe>Pb>Ni>Co>Ca>Cd>Zn>Mn>Mg. Hamilton-Taylor et al. (2002) determined the effects of ionic strength (I) and hardness ion competition on the humic complexation of cobalt in solution. A humic acid was extracted from a moorland peat, a fixed cobalt concentration of 5.1×10^{-7} M was used, and pH was maintained within a narrow range of 7.7 to 8.0. Five different I conditions were tested: 0.005, 0.05, 0.15, 0.35 and 0.7 M. Metal-humic binding was determined by equilibrium dialysis using a 2000 molecular weight cut-off. Experiments lasted four days. In a NaCl medium of pH ~ 7.8, cobalt-humic binding decreased markedly with increasing ionic strength with ~90% binding at I of 0.005 M, and ~40% binding at I of 0.7 M. For similar ionic strengths, more pronounced decreases were obtained with a Na, Mg and Ca mixture. Factors evoked by the authors for explaining the above dependence on ionic strength included competition for humic binding sites from Na^+, Mg^{2+} and Ca^{2+}, changes in free cobalt concentrations due to chloride and carbonate complexation, an electrostatic effect on the humic molecule and a decrease in the activity coefficient of the cobalt ion with increasing I.

Modelling speciation in solution

Given the great influence of chemical speciation on metal bioavailability in aquatic systems, the speciation of cobalt in a natural context was determined. The Windermere

Humic Aqueous Model, version VI (WHAM VI: Tipping 2002), has been used to model chemical speciation in Canadian waters of various physico-chemical characteristics (Table 5). Appendix I provides detailed descriptions of water types, as well as details of the modeling with WHAM VI.

Table 5. Model results for chemical speciation of cobalt in representative surface waters of Canada using WHAM VI

Water type		General physico-chemical characteristics			Proportion of total aqueous cobalt (%)		
		Hardness (mg $CaCO_3$/L)	DOC[1] (mg C/L)	pH	Free ion	Bound to HA[2]& FA[3]	Complexed by inorganic ligands
Prairie Clear Lake, Alberta		274	13.6	8.6	28	15	57
Lake Ontario		128	1.91	8.2	56	4.5	38
Cana-dian Shield	Colombière R. QC	36.9	18.2	7.0	61	26	13
	Allard River, QC	14.3	14.3	6.4	64	33	3.0
Low mineralized waters of Canada (Lake Ontario 10%)		12.8	1.0	7.3	85	9.0	5.4

1 dissolved organic carbon;
2 humic acid;
3 fulvic acid

Modeled data indicate that the importance of inorganic cobalt complexation increases with water hardness (Table 5). With similar levels of dissolved organic carbon (DOC), the proportion of dissolved cobalt bound by humic (HA) and fulvic (FA) acids in a hardwater lake (Alberta) is less than half that determined for a slow-moving soft water river (Québec) (Table 5). Increased water hardness and mineralization in these Canadian examples would favor competition by Mg and Ca for HA and FA binding sites, increased cobalt complexation by inorganic ligands and a decrease in the activity coefficient of the cobalt ion, all contributing to diminish the importance of cobalt binding to DOC, an explanation consistent with the findings of Hamilton-Taylor et al. (2002).

Tipping et al. (1998) used the WHAM Model V to estimate the chemical speciation of cobalt in the surface waters of the Humber River system in the United Kingdom. General characteristics and aqueous concentration data for this river were obtained from the peer-reviewed literature. For riverine water conditions similar in chemistry to those of Clear Lake and Lake Ontario (shown in Table 5), the authors estimated that about 25% of aqueous cobalt was present as Co^{2+}, ~ 70% was bound to carbonate ligands, and that complexes with fulvic acid were relatively unimportant - accounting for less than 5% of the total. Notwithstanding the fact that there are differences in the water types compared,

these results point out discrepancies between modelling with WHAM V and WHAM VI. In principle, Model VI takes better account of competition among metals, as well as between metals and H^+, binding-site heterogeneity and effects of ionic strength (Tipping 2002).

Sediments

It has been known for a long time that sediments act as sinks for trace metals in aquatic systems (Förstner and Wittmann 1981). The suspended particulate flux in surface waters acts as a 'conveyer-belt' mechanism whereby metals are 'scavenged', being adsorbed by or incorporated into particles generated *in situ* or of allochthonous origin. In turn, these particles fall through the water column and eventually settle to bottom sediments (Santschi 1984). Consistent with Santschi's findings, an *in situ* experiment with cobalt-57 showed that about 80% of the radioisotope was transferred from the water column to bottom sediments 20 days after its initial introduction in a lake enclosure open to surface sediments (Diamond et al. 1990).

Available partition coefficients for suspended sediment-water (K_{spw}) are high for cobalt with log K_{spw} values ranging from 4.18 to 5.83 (Table 2). The partition coefficients for sediment-water, Log K_{sdw}, are less than those for suspended matter, ranging from 2.92 to 3.48 (Table 2), which suggests that cobalt will remain for the most part in bottom sediments after having entered this compartment.

Once in sediments, and similarly for most trace metals, cobalt may be found in a variety of forms in this compartment: dissolved in interstitial waters; in exchangeable fractions on clays, hydrated oxides of iron and manganese and humic acids; bound to carbonates; bound to iron and manganese oxides, bound to particulate organic matter; complexed with sulphides including acid volatile forms, and in the crystal lattice of primary and secondary minerals (Tessier et al. 1979; Förstner and Wittmann 1981; Ditoro et al. 1992). Profiles of Co, Fe and Mn were determined in pore waters of fresh and aged marine sediment cores using the diffusive gradient in thin film technique (DGT). The close correspondence between the Co and Mn profiles suggested that the formation and dissolution of authigenic Mn (oxyhydr)oxide influenced cycling of cobalt in oxic/suboxic surface sediments (Stockdale et al. 2010).

Soils

Similar to sediments, soils are major sinks for metals released to air from natural sources and anthropogenic activities. After entry of metal compounds into soils, transformation processes will involve dissolution, partitioning leaching and ageing. The latter designates reactions transferring metals from labile pools to relatively insoluble pools (Smolders et al. 2007). In general, metal bioavailability is governed by the mobility and solubility of different geochemical forms (Smolders et al. 2007). Smolders et al. (2007) amended a sandy soil with 100 mg/kg $CoCl_2$. Concentrations of cobalt in pore water after 2 and 24 weeks of incubation were respectively 9.2 and 11.2 mg/L. This indicates that after a two

week period, ageing processes were ineffective in further reducing soil pore water concentrations.

The behaviour of cobalt in soils is linked to chemical and physical properties of both the soil and the cobalt-containing compound entering this compartment. In a study of 54 soil series obtained from England and Wales, it was found that Co concentrations extracted by acetic acid were strongly and negatively correlated with soil pH and manganese content (Suttle et al. 2003 cited in Gál et al. 2008).

Available partition coefficients for soil-water range from 0.41 to 3.49 (log K_{SW}; Table 2). This large variability is due in part to differences in soil and soil solution properties (pH, soil organic matter and other sorbent phases, DOC, ionic strength) and the nature of the metal added (Degryse et al. 2009). Modelling of cobalt in a soil solution of a generic composition was performed using the WHAM model VI. It predicted that the affinity of DOM for metals increases in the order: cobalt < Ni < Cd ; Zn << Pb ; Cu. Complexation of cobalt in soil solution was expected to be relatively unimportant at pH < 7. However, the training set used to predict the complexation of cobalt by DOM was limited. Empirical data indicated that cobalt in soil solution may be complexed more with DOM than predicted by the WHAM speciation code (Degryse et al. 2009).

Environmental Persistence

A metal or metalloid ion is considered infinitely persistent because it cannot degrade any further. For most metal-containing compounds, it is the potentially bioavailable metal ion that is liberated (in greater or lesser amounts) upon contact with water that is the moiety of toxicological concern. A parent compound from which persistent metal ions are released is itself considered to meet regulatory persistence criteria (Environment Canada 2003).

Elemental cobalt, cobalt chloride and cobalt sulfate are considered persistent because the cobalt ions that are released into solution when they dissolve cannot be irreversibly degraded. Biodegration, photodegradation and hydrolysis as a function of pH are not applicable to these inorganic metal-containing substances.

Therefore, elemental cobalt, cobalt chloride and cobalt sulfate meet the persistence criteria for all media (i.e., air, water, soil and sediment) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Bioavailability aspects

As for studies on environmental fate, the studies that investigate the bioavailability of cobalt, as well as its bioaccumulation, are conducted with a variety of soluble cobalt compounds. Even if these compounds are in some cases not the ones being assessed in this report, all soluble cobalt compounds are expected to generate dissolved cobalt species that should behave similarly in a given environmental medium, especially in water.

Water compartment

The Biotic Ligand Model (BLM) was developed in recognition that the bioavailability and bioreactivity of metals control their potential to cause adverse effects. Basically, the BLM incorporates the competition of the free metal ion with other naturally occurring cations (e.g., major cations and H^+), together with complexation by abiotic ligands (e.g., dissolved organic matter, chloride, carbonates, sulfate) for binding with the biotic ligand, assumed to represent exposure at the site of toxic action for the organism (Paquin et al. 2002). No published information has been found regarding the development of a BLM for cobalt in the aquatic medium. However, toxicity studies conducted to date suggest that increased water hardness protects against acute cobalt toxicity (e.g. Borgmann et al. 2005), likely because of the existence of competitive interactions between Co^{2+} and hardness cations for binding with the biotic ligand.

Dissolved organic matter (DOM) is typically considered to protect aquatic organisms from metal stress by decreasing free metal ion concentration and thus decrease metal bioavailability. Nonetheless, in his review Campbell (1995) noted that quantitative studies on the subject are more or less evenly divided between examples of enhanced protection in the presence of DOM and examples of enhanced toxicity in the presence of DOM. The author suggested that it is imprudent to treat natural DOM as a simple hydrophilic ligand because this colloidal fraction is multifunctional and its role is not limited to complexing metals in the bulk solution. The following example with cobalt is consistent with this view.

Guo et al. (2001) studied the effects of DOC on the bioaccumulation of trace metals, including cobalt, by American oysters using radiotracer techniques. Seawater was ultrafiltered (< 1 kDa), UV irradiated and diluted with ultrapure seawater in order to have a 'DOC-free' test water of ~ 20% salinity. Four DOC treatments were prepared by adding different volumes of high molecular weight DOC (1 kDa - 0.2 µm) to the treated seawater; tests levels were 0 (~ 0.05), 0.5, 5 and 10 ppm DOC. Juvenile specimens of *Crassostrea virginica* of similar body shape and weights (20-25 g) were obtained from a natural population. Four individual oysters were used in each treatment and exposures lasted 8 hours. Dry weight concentration factors (DCF) were calculated based on radioactivity of metals in soft tissues to the radioactivity of metals in water. Average uptake rate constants (mL/g/h) were derived from plots of DCF versus time.

Measured DCF values for cobalt (and for Cd, Cr, Ag, and Zn) increased as DOC concentrations increased. The cobalt DCF for the DOM-free treatment was 22 mL/g; with addition of DOC, DCFs ranged from 32 to 54 mL/g. Uptake rate constants for cobalt showed an initial drop at lower DOC levels (< 10 ppm) and an increase at the highest DOC level of 10 ppm. The authors suggested that at low [DOC] (< 10 ppm), free ionic, inorganic and/or organic cobalt complexes drive metal uptake. At these DOC levels, complexation of metals with organic matter decreases metal uptake. At high [DOC] (≥ 10 ppm), colloidally complexed cobalt becomes bioavailable via direct uptake of this colloid or via pinocytosis in gills.

Studies have demonstrated that bioavailability of colloidal metals is similar to or higher than that of metals in the dissolved phase for a variety of organism types: zebra mussels (Roditi et al. 2000), marine phytoplankton and zooplankton (Wang et al. 2000), and marine crustaceans (Carvalho et al. 1999).

To summarize, available published information suggests that cobalt complexes with humic and fulvic acids, in addition to Co^{2+} ions, may be available for uptake by many types of aquatic organisms. Taken together, these two potentially bioavailable fractions can comprise from less than half (e.g., Alberta Prairie) to nearly all (e.g., Canadian Shield) of the dissolved and colloidal cobalt in Canadian surface waters. Furthermore, the main hardness ions Ca and Mg are likely to exert a protective effect against the aquatic toxicity of cobalt.

Soil compartment

The development of a 'terrestrial' BLM is conceivable for modelling biouptake and toxicity of cobalt in soil porewater. Efforts have been made in that direction in studies examining the effects of cobalt on the root growth of the barley (*Hordeum vulgare*) in nutrient solution, and on the survival of the potworm *Enchytraeus albidus* exposed to nutrient solution added to acid washed and precombusted sand (Lock et al. 2006, 2007). The exposure media in these experiments were very well chemically defined but too simplistic to simulate the uptake and toxicity of cobalt to plants and earthworms in real soils, a caveat acknowledged by the authors. For example, uptake of cobalt by the worms by ingestion of soil particulate matter was not considered. These studies found that ions such as Ca^{2+}, Mg^{2+}, K^{+} or H^{+} increased LC_{50} values based on concentrations of freely dissolved cobalt ions, for both test species. These results were explained by the existence of competitive interactions between these major ions and Co^{2+} for binding sites at the organism-water interface, the overall effect being a decreased toxicity of the free metal ion (Lock et al. 2007). Dissolved organic matter was not a variable tested in these experiments.

Using another approach, many soil toxicity tests were conducted in support of the regulatory assessment of nickel conducted by the European Union (European Commission 2009). Soils covering large ranges of pH and Cation Exchange Capacities (CEC) were used. A linear regression model was developed from this dataset of experimental toxicity values, having the general format:

$$\text{Toxicity value} = a + b*pH + c*CEC$$

An ageing factor was then applied to the predicted toxicity value, this factor being derived from the duration of ageing, soil pH and soil Cationic Exchange Capacity (CEC) (Vangheluwe et al. 2007). Smolders et al. (2009) demonstrated that this approach for evaluating the toxicity of nickel in soils can also be applied to cobalt.

It has to be noted that risks to soil organisms were not estimated in this assessment because available releases and source apportionment information were not sufficient to evaluate potential for harm related to the cobalt substances being assessed. As well, soil monitoring information is likely more related to other cobalt-containing substances (e.g.

Cobalt oxides) and so it was considered not useful for assessing the substances targeted in this assessment.

Potential for Bioaccumulation

Cobalt essentiality

Cobalt is essential in small amounts for nitrogen fixation by bacteria, blue-green algae, and symbiotic systems such as those in the root of leguminous plants (IPCS 2006). It is also an essential micro-nutrient element for animals and is required for the formation of vitamin B_{12} and for its participation in enzymatic processes (Adam et al. 2001; Gal et al. 2008; Mathews et al. 2008; Metian et al. 2009).

Water compartment

Bioaccumulation of metals - like that of organic substances - is of potential concern because of the possibility of chronic toxicity to the organisms accumulating these substances in their tissues and the possibility of toxicity to predators eating these organisms. Bioaccumulation potential is typically quantified by determining either a bioaccumulation factor (BAF), which is the preferred endpoint as per *Persistence and Bioaccumulation Regulations* (Canada 2000), or a bioconcentration factor (BCF). However, these ratios are currently the object of criticism when applied to metals because they are considered of little usefulness in predicting metal hazards (Schlekat et al. 2007). For example, some metals may naturally be highly accumulated from the surrounding medium because of their nutritional essentiality. Furthermore, both essential and non-essential metals may be regulated within relatively narrow margins by the homeostatic and detoxification mechanisms that many organisms possess. It follows that when ambient concentrations of metals are low, BCFs and BAFs are often elevated. Conversely, when ambient metal concentrations are high, BCFs and BAFs tend to decrease (BAF: BCF: McGeer et al. 2003; DeForest et al. 2007). Thus, inverse relationships may be observed between BCF and BAF values and metal exposure concentrations, and this complicates the interpretation of BCF/BAF values. Natural background concentrations in organisms may contribute to these negative trends (e.g., Borgmann and Norwood 1995). In addition, inverse relationships can occur for non-essential elements as well because there are a finite number of binding sites for these metals within an organism that could become saturated at higher concentrations (e.g., Borgmann et al. 2004, MacLean et al. 1996).

Taking account of these issues, a mechanistically-based saturation model for the bioaccumulation of metals using the freshwater amphipod *Hyalella azteca* as a test organism has been developed (Borgmann et al. 2004; Norwood et al. 2007). This model can estimate a BCF based on background-corrected metal accumulation at low aqueous concentration, which avoids the above-mentioned concentration dependence. In addition, these authors have shown that (i) lethality occurs when tissue concentrations surpass a

critical body concentration (CBC) and that (ii) CBCs appear relatively constant for a variety of different non-essential or marginally essential metals in spite of large differences in the waterborne concentrations that result in chronic toxicity (e.g., Schlekat et al. 2007). It can be deduced from these two points that when the uptake of a given metal is more efficient, a smaller water concentration is required to reach the chronic toxicity threshold in tissue. Consistent with this statement, these researchers have observed a strong negative relationship between estimates of chronic toxicity and BCFs/BAF values for non- or marginally essential metals and metalloids (in laboratory: Norwood et al. 2007; Schlekat et al. 2007; in field settings: Couillard et al. 2008). This relationship holds because total metal body concentration in *Hyalella* is likely related to the concentration of the metal at the site of toxic action. In principle, animals with metal handling strategies not including important pools of metals stored in detoxified forms, may show close relationships between bioaccumulation ratios (BAFs and BCFs) and chronic toxicity (Couillard et al. 2008).

The selection of studies for assessing the bioaccumulation potential of cobalt builds on the above knowledge and on accepted methodologies for deriving BCFs and BAFs (OECD 1993; OECD 1996; Arnot and Gobas 2006). Appendix II summarizes criteria and considerations used for BCF and BAF data quality assessment. In recognition that these ratios are less meaningful for organisms with large and inert metal compartments, studies with such metal accumulators have been left aside. When information was available, only metal concentrations in soft tissues were considered for invertebrates with shells or important exoskeletons.

To characterise the bioaccumulation and biomagnification potential of cobalt, 38 studies were considered; 20 of these were used to provide the data for this bioaccumulation assessment. A complete summary of all bioaccumulation data used is provided in Appendix III, where values are presented on a wet-weight basis; additionally, dry-weight values for terrestrial organisms are presented in square brackets. Appendix IV provides a summary of rejected studies, and the reason for their rejection. The data presented are for cobalt as an element and not for the individual substances: elemental cobalt, cobalt chloride and cobalt sulfate. As explained in previous sections of this report, these substances will dissolve in water and will release cobalt ions. These ions are considered potentially bioavailable and can be taken up by organisms. Unless otherwise stated, all BCF/BAF values reported are based on measured concentrations of the Co element.

Considering all aquatic data in Appendix III, 31 acceptable bioaccumulation factors were reported for various species of algae, invertebrates, fish, and zooplankton. These values ranged from 7.4 to 3110 L/kg, with a mean value of 878 L/kg and a median value of 720 L/kg. Five biota-to-sediment accumulation factors (BSAF-sed.) were reported. One of these BSAF-sed values was for the marine invertebrate *Pecten maximus* (king scallop), with a value of 0.067 (Metian et al. 2009). However, being a filter feeder, the main route of cobalt exposure to *P. maximus* is uptake from surrounding water, as opposed to sediment. Therefore, this BSAF for sediment was considered to be irrelevant. More usefully, the same study also provided a BCF for *P. maximus* of 40 L/kg (for soft tissue), which is included in Appendix III. Four other BSAF-sed values were observed in

freshwater invertebrates. BSAF-sed values ranged from 0.091 to 0.645, with a mean value of 0.232 and a median value of 0.138.

If marine and freshwater data are pooled, then for aquatic invertebrates, 16 BCF and BAF values were obtained, ranging from 21.8 to 2280 L/kg with an average value of 724 L/kg and a median value of 441 L/kg (wet weight). In comparison, values for fish (n=11) ranged from 7.4 to 3110 L/kg, with an average value of 1010 L/kg and a median value of 849 L/kg. Many studies have noted that homeostatic mechanisms likely exist to regulate cobalt accumulation, due to the fact that it is an essential element (Adam et al. 2001; Campbell et al. 2005; Nfon et al. 2009).

One study, done by Norwood et al. (2006), was unique in its use of a mechanistically-based saturation model for the bioaccumulation of cobalt. The test organism was the freshwater amphipod *Hyalella azteca*. The wet-weight BCF was calculated according to the equation:

$$BCF = (max)(DW^{-1})1000K^{-1}$$

Where max is the maximum above-background accumulation of the metal in the organism, measured in nmol/g, DW^{-1} is the mean dry-to-wet weight ratio for the organism, and K is the half saturation constant (i.e. the metal concentration in the water at which the concentration in the organism is halfway between the maximum and the background accumulations), measured in nmol/L.

So, it is seen that this model estimates a BCF based on background-corrected metal accumulation at low aqueous concentrations; thus, unlike with other approaches, background contaminant concentrations will not dictate the BCF values observed. In this case, the wet-weight BCF for *Hyalella azteca* was found to be 515 L/kg.

Another study, done by Corisco and Carreiro (1999) was reviewed and found to be of acceptable quality; here, a BCF of 17 500 (dry weight) was reported for the green algae *Selenastrum capricornutum*, when the algae was in its exponential growth phase. This corresponds to a wet-weight value of 1750 L/kg, since a dry-to-wet weight ratio of 0.1 can be used for algae species (Maeda et al. 1997). While this dry-weight concentration factor appears high, these results would not suggest that cobalt should be classified as meeting the bioaccumulation criteria, as the wet-weight value is below 5000. The BCF observed for the same species in its stationary phase (no growth) was reduced, at 187 L/kg (wet-weight).

Another experiment that considered an algae species was performed by Nucho et al. (1988), on *Scenedenesmus obliquus*. These micro-algae were dosed with radioactive cobalt, and BCFs were calculated as the ratio of the contaminant concentrations in the organism and water. The results provided a maximum BCF of 39 300, dry weight (or 3 930, wet-weight). However, upon review, this study was rejected. The elevated BCFs presented likely do not reflect a potential for chronic toxicity, but rather, an important need for an essential element. This reasoning is based on the following three points

mentioned in the paper: (1) cobalt is reported to be an essential metal for this algae; (2) the culture medium was intentionally free of cold cobalt in order to avoid isotopic competition during the tests. This likely led the algal cells to consume the radioactive cobalt at an elevated rate during exposure in order to meet their nutritional needs, therefore inflating the BCFs; (3) *S. obliquus* is reported by the authors to be used for remediating industrial waters and polluted surface waters. As such, they are likely hyper-accumulators, storing large quantities of metals in an inert form. Assuming that this is the case, the BCFs determined with this species under these conditions are not appropriate to assess the bioaccumulation potential (see Appendix II).

Notably, one study done by Szefer (1991) returned somewhat higher BAF values for several marine organisms. Values calculated for algae, zooplankton, one crustacean species, as well as molluscs and fish, ranged from 70 to 4700 L/kg. However, this study was judged to be unacceptable for use (see Appendix II). More specifically, for this study, metal concentrations in the water and test organism were not simultaneously measured. As well, the study used measurements taken from before 1977; such data are considered of lower reliability because of the numerous analytical difficulties in these times, brought about notably by sources of inadvertent contamination, poor reproducibility, and problems associated with filtration and separation of metals in water (e.g., Batley and Gardner 1977; Beneš and Steinnes 1974; Hume 1973; Stevenson 1985). Thus, none of the data from this paper was considered further in this assessment.

In the study carried out by El-Shenawy (2004), metal concentrations were measured in the bivalve *Ruditapes decussatus*, and in surrounding waters at two different contaminated sites for the calculation of BAFs. A lower BAF was observed at the site with a higher ambient cobalt concentration. This inverse relationship between BAF and ambient cobalt concentration provides evidence for the existence of regulation mechanisms in this invertebrate, as previously explained.

Several of the studies used field observations to calculate relevant values. While these data are environmentally realistic, the presence of multiple contaminants, especially other metals, likely influenced the BAF values observed for cobalt. Along these lines, one laboratory experiment by Fraysse et al. (2002) investigated the effect of the presence of cadmium and/or zinc on cobalt accumulation. Two species of freshwater bivalves (*Dreissena polymorpha* and *Corbicula fluminea*) were exposed to either cobalt alone, cobalt plus cadmium, cobalt plus zinc, or cobalt plus cadmium and zinc. In the end, maximum concentration factors were observed when organisms were exposed to cobalt alone; and, the addition of zinc alone had the greatest inhibitory effect on cobalt uptake (though cadmium and cadmium plus zinc treatments also had an inhibitory affect). Thus, it is important to consider both polymetallic field exposures and controlled laboratory exposures when evaluating cobalt accumulation data.

Trace Metals in the Environment (Smith and Carson 1981), is a review document that compiles a large amount of data on the bioaccumulation of cobalt in aquatic organisms. Here, it is reported that BCFs of freshwater molluscs range from 100 to 14 000 L/kg (whole body, dry-weight). These values correspond to soft-tissue values of 1 to 300, dry-

weight (Smith and Carson 1981). The values of particular interest in this assessment should be expressed as soft-tissue, wet-weight concentration factors. If a dry-to-wet weight conversion factor of 0.2 is used for invertebrates and fish (e.g. Campbell et al. 2005; Ikemoto et al. 2008), the appropriate range of BCF values to consider for freshwater molluscs are 0.2 to 60, according to the data cited in Smith and Carson (1981). However, the reliability of these data is uncertain, as the majority of the studies cited originated from before 1977, a time when analytical quality is regarded as uncertain.

Smith and Carson (1981) also provided bioaccumulation factors for marine fish and freshwater fish (100–4000 and <10–1000, respectively). Once again, the analytical quality of the data cited is uncertain as many of the studies originated from before 1977.

Of the papers cited in Smith and Carson that provided bioconcentration factors for aquatic organisms, and were completed in 1977 or later, five were reviewed. These were: Cherry and Guthrie (1977), Cherry et al. (1979), Kimura and Honda (1977), Papadopoulou and Kanias (1977), and Shuman et al. (1977). Two of these were found to be of acceptable quality. Papers that were unavailable for review included the work of: Vaganov et al. (1978), Ishii et al. (1978), Proctor and Sinha (1978), and Nakahara and Cross (1978).

Cherry and Guthrie (1977) provided BCF and BSAF values for plants, vertebrates, and invertebrates, from a site contaminated by fossil fuel plant effluent and coal ash. However, this study was considered unacceptable for use, as the chemical analysis was performed prior to 1977, and thus is considered to be of uncertain quality. In the work of Shuman et al. (1977), chemical analyses were performed in 1975 so this paper was rejected for the same reason.

Cherry et al. (1979) measured the cobalt concentrations in a range of biota from sites contaminated by both a thermal effluent, coming from a fossil fuel power plant, and by a coal ash effluent. This study was found to be of acceptable quality, though the results from one sampling site were ignored, where greater thermal pollution resulted in water temperatures outside the range of what would be considered typical for Canadian environments. For *Enallagma* species (aquatic insects), the BAF of cobalt was found to be 29.3 L/kg. For *Libellula* species (dragonflies), the maximum BAF observed was 24.5. For *Chironomidae* (lake flies), the maximum BAF was 148. Finally, for *Procambarus* sp. (crayfish), a BAF of 21.8 was found. As well, this paper provided biota-sediment accumulation factors. Maximum values observed were: 0.221 for *Enallagma* sp., 0.645 for Chironomidae, 0.091 for crayfish, and 0.138 for *Libellula* sp.

A second paper cited in Smith and Carson (1981) that was available for review and of acceptable quality was prepared by Kimura and Honda (1977). Here, the authors considered the accumulation of cobalt by rainbow trout eggs. The uptake and depuration of cobalt-60 in fish eggs was followed for approximately 30 days, while the metal concentration in the eggs and rearing water was also measured. BCF values were determined both as a ratio of uptake and depuration kinetics, and also as the ratio of metal

concentrations in the organism and water. BCF values of 7.4 (using the former calculation method) and 7.0 (using the latter method) were found.

Papadopoulou and Kanias (1977) studied the accumulation of cobalt in the tunicates *Microcosmus sulcatus* and *Ciona intestinali*. BCFs of less than 10 were reported for both organisms, however, this study was not found to be of acceptable quality, as sampling of the water and organisms was not done simultaneously. Also, all measurements were taken before 1977, thus the analytical quality is uncertain. Finally, *M. sulcatus* is not a test species that is relevant to Canadian waters, as it is primarily found in subtropical waters of the Western Indian Ocean and the Mediterranean Sea (Agbayani and Laxamana 2009).

Soil Compartment

In terrestrial environments, four acceptable biota-to-soil accumulation factors (BSAF-soil) values were identified for two species, *Xerocomus badius* (bay bolete), and *Morus alba* (white mulberry). Measurements for *X. badius* ranged from 0.007 to 0.81, with an average value of 0.15 in the cap, and 0.11 in the stalk (unitless, based on wet-weight). For *M. alba,* maximum BSAF-soil values of 0.28 and 0.08 were found. One soil study considered the cobalt concentration in a soil solution, thus providing bioaccumulation factors for three different plant species. These values ranged from 0.100 to 0.146, wet-weight. All values obtained from soil studies were reported using dry-weight measurements and then converted to wet-weight values. It is observed that the average BSAF-soil and BAF values of these acceptable studies are all less than one.

In the research done by Pereira et al. (2009), soil samples were taken from ten sites at an abandoned uranium mine; the soils were then used to grow lettuce (*Lactuca sativa*) and maize (*Zea mays*) in a laboratory experiment. In this experiment, BSAF values of greater than one were observed for only one of the ten soil types tested. This soil site had both the minimum pH (4.81), and the minimum organic matter content (0.78%) of the soils sampled. It has been widely reported that organic matter content and pH will affect cobalt bioavailability (e.g. Gal et al. 2008; Malinowska et al. 2004); so, the unusually high BSAF values observed may be attributable to these soil characteristics increasing cobalt bioavailability. The BSAFs reported for this acidic organic-poor soil were 3.50 and 1.03 (wet-weight) for *L. sativa* and *Z. mays*, respectively. Overall, the 10 soils tested had average BSAFs of 0.39 and 0.11 (wet-weight, for *L. sativa* and *Z. mays*, respectively). However, neither the cobalt concentrations measured in the plant tissue nor in the soils were directly reported. This precludes the possibility for correction for background cobalt concentrations, resulting in elevated BSAF-soil values. Because this paper did not provide this necessary information, these results will not be further considered.

Ashfaq et al. (2009) also demonstrated that lower soil pH gives rise to greater cobalt accumulation. This microplot study measured the accumulation of cobalt in white mulberry plants (*Morus alba*) from soils irrigated with cobalt-containing wastewater. In one set of measurements, the pH of irrigation water was varied from 3 to 5; in another set, the cobalt concentration of irrigation water was varied from 25 to 400 mg/L. In

experiments that used variable pH, a maximum BSAF-soil of 0.28 (wet-weight) was found at pH 3, the minimum pH tested (the total dissolved cobalt concentration of irrigation water was 100 mg/L). In experiments that used variable concentrations of cobalt in the irrigation water, a maximum BSAF-soil of 0.08 (wet-weight) was measured at the minimum concentration of cobalt tested, 25 mg/L (pH was not reported).

Potential for Biomagnification

Three biomagnification factors (BMF) were found in the literature for cobalt in marine environments, with values ranging from 0.004 to 0.025. One BMF was identified for freshwater species, with a value of 0.087. Table 6 summarizes all data considered for assessing the biomagnification potential of cobalt, including trophic magnification factors (TMF). All values are expressed on a wet-weight basis.

Table 6. Summary of experimental data selected for estimating the biomagnification potential of cobalt[*,]**

Organism		Study Type		End Point	Value (wet wt)	Reference
Predator	Prey					
Aquatic Organisms						
Freshwater zooplankton	SPM	Field	Su	BMF	0.087	Nguyen et al. 2005
Chinook salmon, *Oncorhynchus tshawytscha*	Commercial fish feed	Field	Su	BMF	0.025	Kelly et al. 2008
Carp, *Cyprinus carpio*	Mollusc, *Lymnea stagnalis*	Lab	SS	BMF	≈ 0.01	Baudin and Fritsch 1989
Atlantic salmon, *Salmo salar*	Commercial fish feed	Field	Su	BMF	0.004	Kelly et al. 2008
Coho salmon, *Oncorhynchus kisutch*	Commercial fish feed	Field	Su	BMF	0.004	Kelly et al. 2008
Small-spotted catshark *Scyliorhinus canicula*,	Gilthead sea bream, *Sparus auratus*	Lab	Ki	BMF	<1	Mathews et al. 2008
Turbot, *Psetta maxima*	Gilthead sea bream, *Sparus auratus*	Lab	Ki	BMF	<1	Mathews et al. 2008
Gilthead sea bream, *Sparus auratus*	Gilthead sea bream, *Sparus auratus*	Lab	Ki	BMF	<1	Mathews et al. 2008

Food Web Studies					
Marine Pelagic food chain (Baltic Sea)	Field	Su	TMF	1.1[1]	Nfon et al. 2009
Marine Pelagic Arctic food chain (Baffin Bay)	Field	Su	TMF	0.93[2]	Campbell et al. 2005
Freshwater food chain (Mekong Delta)	Field	Su	TMF	0.95[a]	Ikemoto et al. 2008
Marine pelagic and benthic food chain (East China Sea)	Field	Su	TMF	0.71; 1.45[c]	Asante et al. 2008

***Abbreviations:** BMF: Biomagnification factor; Ki: Study of kinetics of uptake and depuration; SPM: Suspended particulate matter; Su: Field survey of organism, water, sediment, etc.; TMF: Trophic magnification factor

**BMFs expressed on a dry weight basis have been converted to a wet weight basis using the following conversions: per one gram of wet material, assume 0.2 g dry for zooplankton, invertebrates and fish (e.g., Ikemoto et al. 2008; Campbell et al. 2005); and, 0.1 g dry for SPM and algae (assuming that SPM composition approximates that of superficial sediments and using the data of Couillard et al. 2008; Maeda et al., 1997).

1: Correlation between trophic level and Cobalt concentration demonstrated, but with no statistical significance

2: Study reported that no relationship was demonstrated for cobalt in this food web, due to the small change in cobalt concentration at each trophic level and due to highly variable data. The TMF value is calculated as 10^B, where B is the slope of the log [Co] vs. nitrogen isotope ($\delta^{15}N$) regression (Nfon et al. 2009). In this case, B was reported to be -0.03, with statistical significance ($p<0.05$). From the equation provided by Nfon et al. (2009), this corresponds to a TMF value of 0.93. The r^2 value for this regression was 0.04.

[c] Study reported contradictory results: a positive and a negative relationship were observed between cobalt concentration in the organism and trophic level. The TMFs were calculated according to Nfon et al. 2009. B was reported to be 0.16, with statistical significance ($p<0.01$, r2 = 0.15) for deep-water fish whereas B = -0.15 for all deep-water species ($p<0.05$, r2 = 0.50). The corresponding TMF values were respectively 1.45 and 0.71.

One study in a marine environment measured particularly low BMFs of 0.025, 0.004, and 0.004 for three salmon species (Kelly et al. 2008). This study examined farmed salmon, which had been raised on a diet of commercial fish feed. As the fish were not raised in a controlled laboratory setting, this data will be regarded as originating from a field study; however, it is worth noting that the fish were not raised in a truly natural environment, and commercial fish feed does not truly reflect a natural salmon diet. The BMFs provided were calculated as the ratio of the mean wet-weight cobalt concentrations in salmon flesh and in a commercial salmon diet. The abnormally low BMFs found in this study may be the result of tissue sampling being done for fish muscle only. The authors commented that many metals are stored preferentially in body compartments other than muscle; other studies have supported this (e.g. Campbell et al. 2005; Metian et al. 2009). Thus BMFs calculated using muscle measurements only may not provide true reflections of the metal's potential for biomagnification.

With this in mind, the BMF values reported by Kelly et al. (2008) for farmed Atlantic salmon (*Salmo salar*), Coho salmon (*Onocorhynchus kisutch*), and Chinook salmon (*Oncorhynchus tshawytscha*) (0.004, 0.004, and 0.025, respectively), do not show evidence for biomagnification potential. In comparison, the study reported BMFs for methylmercury of 1.3, 0.86, and 1.9 for the same species.

Additionally, in a laboratory setting, Mathews et al. (2008) investigated the potential for cobalt to biomagnify when passed from radiolabelled prey fish (*Sparus auratus*) to predator fish (*Scyliorhinus canicula, Psetta maxima,* and *S. auratus*). While the BMF values were not directly indicated, they were reported to be consistently less than 1 for cobalt.

The Scientific Criteria Document for the Development of a Provincial Water Quality Objective for Cobalt (Fletcher et al. 1996), produced by the province of Ontario, is another document that provides reference to various studies on cobalt bioaccumulation and biomagnification. This document cites the work of Smith and Carson (1981); additionally, references are made to Tong et al. (1972 and 1974), which indicated a lack of biomagnification for cobalt. However, these studies were not available for review, and as they were done before 1977, their analytical quality can be considered unreliable. Additionally, a study done by Baudin and Fritsch (1989) is referenced. This study was available for review, and was found to be of acceptable quality. Here, when the carp *Cyprinus carpio* received cobalt from contaminated food (the mollusc *Lymnea stagnalis*), the biomagnification factor was reported to have been in the order of 10^{-2} (though the actual value was not reported). Additionally, it was concluded that water is the dominant pathway for cobalt uptake, and that accumulation from food and water is additive.

A number of studies also attempted to quantify the trophic magnification factor of cobalt (TMF). Briefly, this value depends on the correlation between trace element concentrations and nitrogen isotopes ($\delta^{15}N$), measured in an array of members of a given food web (Nfon et al. 2009), and has the simple equation:

$$TMF = 10^{B},$$

where B is the slope of the regression of the log[trace element concentration (µg/g wet weight)] against $\delta^{15}N$ (Nfon et al. 2009). As the $\delta^{15}N$ count increases predictably with each trophic level in a food chain, a significant correlation between these two variables can be indicative of the potential for biomagnification (if TMF >1) or biodilution (if TMF <1) (Nfon et al. 2009).

Nfon et al. (2009) estimated the TMF values for several elements in a pelagic food chain from the Baltic Sea. The wet-weight element concentrations in phytoplankton, zooplankton, mysis (*Mysis* sp.) and herring (*Clupea harengus*) were measured, as well as the $\delta^{15}N$, $\delta^{13}C$, and lipid fractions. The TMF for cobalt was found to be 1.12; but the correlation coefficient was low (r^2=0.10) and the relationship was not statistically significant ($p = 0.165$). Therefore, based on these data Nfon et al. (2009) concluded that there was no evidence of cobalt biomagnification. In comparison, mercury was calculated to have a TMF of 1.50 ($p < 0.001$).

Campbell et al. (2005) studied a pelagic Arctic marine food web from Baffin Bay. The study surveyed phytoplankton, zooplankton, three species of marine invertebrates, one fish species, eight species of birds, and one species of seal. Metal concentrations were measured in whole organisms, and in muscle and liver tissues of birds and mammals. Here, the slope of the log [Co] vs. $\delta^{15}N$ was found to be -0.03, with statistical significance ($p<0.05$). Using the preceding equation provided by Nfon et al. (2009), this corresponds to a TMF value of 0.93. However, due to the small change in cobalt concentration at each trophic level and due to highly variable data, the authors concluded that these results did not consistently demonstrate that cobalt will bioconcentrate or biodilute through the food chain. On the other hand, it was demonstrated that mercury

does biomagnify: the slope of the log[total Hg] vs. $\delta^{15}N$ regression was 0.197, corresponding to a TMF of 1.57 ($p \leq 0.001$). This study also attempted to correlate element concentrations with $\delta^{13}C$ values in seabird liver and muscle tissues (the $\delta^{13}C$ indicating dietary carbon source), though no significant relationship was demonstrated for cobalt.

Ikemoto et al. (2008) considered the freshwater food web of the Mekong Delta in South Vietnam, examining phytoplankton, snails, five species of crustaceans, and fifteen species of fish. A TMF of 0.95 resulted, but again there was no statistical significance (r^2=0.013, p=0.506). Thus the results showed no biomagnification or biodilution of cobalt through the food chain.

Finally, Asante et al. (2008) studied the accumulation of various metals in shallow and deep water organisms from the East China Sea. Fish, Cephalopods, Coelenterates, Crustaceans, Echinoderm and Gastropods species were collected. Whole body cobalt concentrations were measured. Contradictory results were observed as positive and negative relationships were caclulated between cobalt concentration and trophic level. A positive correlation was observed for deep-water fish (TMF of 1.45) whereas a negative correlation was observed when considering all deep-water species (TMF of 0.71). The authors suggested that cobalt might be accumulated in fish at higher trophic levels. However, results are conflicting.

The relatively high consistency of the results reported in the studies presented above leads to the conclusion that cobalt does not present a risk for biomagnification.

Conclusion. There are several lines of evidence to suggest that the bioaccumulation potential of cobalt in natural ecosystems is relatively low. First of all, low BAFs have been reported in eight laboratory (steady state) studies and four field studies; five BSAF-sediment values have been found to be well below 1; and, four (out of four) average BSAF-soil values have been reported to be well below 1. In addition, results from six field investigations plus two laboratory studies indicate the absence of biomagnification of cobalt in natural food webs. Finally, cobalt is an essential micro-nutrient, the uptake of which is expected to be regulated to some extent by many organisms. It is therefore concluded that elemental cobalt, cobalt chloride and cobalt sulfate do not meet the bioaccumulation criteria (BAF or BCF $\geq$ 5000) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential to Cause Ecological Harm

Ecological Effects Assessment

A - In the Aquatic Compartment

There is experimental evidence that cobalt causes harm to aquatic organisms following short-term (acute) and longer-term (chronic) exposure at very low concentrations. Many empirical data are available in the literature for acute and chronic toxicity of cobalt chloride, cobalt sulfate and other cobalt compounds. Because all of these compounds are soluble in water, all data from reliable chronic studies were considered in order to derive a critical toxicity value (CTV), since they all lead to the formation of potentially bioavailable dissolved cobalt species, in particular, the free ion, Co^{2+}. Robust Study Summaries (RSS) were completed for all studies from which the toxicity data used to develop a predicted environmental no effect concentration (PNEC) were obtained, and are available upon request.

Reliable acute (short-term) studies were identified for 15 species including 12 invertebrate species and 3 fish species. Toxicity values range from 89 to 585 800 µg/L as total dissolved cobalt (Nautilus Environmental 2009). Chronic (long-term) data are of greater interest in this assessment because they are a more sensitive indicator of potential for harm from long-term exposures. Table 7 summarizes reliable chronic aquatic toxicity data for cobalt to freshwater organisms; 15 species were identified including 5 plants/algae species, 7 invertebrate species and 3 fish species. It should be noted that concentrations in the cited studies are expressed in micrograms of cobalt per litre (µg Co/L). Therefore, the CTV derived from these data is for total cobalt as an element rather than for the compounds tested (e.g. $CoCl_2$).

Table 7. Empirical data for aquatic chronic (long-term) toxicity to freshwater organisms.*.

Test Organism	Test Compound	Hardness (mg $CaCO_3$/L)	pH	T (ºC)	Endpoint and duration	Value[1] (µg Co/L)	Reference
Fish							
Zebrafish *Brachydanio rerio*	$CoCl_2$*$6H_20$	100	7.5-7.7	25.4-26.4	MATC 16d (survival)	340	Dave and Xiu 1991
	$CoCl_2$	103 ± 6.1	7.8 ± 0.1	27-29	EC_{10} 33d (biomass)	1084	CDI 2009b
Fathead minnow *Pimephales promelas*	$CoCl_2$	109	7.6-8.5	24-27	EC_{10} 34d (survival)	351	CDI 2009c
	$CoSO_4$	236[2]	8.14	24.4	IC_{10} 28d (growth)	480	Kimball 1978
Rainbow trout *Oncorhynchus mykiss*	$CoCl_2$	115	7.6-7.8	10-14	EC_{10} 81d (biomass)	2 171	CDI 2009d
Invertebrates							
Amphipod *Hyalella azteca*	$CoCl_2$*$6H_20$	122	8.2	25	IC_{25} 28d (growth)	2.9	Norwood et al. 2007
	$CoCl_2$	125 ± 10	7.15-7.69	25 ± 1	EC_{10} 28d (survival)	5.5	CDI 2009e
Water flea *Daphnia magna*	$CoSO_4$	198[2]	8.31	20.3	LOEC 28d (reproduction)	4.4	Kimball 1978
	$CoCl_2$	230-250	7.22-7.64	20 ± 1	EC_{10} 21d (reproduction)	54	CDI 2009e
Water flea *Ceriodaphnia dubia*	$CoCl_2$	108	8.0-8.7	25 ± 1	EC_{10} 21d (reproduction)	7.9	CDI 2005
Snail *Lymnea stagnalis*	$CoCl_2$	140	7.64-7.88	20 ± 1	EC_{10} 28d (growth)	22	De Schamphelaere et al. 2008
Midge *Chironomus tentans*	$CoCl_2$	32-34	7.58-8.17	23 ± 1	EC_{10} 20d (growth)	123	Pacific Ecorisk 2005
Oligochaete *Aeolosoma sp*	$CoCl_2$	54	7.4-7.8	24-25	EC_{10} 14d (reproduction)	155	CDI 2008b
Rotifer *Philodina acuticornis*	$CoCl_2$	25	7.4-7.9	20	EC_{50} 4d (reproduction)	59 000	Buikema et al. 1974

Test Organism	Test Compound	Hardness (mg $CaCO_3$/L)	pH	T (ºC)	Endpoint and duration	Value[1] (µg Co/L)	Reference
Plants/Algae							
Duckweed *Lemna minor*	$CoCl_2$	SSI standard media	6.52-6.68	24 ± 2	EC_{10} 7d (growth)	4.9	CDI 2009e
Green algae *Pseudokirchneriella subcapitata*	$CoCl_2$	25[3]	7.51-7.72	25 ± 1	EC_{10} 4d (growth)	23	CDI 2009e
Giant Duckweed *Spirodela polyrhiza*	$CoCl_2$	12[4]	7.0	25	EC_{50} 4d (growth)	140	Gaur et al. 1994
Green algae *Chlamydomonas reinhardtii*	$CoCl_2$	12[4]	6.8	25	EC_{30} 5d (growth)	1 120	Macfie et al. 1994
Green algae *Chlamydomonas acidophila*	$CoCl_2$	200[5]	4	20	EC_{50} 4d (growth)	4 096	Nishikawa and Tominaga 2001

***Abbreviations:** EC_{xx}: The concentration of a substance that is estimated to cause some effect on XX% of the test organisms; IC_{xx}: The inhibiting concentration for a specified percent effect. A point estimate of the concentration of a test substance that causes XX% reduction in a quantitative biological measurement such as growth rate; MATC: The maximum allowable toxicant concentration, generally presented as the range between the NOEC(L) and LOEC(L) or as the geometric mean of the two measures; NR: Not reported

1: The lowest value or geometric mean is used for multiple tests with the same species, as per text (CCME 2007).

2: Only the alkalinity (mg/L) was reported in this study.

3: Calculated using the OECD 201 media Ca, Mg, Fe and Mn concentrations. Sources: http://oberon.sourceoecd.org/vl=1752526/cl=22/nw=1/rpsv/ij/oecdjournals/1607310x/v1n2/s2/p1; http://www.groundwatersoftware.com/calculator_8_water_hardness.htm

4: Calculated using the APP media Ca, Mg, Fe and Mn concentrations. Sources: http://oberon.sourceoecd.org/vl=1752526/cl=22/nw=1/rpsv/ij/oecdjournals/1607310x/v1n2/s2/p1; http://www.groundwatersoftware.com/calculator_8_water_hardness.htm

5: Calculated using the Ca, Mg, Fe and Mn concentrations. Source: http://www.groundwatersoftware.com/calculator_8_water_hardness.htm

A species sensitivity distribution (SSD) was developed using the chronic toxicity data shown in Table 7 for a total of 15 species: three fish, seven invertebrates and five plant/algae species (Figure 1). When more than one value for an endpoint was available for a single species, the final value to be used in the SSD was chosen following the guidance by the Canadian Council of Ministers of the Environment (CCME 2007). When test conditions are the same or similar (e.g. duration, endpoint, pH, hardness, etc.) the geometric mean may be taken, whereas when differences occur, the lowest value is chosen. In all cases above, the lowest value was used for the SSD generation. It is well documented that the toxicity of metals depends on the pH and ionic strength of the external media (CDI 2009b; DiToro et al. 2001). As a result, toxicity data used as input in a SSD may be normalized for the effects of pH, ionic strength and hardness, and dissolved organic carbon (Vangheluwe et al. 2007) depending on assessment needs. However, this was not done for this assessment as sufficient information could not be found for cobalt to adjust the data to account for these toxicity modifying factors. As indicated in the Bioavailability section, hardness appears to be a particularly important toxicity modifying factor for cobalt, with high hardness having a protective effect. The hardness of the waters tested was typically in the very soft to hard range (range: 12 – 250 mg/L; average: 95 mg/L, see Table 7), which is well within the range estimated for representative Canadian receiving waters (12.8 – 274 mg/L, see Table 5). As well, pH may have a large influence on the toxicity of cobalt while keeping other factors constant (Khangarot et al. 2003). The pH range of the waters tested (range: 6.5 to 8.5; average: 7.6, see Table 7) is very similar to the representative Canadian receiving waters (6.4 to 8.6, see Table 5) if we exclude the single value of 4 for an acidophilic algae test.

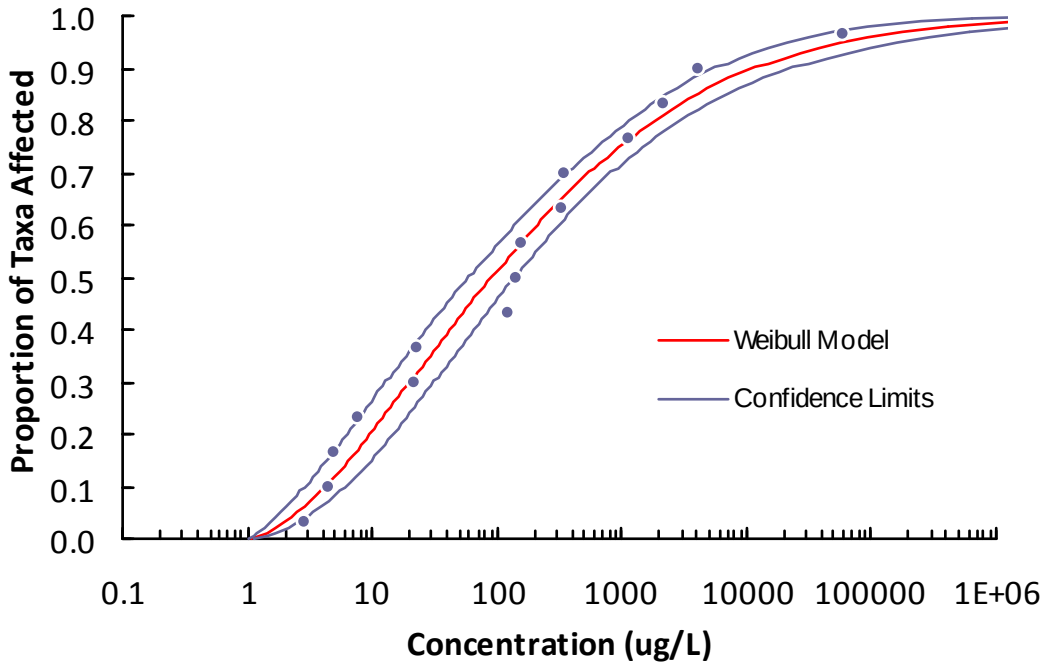


Figure 1. Species sensitivity distribution (SSD) for cobalt based on chronic toxicity data for freshwater aquatic organisms. The Weibull model fit to data is shown on the graph along with the 95% confidence intervals.

The software SSD Master v2.0 (SSD Master 2008) was used to plot the SSD. Several cumulative distribution functions (CDFs) (normal, logistic, Gompertz, Weibull and Fisher-Tippett) were fit to the data using regression methods. Model fit was assessed using statistical and graphical techniques. The best model was selected based on consideration of goodness-of-fit and model feasibility. Model assumptions were verified graphically and with statistical tests. The Weibull model provided the best fit of the models tested (Anderson-Darling Statistic (A^2) = 0.225) and the 5th percentile (HC_5), i.e., hazardous concentration to 5% of species, of the SSD plot is 2.5 µg/L with lower and upper confidence limits of 1.9 and 3.4 µg/L, respectively (Figure 1). The HC_5 of 2.5 µg/L calculated from the SSD is selected as the predicted no-effect concentration (PNEC) for toxicity to freshwater organisms.

B - In Other Environmental Compartments

Available exposure and source apportionment information were not sufficient to evaluate potential for harm to soil and sediment organisms related to the cobalt substances being assessed. Available information on the releases of the assessed substances to soils was limited and tools to predict soil concentrations were not used. As well, monitoring information was related to a mixture of cobalt-containing substances (e.g. cobalt oxide, hydroxide, sulfate) and so was considered not to be useful for assessing the substances targeted in this assessment. Therefore, a PNEC for soils was not derived in this assessment.

Monitoring values in sediments were not collected at industrial sites where the cobalt substances considered in this assessment were used (e.g. near mining areas). In addition, other sources of dissolved cobalt (originating from other compounds) could be present and contributing to sediment concentrations. Considering that aquatic concentrations resulting from the releases of the substances being assessed were modelled and high uncertainties are associated with extrapolating sediment concentrations from those in water, a PNEC for sediments was not developed for this assessment.

Ecological Exposure Assessment

As this assessment pertains to elemental cobalt, cobalt chloride and cobalt sulfate, this section will focus on exposure scenarios resulting from those anthropogenic activities identified as emitting mainly these forms of cobalt (see Releases to the Environment section). As well, this section will focus on the aquatic compartment as the medium of greatest concern for these substances, because it is mainly to this compartment that these substances are released Cobalt releases to air are expected to be a mixture including oxide and hydroxide forms (see releases section on page 19-20), and monitoring data for soil may also not be representative of the forms being assessed. Source apportionment can therefore be considered as a knowledge gap here.

Cobalt concentrations have been measured in a variety of locations and environmental media in Canada. As for other metals, monitoring data for cobalt are typically reported as total cobalt element or total dissolved cobalt. It is not possible to determine the extent to which cobalt measured in the environment originated from the cobalt compounds assessed in the present document.

Presence in the environment

Worldwide, the cobalt concentrations in relatively pristine areas are reported as 20-25 mg/kg in soil, less than 1 µg/L in surface freshwater, 0.3-1.7 µg/L in rainwater and ~1 ng/m^3 in the atmosphere in remote areas (IPCS 2006).

Levels measured in selected regions of Canada where some of the industries that manufacture or use the cobalt compounds considered in this assessment are located are summarized in Table 8. Although some of the high-end concentrations may be related to point-source contamination, the majority of the data (i.e., values up to at least the 50th percentile) are likely minimally affected by anthropogenic inputs.

Since cobalt is a naturally occurring substance, biogeochemical background levels in soil, water, sediments and groundwater contribute to overall exposures. These levels were accounted for in the screening assessment by adding estimated median background concentrations to model-predicted aquatic exposure concentrations based on point-source release. Information on environmental cobalt concentrations in minimally impacted areas is presented below. Since these areas could include samples from impacted sites, the median was taken instead of the 90th percentile.

Table 8. Concentrations of total cobalt in surface waters of selected minimally impacted areas[1] of Canada

Location[2]	Concentration range (µg Co/L)	Percentiles (µg/L)[3]			N	Reference
	Min-Max	5th percentile	Median	90th percentile		
1	0.024-3	0.035	0.16	1	220	NWRI 2009
2	0.026-2.0	0.0393	0.1	1	87	NWRI 2009
3	<d.l.-0.491	<d.l.	0.1	0.2	123	OMOE 2004
4	0.00013-6.9	0.0466	0.496	1.31	7389	OMOE 2009

n/a: not available
d.l.: detection limit
N: number of samples
1: These areas were chosen for their physical / chemical similarities with the areas for which exposure scenarios were developed or because some of the the sources assessed are within these regions.
2: Locations of the areas could not be provided to prevent disclosure of information on site locations and facilities in Tables 9 & 11.
3: Fraction: filtered (0.45 µm) for the 2 first locations and unfiltered for the 2 latter.

Exposure scenarios

As discussed in the Releases to the Environment section, some facilities in Canada extract ore containing cobalt from the earth, and then transform it into cobalt sulfate or cobalt chloride. The product is sent to another facility to produce elemental cobalt.

Releases to water from industrial activities are expected to be far more important than releases from consumer uses (e.g. batteries, paints, desiccants), which are expected to be negligible. Therefore, only industrial exposure scenarios were developed.

Seven site-specific industrial releases scenarios were developed to estimate aquatic concentrations of cobalt (Table 9) from three general areas or activities: (i) cobalt sulfate intermediate manufacturing and elemental cobalt refining; (ii) alloy and super-alloy manufacturing; (iii) cobalt hydroxide production (for batteries). For most scenarios, exposure concentrations had to be estimated because monitoring data directly relevant to these sites were not available.

i) Cobalt Production

The first scenarios are based on the information specific to five Canadian nickel/copper/cobalt smelter/refinery facilities where the highest cobalt releases are expected to occur (see Sites No.1-5 in Table 9). Elemental cobalt losses to industrial wastewater are considered only when it is in the form of a powder, because this form increases the elemental cobalt solubility. Soluble elemental cobalt and cobalt sulfate loss to industrial wastewater are estimated to be 0.081% of the total quantity used, resulting from handling during transport and wastewater from milling, separation by floatation and roasting operations (see Releases to the Environment section). NPRI and other data are used to reflect actual releases after wastewater treatment, so that the removal rate is included in the emission factor of 0.081%. The receiving water at industrial sites has a 2 to 10-fold dilution capacity, depending on the receiving waterbody size. This is in relation to the concentration in the wastewater treatment system effluent for which flows vary from approximately 12 824 to 260 000 m^3 per day for the five facilities being considered, depending upon the size of the treatment operation. It is assumed that the releases occur 250 days per year, which is typical for small and medium-sized facilities or 365 days per year for large-sized facilities. Based on the above assumptions, and taking into account the actual substance quantities manufactured for industrial use in Canada, estimated aquatic concentrations are between 0.3 and 54.3 µg/L (Environment Canada 2010a). Respective median background values for the locations (from Table 8, above) were added to the estimated aquatic concentration to calculate PEC values ranging from 0.44 to 54.4 µg/L. Values estimated are summarized in Table 9 below. The PEC for site No. 4 (4.3 µg/L) is lower than a measured value (10.9 µg/L) for this site (Table 9, footnote no. 3).

ii) Alloy and Super-alloy Manufacturing

Another scenario was developed using the information specific to the use of elemental cobalt powder to make alloys, where the highest releases are expected to occur for that specific activity (see Site No.6 in Table 9). The loss to sewer water is estimated to be 0.1% of the total quantity used, resulting from the weld dust and washing (see releases to the environment section). The scenario has the same assumptions as the smelting and refining scenario above (removal rate from wastewater treatment system and dilution capacity for the effluent). A wastewater treatment system flow of approximately 21 372 m^3 per day given the size of the treatment operation has been used. Based on the above assumptions and using the actual quantity for industrial use in Canada yielded an estimated aquatic concentration of 0.9 µg/L and a PEC of 1.0 µg/L when considering the addition of the median background value for the location (Environment Canada 2010a) (see Table 9).

iii) Battery Manufacturing

A final scenario was developed for chemical industry that produces cobalt hydroxide from elemental cobalt powder for use in the manufacture of batteries (see Site No.7 in Table 9). Measured and conservatively calculated concentrations in the industrial wastewater effluent were provided in a submission by the industry (Environment Canada

2010a). The highest concentration reported for the last 6 years (1.2 µg/L, see Table 9) was selected as the estimated aquatic concentration for this scenario (Environment Canada 2010a). Adding the median background for the location yielded a PEC of 1.7 µg/L.

Table 9. Exposure scenarios based on modeled industrial surface water releases, resulting EAC, PEC and monitored water quality parameters[1,5].

Site No.	Type of facility/industry	Combined mass range of the substance(s) at the facility	EAC[2] (as total µg Co/L)	Background[3] (as total µg Co/L)	PEC[4] (as total µg Co/L)	pH[5]	T[5] (˚C)	Hardness (mg/L $CaCO_3$)
1	Smelter/refinery #1	100 000-1 000 000 kg/year	5.4	0.1	5.5	7.9	7.1	160
2	Smelter/refinery #2	1 000 000-10 000 000 kg/year	5.4	0.1	5.5	7.9	7.1	160
3	Smelter/refinery #3	100 000-1 000 000 kg/year	0.28	0.16	0.44	7.7	14.4	N/A
4	Smelter/refinery #4	1 000 000-10 000 000 kg/year	3.8	0.5	4.3[6]	7.1	15.8	463
5	Smelter/refinery #5	1 000 000-10 000 000 kg/year	54.3	0.1	54.4	8.4	21.9	117
6	Cobalt alloy manufacturer	10 000-100 000 kg/year	0.9	0.1	1.0	8.1	N/A	115
7	Manufacturer of battery component	100 000-1 000 000 kg/year	1.2	0.5	1.7	8.2	11.3	80.7

1: Water quality parameters are measured within 10 kilometers from the sites of release.
2: Estimated Aquatic Concentration
3: From Table 8, above (median).
4: Predicted Environmental Concentration (PEC) = EAC + Background
5: References for water pH, temperature and hardness could not be provided to prevent disclosure of information on site locations and facilities.
6: The monitored unfiltered total cobalt concentration at the site of discharge was 10.9 µg/L (collected in spring 2004, one sample, downstream of a wastewater treatment system's effluent, reference not provided to prevent disclosure of information on site locations and facilities).

For comparison and to emphasize the fact that modeled aquatic cobalt concentrations similar to those presented in Table 9 may occur in the Canadian environment, general monitoring data for some of the more highly contaminated surface waters of Canada are presented in Table 10. Note that these concentrations likely resulted from releases associated with the manufacture or use of many cobalt-containing substances and likely include substances that are not considered in this document.

Table 10. Total dissolved cobalt concentrations for the highest cobalt contaminated aquatic environments in Canada

Location	Facility / Industry	Medium	Co range (µg/L)	Percentiles (µg/L)			N[2]	Reference
			min-max	5th	median	90th		
Rouyn-Noranda, QC	Ni/Cu Smelter	Sediment porewater[1]	0.006-76.73	0.28	1.27	11.6	88	Natural Resources Canada 2001
		Surface Water	0.025-1.33	0.025	0.065	0.83	98	Natural Resources Canada 2001
Sudbury, ON	Ni/Cu/Fe Smelter	Surface Water	<1.5-31	0.5	0.75	17	95	City of Greater Sudbury 2001 and 2004
Cobalt, ON	Silver mining camp	Surface Water	0.25-2028	0.25	41	1678	69	Percival et al. 1996

1: Sediment porewater: the aquatic PNEC was used to estimate an exposure concentration assuming that sediment organisms are as or more sensitive than aquatic organisms.
2: Number of samples

As it can be seen, the data from three monitoring areas (90th percentile) are in the same range or higher than the concentrations predicted and indicated in Table 9 (PECs). It has to be noted that surface water cobalt concentrations in lakes from the Rouyn-Noranda area presented above (90th percentile of 0.83 µg/L, Table 10), are likely mainly due to atmospheric deposition from smelters since these lakes do not receive cobalt inputs from liquid mining effluents. Therefore, contamination in these lakes located up to 100 km from the smelter, is likely be due to a mixture of cobalt forms (Natural Resources Canada, 2001). On the other hand, in the Sudbury area, the sites sampled are located in the vicinity of the smelters. Liquid effluents containing cobalt are most likely contributing to most of the surface water concentration levels (90th percentile of 17 µg/L, Table 10) in this area. Liquid effluents are mainly related to the substances assessed in this document (elemental cobalt in the form of powders, cobalt chloride and cobalt sulfate). However, other cobalt-containing substances may be present as well. Abandoned mine tailings near the town of Cobalt site (Ontario) are likely the source of much of the cobalt in surface waters measured by Percival et al. (1996).

Characterization of Ecological Risk

The approach taken in this ecological screening assessment was to examine various supporting information and develop conclusions based on a weight-of-evidence approach and using precaution as required under CEPA 1999. Lines of evidence considered include results from risk quotient (RQ = PEC/PNEC) calculations for key exposure scenarios, as well as information on persistence, bioaccumulation, toxicity, sources and fate of the substances.

Table 11 presents the results of risk quotient calculations based on key industrial exposure scenarios – with emphasis on the metal production industry. Risk quotients (RQs) were calculated for seven industrial facilities believed to manufacture and/or use elemental cobalt, cobalt chloride and/or cobalt sulfate in Canada. For this, site-specific estimates of exposure were made for the the actual receiving water body near each of the facilities, yielding PECs varying from 0.44 to 54.4 µg/L (see Exposure Characterization Section; Environment Canada 2010a). Results show that for four out of seven scenarios, RQs are higher than one based on exposure related to releases of the three substances combined. The RQs calculated from modelled aquatic PECs, for smelters/refineries, indicate that expected total dissolved cobalt concentrations in water bodies near sources of releases of the three substances being assessed may exceed estimated no effect levels for sensitive aquatic organisms.

Table 11. Risk quotients (RQs) calculated for key industrial exposure scenarios[1] in the aquatic compartment.

Site No.	Type of facility/industry	PEC	PNEC[1] (µg/L)	RQs[2]
Site 1	Smelter/refinery #1	5.5	2.5	**2.20**
Site 2	Smelter/refinery #2	5.5		**2.20**
Site 3	Smelter/refinery #3	0.44		0.18
Site 4	Smelter/refinery #4	4.3		**1.72**
Site 5	Smelter/refinery #5	54.4		**21.76**
Site 6	Cobalt alloy manufacturer	1.0		0.40
Site 7	Manufacturer of battery component	1.7		0.68

1: PNEC as developed in the effect characterization section
2: RQ = PEC/ PNEC.

Both PECs and PNECs have been expressed in terms of total dissolved cobalt concentrations since the limited data available did not allow for bioavailability corrections. Given sufficient data, aquatic PNECs can be adjusted for bioavailability using a Biotic Ligand Model or empirical equations that take into account pH and hardness differences. This would have permitted site-specific correction of PNECs. Instead, a comparison between the hardness and pH data from Table 7 and the site-specific information in Table 9 can be made. In general, the site-specific pH (range 7.1-8.4) and hardness (range 80.7-160 mg/L) of the receiving waters are within the ranges of the waters used in the toxicity tests listed in Table 7. However, there is one exception.

The hardness of the receiving waters for site 4 (463 mg/L) is significantly higher than the hardness of the waters used in the toxicity tests listed in Table 7 (range: 12-250; average: 95 mg/L). Correction for hardness would result in some level of increase in the PNEC for this site, with a resulting decrease in the risk quotient.

No ecological PEC, PNECs and RQs were developed for the soil, sediment and air compartments because of limitations in the information available and the expectation that the substances being assessed are not significantly emitted to air, nor further deposited onto the ground. However, exposure values for air are considered in the human health assessment below.

Cobalt ions are expected to be persistent in water, soil and sediment and so have the potential to accumulate from year to year and increase exposure in the latter two compartments. They have been demonstrated to have a high toxicity to sensitive aquatic organisms. The calculated risk quotients, which are based on predicted concentrations of total dissolved cobalt for both exposure and effects, indicate a potential risk to aquatic organisms near smelting/refining operations.

This assessment grouped three substances based on their common moiety of concern: total dissolved cobalt. However, the scope of the assessment is limited to elemental cobalt and the chloride and sulfate salts. Efforts were made throughout this ecological assessment to focus on the three substances and link assessment endpoints and exposure scenarios to the activities involving them. To the extent possible, only releases of potentially bioavailable cobalt related to the three cobalt substances were considered. Other anthropogenic sources of the metal to the environment were not systematically included, neither through use of monitoring data to estimate PECs nor in modelled scenarios. Of particular note, almost all monitoring studies report total cobalt. Such information cannot be attributed to the specific forms being assessed. The extent to which any of the three substances would individually contribute to the risk posed by the total dissolved cobalt remains uncertain.

The high manufacture and importation volumes of the three substances in Canada– particularly elemental cobalt and cobalt sulfate - along with information on their uses and the calculated RQs, support the likelihood that anthropogenic release of these substances result in concentrations of the metal at levels higher than local background concentrations in the Canadian environment. However, these substances likely constitute only a fraction of all the anthropogenic sources of cobalt in the Canadian environment. Information reported to the 1984-86 DSL survey (Environment Canada 1988) on the various cobalt compounds suggests that the three cobalt substances that are the subject of this assessment represent about ~30% of the total quantity of cobalt currently in use in Canada. The total quantity of cobalt released from all possible cobalt-containing substances was not systematically considered in this assessment. Given the concern identified in this assessment for total dissolved cobalt ions, and recognizing that many other cobalt-containing substances may contribute to the loadings of total dissolved cobalt in the aquatic compartment in Canada, a moiety-based assessment of cobalt is desirable. Such an assessment would examine the combined exposures from a much

wider range of sources covering all substances that could contribute to loadings of the moiety in the environment. It would also be possible to assess the sediments and soil compartments in such an assessment.

Based on the above information and considerations, it is concluded that elemental cobalt, cobalt chloride and cobalt sulfate are not individually causing ecological harm in Canada.

Their relative importance as contributors to the environmental loading and effects of total dissolved cobalt does however warrant further examination in a future moiety-based assessment.

Uncertainties in Evaluation of Ecological Risk

The information on the influence of abiotic factors (e.g. pH, hardness) on cobalt ecotoxicity was too limited to permit systematic evaluation of potential for aquatic toxicity in different types of water compositions across Canada. However, in general, the site-specific pH and hardness of the receiving waters is within the ranges of the waters used in the toxicity tests. Additionnaly, there is evidence that in addition to Co^{2+} ions, cobalt complexes with humic and fulvic acids may be available for uptake by some types of aquatic organisms. These two forms are estimated to comprise more than half of measured total dissolved cobalt concentrations in Canadian surface waters (see Bioavailability section).

Note that NPRI data for “cobalt and its compounds” along with section 71 specific release information were used to derive release factors used to estimate releases for most of the sites. In addition, it should be noted that PECs at each site are based on estimates of the combined releases for all cobalt substances considered in this assessment where possible because each can lead to the formation of dissolved cobalt species, including, the free ion, Co^{2+}. There is uncertainity that these release factors actually include only the substances assessed and no other cobalt substances. It is still unclear the extent to which the substances assessed are contributing to the total dissolved cobalt levels in the effluents. It should be remembered that it is on the basis of their common moiety of concern that these three cobalt substances were grouped for exposure and RQs determinations.

Since risks to benthic organisms were not assessed, there is uncertainty about whether releases of cobalt are harming sediment-dwelling biota. Accumulation of cobalt in sediments over time may increase exposure and associated risks, as sediment acts as a sink for metals (see fate section). Whether this occurs depends on the rate of accumulation of “clean” sediments (that will tend to reduce the concentration of cobalt over time), and the rate of sediment burial that eventually makes the contaminated layer inaccessible to most biota as well as diagenetic processes.

There is uncertainty about the exposure resulting from the cobalt released to soils from the substances assessed. Releases of the substances assessed to soil could not be

estimated and modelled with the current exposure tools available. In addition, releases of cobalt to soil occur as a mixture of different cobalt forms possibly including oxides and hydroxides. These forms were not assessed in this document but could be considered in a future moiety-based assessment.

Potential to Cause Harm to Human Health

Exposure Assessment

Environmental Media and Food

The analytical methods used to measure cobalt concentrations in environmental media and foods are not able to identify the different forms of cobalt (e.g. elemental, oxide, oxidation state or salt type). Therefore, intake estimates via environmental media and foods represent total cobalt. The solution behaviour of anhydrous and hydrated forms of cobalt are considered indistinguishable, as dissolution of either form produces a solution of hydrated ions and water (NTP 2002); therefore information related to the hydrates was considered relevant to informing the assessment of exposure to cobalt sulfate and cobalt chloride.

Atmospheric cobalt is generally associated with particulate matter and not as the free salts or metal (OMOE 2002c; ATSDR 2004). After inhalation, large particles may be cleared from the lungs via mucocilliary transport, and enter the digestive tract adding to the oral intake. Additionally, only a fraction of the cobalt measured in the particulate matter is soluble and available for absorption. In the United States, mean air concentrations of cobalt in urban settings is reported to range from less than 1 to 2 ng/m^3, and up to 10 ng/m^3 near industrial sources (ATSDR 2004). A human health risk assessment was conducted by the Ontario Ministry of Environment in Port Colborne, Ontario in order to evaluate potential impacts of a local refinery (OMOE 2002a). This Canadian study reported the average and maximum concentrations of cobalt in total suspended particulate matter sampled in local schools during the summer of 2000 to be 7.5 ng/m^3 and 10 ng/m^3 respectively (OMOE 2002b). Because cobalt was not extensively sampled in this Port Colborne study, the authors derived intake estimates using data collected by the National Air Pollution Surveillance (NAPS) network at nine locations across Ontario collected between 1995 – 1999, which reported the maximum and average concentrations of cobalt in air to be 17 ng/m^3 and 2 ng/m^3, respectively (OMOE 2002b). More recently, as part of NAPS, between 2003 and 2008 over 4500 measurements of cobalt from eighteen sites across Canada were collected and analyzed; 95th percentiles for each site ranged from 0.04 ng/m^3 on Sable Island, NS to 0.68 ng/m^3 in Halifax, NS; and the maximum concentrations for each site ranged from 0. 05 ng/m^3 on Sable Island, NS to 5.5 ng/m^3 in Dow Settlement, NB (NAPS 2003 – 2008). Of the major Canadian urban centres sampled, the 95th percentile, maximum concentrations were reported to be: Montreal (0.04 ng/m^3, 0.43 ng/m^3), Ottawa (0.08 ng/m^3, 0.20 ng/m^3), Toronto (0.10 ng/m^3, 0.47 ng/m^3), Edmonton (0.45 ng/m^3, 2.82 ng/m^3) and Vancouver (0.09 ng/m^3, 5.41 ng/m^3) (NAPS 2003 – 2008).

No data were identified reporting indoor air concentrations of cobalt in Canada; however, preliminary analysis of indoor and outdoor measurements of cobalt in PM2.5 and PM10 (particulate matter suspended in air up to 2.5 µm and 10 µm respectively) from Windsor, Ontario indicate higher cobalt concentrations in outdoor air than indoor air (2010

personal communication from Environmental and Radiation Health Sciences Directorate, Health Canada, to Existing Substances Risk Assessment Bureau, Health Canada; unreferenced). Consistent with these findings, a study in Singapore comparing indoor and outdoor concentrations of cobalt in PM2.5 reported cobalt levels of 0.10 ng/m^3 in the living room, 0.07 ng/m^3 in the master bedroom, 0.07 ng/m^3 in the second bedroom versus 0.08 ng/m^3 outdoors (Balasubramaniam and Lee 2007). Considering these results, a conservative estimate is obtained by using outdoor air concentrations of cobalt to represent the indoor environment.

The concentration of cobalt in air is subject to meteorological conditions and seasonal variations; therefore, exposure estimates are derived using 95th percentile concentrations. Maximum concentrations are considered most relevant when the exposure can be associated with a specific event or activity pattern. It is acknowledged that assuming complete availability and absorption of airborne cobalt represents a conservative approach. The highest 95th percentile cobalt concentration from the 2003 – 2008 NAPS data, 0.68ng/m^3, measured in Halifax, was used to estimate air intake of cobalt by the general Canadian population.

Drinking water measurements of cobalt correspond to soluble salts and suspended particulate matter. While there is currently no Canadian guideline for cobalt in drinking water (Health Canada 2008), cobalt concentrations were measured as part of the Canadian Total Diet Studies (TDS, see Foods intake for description). Average tap water measurements reported ranged from < 0.3 up to 1.5 µg/L, encompassing results from studies in 1986 to 1988 (Dabeka and McKenzie 1995), 1993 – 1999, 2000, 2001 and 2002 (Health Canada 2009b). Concentrations of cobalt in water collected at local water treatment facilities were also reported for St. John's (2001), < 0.03 µg/L and Vancouver (2002), < 0.6 µg/L (Health Canada 2009b). These area water measurements of cobalt are consistent with reports published by Canadian municipal water authorities, in annual reports, which ranged from < 0.02 µg/L to < 2 µg/L (Montréal 2000; Winnipeg 2002; Winnipeg 2003; Calgary 2004; Montréal 2004; Montréal 2005; London 2006; Montréal 2006; London 2009; Vancouver 2009; Victoria 2009). Victoria, BC reported the median of 9 samples in 2008 to be <0.5 µg/L, the 10 year (1999-2008) median value of 73 samples was <0.5 µg/L and the range over the 10 years was <0.02 – 20 µg/L (Victoria 2009). While the maximum value reported in Victoria was 20µg/L, the ten year median value is less than 0.5µg/L and since cobalt levels in water will depend on rainfall and runoff, the 20µg/L value was not considered representative. Tap water measurements are considered the most representative measurement of annual population exposure to cobalt in drinking water by the general population; therefore, the highest measured value of 1.50µg/L from the Canadian TDS was used in the calculation of daily intake.

Ingestion of dust and soil is known to be an important route of childhood exposure to metals found in paint, gasoline and other industrial sources (Duggan 1983; Mielke and Regan 1998). Cobalt concentration in soils is highly variable and can range from 1-40 µg/g (ATSDR 2004). Mines are located to take advantage of geological formations enriched in minerals of interest, therefore soil concentrations of metals in the vicinity of active or abandoned mines and refineries will be higher. In Port Colborne, Ontario,

which is located near a metal refinery, the highest reported soil concentration was 262 µg/g. This level is related to the long term atmospheric deposition of cobalt from local stack emissions (OMOE 2002b). The concentration of cobalt in Port Colborne soils, because of its association with deposition from the metal refinery, was not considered representative, and therefore was not used in the calculation of exposure estimates for the general population. However, the Ontario Ministry of Environment did evaluate the health impact of releases from this locality (OMOE 2002a).

Several studies have reported soil cobalt concentrations in North America. The average concentration of cobalt in soil in the United States is reported to be 7.2 µg/g (Barceloux 1999) and a study of two samples of street dust from moderately travelled roads in Urbana, Illinois reported an average cobalt concentration of 6.8 µg/g (Hopke et al 1980). Soil samples from thirteen locations in south western Saskatchewan were collected and analyzed to determine trace element concentrations. The soils had been cultivated and fertilized for at least thirty years; the mean and range of cobalt measured were 10.5µg/g and 3.7 to 16 µg/g respectively (Mermut et al 1996). In 1993, house dust samples were collected from 50 residences in Ottawa; street dust and garden soil were also collected within 15 m of each residence, and all samples analyzed for multiple elements including cobalt (Rasmussen et al 2001). The mean and 95th percentiles for house dusts were 8.92 and 13.10 µg/g, street dusts were 8.31 and 11.15 µg/g and garden soils were 8.36 and 11.58 µg/g, respectively. A conservative estimate of exposure to cobalt via ingestion of soil by infants and children is derived using the 95th percentile 13.10 µg/g, reported in dust in Ottawa homes.

Three international reports and one Canadian report of cobalt concentrations in human milk were identified. In Austria, the milk of 27 healthy mothers was analyzed for trace metals, the median and range of cobalt measured were 0.19µg/L and less than 0.07 to 1.20 µg/L respectively (Krachler et al 2000). A German study investigated the transfer of elements from food into human milk in a study of 19 mothers. While no simple correlation was observed between cobalt intake and transfer to milk, the mean and range of the cobalt concentrations reported for the participants was 0.85µg/L and 0.42 to 2.46µg/L respectively (Wappelhorst et al 2002). The range of breast milk cobalt concentrations reported by the World Health Organization (WHO) for samples taken in Guatemala, Hungary, Nigeria, Philippines, Sweeden, and Zaire was 0.02-4.74 µg/L (WHO 1989). A Canadian study reported levels of cobalt in the breast milk of 43 nursing mothers; the authors compare the composition of the milk from mothers of premature and full-term infants during the first three months and the range of median concentrations reported was 0 – 6 µg/L (Friel et al 1999). Eighteen median concentrations were reported; seventeen median values were less than or equal to 2 µg/L and one was 6 µg/L. While it is acknowledged that the highest reported Canadian value of 6 µg/L is unlikely representative of general population exposure, because it is greater than the values reported by the WHO from multiple countries; it is used to provide a conservative estimate of daily cobalt intake by breast fed infants.

Cobalt is an essential component of Vitamin B12; however, as previously described, the analytical methods used to measure environmental cobalt concentrations and cobalt

concentrations in foods (TDS) were not able to distinguish the forms of cobalt. Cobalt is a naturally occurring element in soil and therefore can be present at very low levels in a large number of foods via uptake by plants and livestock. Data for total cobalt levels in food, baby formula and drinking water were reported in the Canadian TDS 1986 to 1988 (Dabeka 1989; Dabeka and McKenzie 1995), 1992 to 1999 (Health Canada 2009b) and 2000 to 2002 TDSs (Health Canada 2009b)). Canadian data obtained from the 2002 TDS (Health Canada 2009b), reported cobalt levels in approximately 210 food and beverage items, purchased in three to four supermarkets (available from: http://www.hc-sc.gc.ca/fn-an/surveill/total-diet/concentration/conc-food-alim_2002-eng.php). The most recent TDS, for the year 2002, is used to estimate daily cobalt intake via food (available from: http://www.hc-sc.gc.ca/fn-an/surveill/total-diet/intake-apport/chem_age-sex_chim_2002-eng.php).

The upper-bounding estimates of daily intake of cobalt from environmental media and foods are presented in Appendix V. The highest exposure groups are estimated to be breast fed infants aged 0 – 6 months and ages 0.5 – 4 years with an estimated daily intake of 0.64 µg/kg-bw per day. The estimated cobalt intake for adults 20-59 years is 0.24 ug/kg-bw per day. Exposure on a body weight basis decreases with increasing age since food is the largest contributor to cobalt intake and younger age groups generally consume more food per kg of body weight.

Confidence in the exposure to cobalt via environmental media (air, water and soil) is high because recent Canadian studies were identified. Confidence in the exposure via food is also high; Health Canada as part of the TDS has monitored and reported cobalt levels in Canadian food products for over twenty years. Confidence in the exposure of breast fed infants is moderate because only one study of 43 nursing mothers in Newfoundland was identified. However, there is high confidence that the highest median value is conservative because all other median values were at least three times lower. Furthermore, the next highest median value is consistent with reports from other jurisdictions.

Consumer Products

The Cosmetic notification system (CNS) identified elemental cobalt in one antiwrinkle mineral mask and cobalt chloride in 9 personal care products including skin moisturizer, hair conditioner, hair grooming, facial scrub, and hair waving preparations (CNS 2009). Elemental cobalt was not added to the antiwrinkle mask; however, cobalt is present in the seaweed used as an ingredient in this product. As elemental cobalt is not naturally occurring (IPCS 2006), the cobalt in the product is unlikely to be in elemental form.

The maximum concentration reported in the CNS was used to derive exposure estimates from products containing cobalt chloride for adult Canadians. As the vapour pressure of cobalt and its salts is very low, and no products applied as a spray were identified, only dermal exposures were estimated using ConsExpo 4.1 (ConsExpo 2006); details are included in Appendix VII. The upper-bounding estimate of cobalt chloride intake from

the use of products applied to the skin is 2.1×10^{-5} mg/kg-bw per day (equivalent to 6.0×10^{-6} Co/kg-bw per day) (Appendix VI).

Confidence in the numerical values for exposure via personal care products is low, as only concentration ranges were reported, and the function of cobalt and cobalt chloride in the products was not known; therefore it is possible that the products contain forms of cobalt other than those addressed in this assessment. Confidence is high that the estimates for exposure via personal care products are protective because the approach assumes that all products contain the maximum concentration in the reported range. In an *in vitro* study in which the penetration of cobalt through skin was tested by applying the metal dispersed in synthetic sweat onto intact human skin, following an EDETOX (Evaluations and predictions of dermal absorption of toxic chemicals) protocol, cobalt ions were measured in the receiving phase at 0.009 to 0.089% of the total ion amount (Filon et al 2009). Thus the use of an absorption factor of 1% is conservative.

Health Effects Assessment

An overview of the toxicological database for elemental cobalt, cobalt chloride, and cobalt sulfate is presented in Appendix VIII. All exposure concentrations are expressed in terms of total cobalt. Much of the available data on cobalt toxicity in laboratory animals is for soluble cobalt (II) salts including the chloride and sulfate, with studies on the nitrate and acetate salts included as supporting information only. These salts are expected to dissociate in physiological media to generate Co^{2+} cations and are therefore considered to be toxicologically equivalent. Studies with both the anhydrous and hydrated forms of the soluble Co (II) salts are considered relevant, as they are expected to be indistinguishable in solution. In biological media, elemental cobalt particles can bind to proteins, and may be oxidized to generate Co^{2+} ions. The systemic effects of elemental cobalt are likely primarily due to cations which are released from the particles and absorbed, whereas local effects may be due to both the ions released and the particles themselves at the point of contact (i.e., lungs or skin) (reviewed in ATSDR 2004, IPCS 2006, IARC 2006).

Oral absorption of cobalt in humans depends on the form of cobalt, the dose, and the nutritional status of the individual. Absorption from the gastrointestinal tract increases with solubility and with iron deficiency. Estimates of the absorption of cobalt chloride in humans range from 5 to 44% of the administered dose. There is no human data on the distribution of cobalt following oral absorption, but studies in laboratory animals indicate increased cobalt levels primarily in liver, as well as in other organs. In humans, orally administered cobalt is primarily eliminated in feces (reviewed in IPCS 2006).

Following inhalation exposure to cobalt, large particles are deposited in the upper respiratory tract where they are subject to mechanical clearance, including transfer to the gastrointestinal (GI) tract. Smaller particles are deposited in the lower respiratory tract where they may be solublized and absorbed, or phagocytosed. Solubility affects clearance from the lung, with faster absorption into blood and subsequent elimination for more soluble cobalt compounds. Data on animals suggest that urinary excretion rates

correlate with the translocation rate into blood, and fecal excretion rates correlate with the clearance rate to the GI tract (reviewed in IPCS 2006).

The International Agency for Research on Cancer (IARC) has classified elemental cobalt and soluble cobalt (II) salts as Group 2B carcinogens (possibly carcinogenic to humans) based on inadequate evidence in humans and sufficient evidence in experimental animals (IARC 2006). Cobalt chloride and cobalt sulfate have been classified by the European Commission as Category 2 for carcinogenicity (should be regarded as if it is carcinogenic to man) (European Commission 2004a,b; ESIS 2006). The US NTP considers cobalt sulfate to be "reasonably anticipated to be a human carcinogen" based on sufficient evidence of carcinogenicity in experimental animals (NTP 2005a).

Available studies on the carcinogenicity of cobalt in humans are based on occupational exposure to cobalt, often in the presence of carbides such as tungsten carbide (WC). Due to co-exposure with other substances, the data were insufficient for IARC to conclude on the carcinogenic potential of elemental cobalt alone. Data on the carcinogenicity of elemental cobalt in experimental animals consist of studies done by injection or implantation (intra-muscular, subcutaneous, intra-osseous, intra-peritoneal, intra-thoracic, and intra-renal); and the only study on carcinogenicity of cobalt chloride in experimental animals was done by subcutaneous injection. Injection or implantation site tumours were observed in some of these studies; however, the relevance of data from these routes of administration to carcinogenicity in humans is unclear.

A 2 year inhalation study was conducted on cobalt sulfate in mice and rats (NTP 1998; Bucher 1999). Exposure to aerosols of 0.11, 0.38, or 1.14 mg Co/m^3 induced a concentration-related increase in benign and malignant alveolar/ bronchiolar tumours in both species and sexes (significant at high-concentration for male mice and rats; significant at mid- and high-concentrations for female mice and rats). There was also a concentration-related increase in incidence of benign and malignant adrenal tumours (pheochromocytomas) in the exposed female rats (significant at the high dose). Although a common age-related tumour in males, pheochromocytomas are much less commonly seen in untreated females. The investigators considered the increased incidence of this tumour type to be an "uncertain" finding because it was seen only in the top dose group and was not supported by increased incidence or severity of hyperplasia (IARC 2006). The NTP concluded there was 'clear evidence of carcinogenicity' in male and female mice and female rats; and 'some evidence of carcinogenicity' in male rats.

Cobalt chloride and cobalt sulfate are classified as Category 3 mutagens ("cause concern for man owing to possible mutagenic effects") by the European Commission (European Commission 2004a,b; ESIS 2006). *In vitro* mutagenicity assays in bacteria with soluble cobalt (II) salts were primarily negative both with and without activation. Mixed results were obtained in bacterial indicator assays for DNA damage (Rec assay in *B. subtilis*). In yeast, mainly positive results were obtained in mutagenicity and gene conversion assays in *S.cerevisiae* strains without activation. In mammalian cells *in vitro*, mutagenicity and cell transformation assays gave mixed results. However, cobalt chloride induced DNA damage (strand breaks and DNA-protein cross links), chromosome damage (micronuclei

and sister chromatid exchanges) and aneuploidy in rodent and human cells in culture. Negative results were obtained for cobalt acetate and cobalt nitrate in chromosomal aberration assays in human cells in culture. Elemental cobalt particles induced DNA damage (strand breaks) and chromosome damage (micronuclei) *in vitro*. (See Appendix VIII for study details and references)

In vivo, a single intraperitoneal injection of cobalt chloride induced micronuclei in mouse bone marrow (Suzuki et al 1993). Cobalt chloride also induced aneuploidy, pseudoploidy and hyperploidy in the bone marrow and testes of hamsters when dosed intraperitoneally over 9 days (Farah 1983); and chromosome aberrations in the bone marrow of mice given a single oral dose (Palit et al 1991a,b,c,d). In *Drosophila melanogaster*, cobalt chloride was positive in the wing spot test (Ogawa et al 1984), and cobalt nitrate was positive for gene mutations, chromosomal deletion, non disjunction or mitotic recombination (Yesilada 2001). Mice exposed to cobalt dust by inhalation for 13 weeks did not have an increase in micronuclei in the peripheral blood (NTP 2005b). There was no indication of increased DNA strand breaks or micronuclei in blood lymphocytes of 35 workers in a cobalt refinery exposed to cobalt dust compared to 27 unexposed workers (De Boeck et al 2000).

The overall evidence shows that cobalt metal particles and soluble cobalt (II) salts have the capacity to cause DNA damage and chromosomal damage *in vitro.* Although *in vivo* data for cobalt particles are limited, the *in vivo* data for cobalt chloride are consistent with the *in vitro* data for soluble cobalt (II) salts.

It is considered likely that cobalt induces DNA damage through the generation of reactive oxygen species (ROS) and increased cellular oxidative stress. Some of the supporting evidence is described below. Both elemental cobalt particles and Co^{2+} ions have been shown to generate ROS under biologically relevant conditions. An aqueous suspension of elemental cobalt particles (0.1 to 1.5 µm) was found to react with dissolved oxygen, forming a strong oxidant, likely $Co\text{-}O\text{-}O^{\bullet}$, and in the presence of either superoxide disumatase or Fe^{2+} ions the oxidant was found to release hydroxyl radicals (Leonard et al 2006). In pH 7.4 phosphate buffer, free Co^{2+} ions promoted the conversion of hydrogen peroxide to the superoxide anion; however in the presence of chelating peptides such as glutathione, conversion of hydrogen peroxide to hydroxyl radicals was observed (Hanna et al. 1992; Shi et al 1993). This Fenton-type mechanism generated ROS in both *in vitro* and *in vivo* studies (Moorhouse et al., 1985; Kadiiska et al.,1989; Kawanishi et al., 1994; Lloyd et al., 1997 – all cited in IPCS 2006).

In vitro and *in vivo*, exposure to soluble cobalt leads to increased indices of oxidative stress (Lewis et al., 1991 cited in IPCS 2006; Hoet et al., 2002 cited in IPCS 2006). In the presence of hydrogen peroxide, cobalt(II) stimulates *in vitro* formation of 8-hydroxy-2'-deoxyguanosine (8-OH-dG) (Ivancsits et al. 2002), and cobalt sulfate induces DNA cross-links (Lloyd et al 1997). *In vivo*, cobalt acetate induced oxidative DNA damage in the liver, kidney, and lungs of rats given a single intraperitoneal injection (Kasprzak et al 1994). Additional suggestive evidence of an oxidative stress mechanism of DNA damage in tumour induction also comes from the examination of tumours from cobalt

sulfate-exposed mice, in which the frequency of base pair transversion (guanine to thymine) in codon 12 of the K-ras oncogene was 55% compared with none in the lung tumours of the control mice (NTP 1998).

A second potential mechanism contributing to the indirect genotoxicity of cobalt is the inhibition of DNA repair processes, possibly through competition with other essential ions and binding to zinc finger domains in DNA repair proteins. *In vitro*, cobalt (II) inhibits the mammalian repair protein Xeroderma pigmentosum group A (XPA), which contains zinc finger domains (Asmuss et al 2000; Kopera et al 2004). Cobalt chloride and cobalt acetate inhibited DNA repair following UV-induced DNA damage in human cells in culture, by inhibiting the incision and polymerization steps, but not the ligation step (Snyder et al 1989; Kasten et al 1997). In a small epidemiological study in which workers were exposed to cobalt dust, individuals with variations in several DNA repair genes had higher incidences of genotoxicity markers in the lymphocytes (Mateuca et al 2005). (reviewed in IARC 2006, IPCS 2006, Beyersmann and Hartwig 2008).

Cobalt choride and cobalt sulfate are classified by the European Union as Category 2 Reproductive toxicants ("should be regarded as if they impair fertility in humans") (European Commission 2004a,b; ESIS 2006). No data on the potential for reproductive toxicity of elemental cobalt or soluble cobalt (II) salts in humans were available; however, effects on the male reproductive system have been observed in rodents. Male mice were given cobalt chloride in the drinking water at up to 800 ppm (0, 6.4, 11.6, or 23.0 mg Co/kg-bw per day) for 12 weeks, then mated with untreated females. At all doses, there were decreased implantations, increased number of resorptions, decreased number of viable fetuses, and decreased sperm counts; and at the 2 higher doses, there was also decreased relative testes weight, and testes necrosis and degeneration (Elbetieha et al 2008). Reduced fertility, decreased sperm concentration and motility, testicular atrophy, degeneration and necrosis were also reported in several other studies in male mice and rats given higher oral doses of cobalt chloride (Nation et al 1983; Domingo et al 1984; Corrier et al 1985; Mollenhaur et al 1985; Pedigo et al 1988; Anderson et al 1992, 1993; Pedigo and Vernon 1993). In a 13-week study in mice exposed to cobalt sulfate aerosols by inhalation, sperm motility was decreased at 1.14 mg Co/m^3 and higher; and at 11.38 mg Co/m^3, there was testicular atrophy, increased abnormal sperm, and decreased testes weight (Bucher et al 1990; NTP 1991).

No data on the potential for developmental toxicity of elemental cobalt or soluble cobalt (II) salts in humans were available, but developmental toxicity studies have been conducted in rats, mice and rabbits. In pregnant rats dosed with cobalt sulfate by gavage at 5.2, 10.5, or 21 mg Co/kg-bw per day during gestation, there was a statistically significant increase in frequency of skeletal retardation, decreased pup body weight at postnatal days 1 and 7, decreased survival from birth to postnatal day 5, and delays in postnatal developmental parameters (ear opening, incisor eruption, descending of testes, swimming performance and auditory reflex), relative to controls. By postnatal day 21, body weight, developmental parameters, and survival rates (day 5-21) had returned to control levels. Some maternal toxicity was observed at the high dose (increased relative weight of liver, adrenals and spleen; serum alterations) (Szakmary et al. 2001).

In an earlier study, when pregnant rats were treated with cobalt chloride at 6.2 to 24.8 mg Co/kg bw per day throughout gestation, there was no effect on fetal growth or size, and no teratogenicity observed despite maternal toxicity (decreased body weight gain and food consumption, and altered haematology) (Patternain et al 1988). However, when female rats were given cobalt chloride from day 14 of gestation to day 21 of lactation at similar doses, pups had decreased body weight, length, liver and spleen weights. Effects in the dams were not discussed in this study, but the authors stated that maternal toxicity had been observed in other studies at similar doses, indicating that developmental effects could be secondary to effects on the dams (Domingo et al. 1985).

In mice, when dams were treated with cobalt sulfate at 10.5 mg Co/kg-bw per day throughout gestation, an increased frequency of pups had reduced body weights (although the average pup body weight was not different from controls). Pups also had skeletal retardation and abnormalities of eyelids, kidneys, cranium and spine. No maternal toxicity was reported. In rabbits, when dams were treated with cobalt sulfate at 4.2 to 42.0 mg Co/kg-bw per day throughout gestation, an increased frequency of pups had reduced body weights (although the average pup body weight was not different from controls). Dams had a significantly decreased body weight gain. No signs of teratogenicity were reported in rabbits (Szakmary et al. 2001).

In humans, cobalt has been shown to stimulate red blood cell production. A transient increase in red blood cell numbers and haemoglobin levels was observed in a study of 6 adult male volunteers dosed orally with cobalt chloride at approximately 1mg Co/kg/day for 3 weeks (Davis and Fields 1958). Similar effects were observed in anephric patients given cobalt chloride as treatment for anaemia at approximately 0.16 to 0.32 mg Co/kg-bw per day for several months (Duckham and Lee 1976; Taylor et al 1977). Pregnant women given cobalt chloride during the third trimester at 0.45 to 0.62 mg Co/kg-bw per day did not have increased haemoglobin and red blood cells (Holly 1955).

In short term and subchronic studies on cobalt chloride in rats, polycythemia and increased haemoglobin were induced at doses of 0.5 mg Co/kg bw/day and above (Stanley et al 1947; Murdock 1959; Krasovskii and Fridlyand 1971).

In the mid-1960s, a series of case reports were published describing lethal cardiomyopathy in subjects in North America and Europe who drank large quantities of beer containing cobalt sulfate, which was added by some breweries as a foam stabilizer. The exposure to cobalt from beer in these subjects was estimated to be 0.04 to 0.14 mg Co /kg-bw per day, based on a cobalt concentration in beer of 1 to 1.5 mg/L and consumption of 8 to 30 pints per day (reviewed in ATSDR 2004, IPCS 2006). Potential influences on the victims' susceptibility included a protein-poor diet and the possibility of existing cardiac damage from alcohol abuse.

In rats given cobalt sulfate in the diet for 24 weeks at 8.4 mg Co/kg-bw per day, cardiac enzyme activity and mitrochondrial ATP production were significantly reduced. The hearts of treated animals were isolated and were found to have left ventricular hypertrophy and impaired ventricular function (Haga et al 1996; Clyne et al 2001). Rats

treated with cobalt sulfate at 26 mg Co/kg-bw per day for 8 weeks or cobalt chloride at 12.4 mg Co/kg-bw per day for 3 weeks had cardiac degeneration (Grice et al 1969; Morvai et al 1993). Guinea pigs given cobalt sulfate at 20 mg Co/kg-bw per day for 5 weeks had abnormal EKGs, increased heart weight, and cardiac lesions (Mohiuddin et al 1970).

In some anaemic patients, cobalt therapy at doses of 2.8 to 3.9mg Co/kg bw per day for 3 to 8 months led to thyroid hyperplasia and enlargement (Gross et al 1955; Kriss et al 1955). Thyroid hyperplasia was also reported in some victims of beer drinkers' cardiomyopathy (Bonenfant et al 1969; Alexander 1972). Thyroid necrosis was observed in mice dosed by the oral route for 15 to 45 days with cobalt chloride at 26 mg Co/kg bw/day (Shrivastava et al 1996).

In a cross-sectional study of 194 workers (166 men and 28 women) in the diamond polishing industry exposed to cobalt dust, a LOAEC of 0.0151 mg Co/m^3 was determined based on a significant increase in the prevalence of eye, nose, and throat irritation and cough; and reduced lung function compared to 59 unexposed control workers (46 men and 13 women). A NOAEC of 0.0053 mg Co/m^3 was also determined. Cobalt exposure groups were defined based on air measurements at the time of the study, and exposure was confirmed by measurement of cobalt in urine. The duration of employ ment was not discussed (Nemery et al 1992). In another cross-sectional study, workers in a cobalt refinery who were exposed to cobalt metal, salts and oxides for up to 39 years at an average concentration of 0.125 mg Co/m^3 had increased dyspnoea and wheezing, and decreased lung function compared to unexposed controls (Swennen et al 1993). Linna et al (2003) also found that asthma symptoms were more prevalent in workers in a cobalt plant who were exposed to cobalt compounds. In a study on the effects of cobalt exposure on the heart, Linna et al (2004) reported no significant differences in the electrocardiograms, blood pressure, heart rate, or clinical chemistry between 203 cobalt-exposed workers and 94 unexposed controls (See Appendix VIII for study details)

Many of the epidemiological studies on inhalation exposure to cobalt have been conducted on workers in the hard metal industry where subjects are co-exposed to elemental cobalt and other substances such as tungsten carbide. It is difficult to assess the effects of cobalt alone from these studies as the toxicity of cobalt metal is increased in the presence of tungsten carbide, and it has been proposed that a mixture of cobalt and tungsten carbide behaves as a unique entity (IARC 2006). Studies on exposure to hard metal were not reviewed for this assessment.

The US National Toxicology Program (NTP) has conducted 13-week and 2-year inhalation studies in rats and mice exposed to cobalt sulfate at 0 to 11.38 mg Co/m^3. In both rat and mouse, all tested concentrations resulted in a 'spectrum of inflammatory, fibrotic and proliferative lesions,' in the nose, larynx and lung with increasing severity at higher exposures (Bucher et al 1990,1999; NTP 1991,1998)

Cobalt has been classified for inhalation and dermal sensitization by the EU ("May cause sensitization by inhalation and skin contact"). Bronchial asthma has been described in workers exposed to various forms of Cobalt, including 'pure' cobalt particles and other

cobalt compounds including cobalt salts. Contact dermatitis in humans is common: in several large studies, patch tests have detected sensitization to cobalt in up to 10% of patients. However, the exposure conditions resulting in sensitization are not clear (reviewed in ATSDR 2004, IPCS 2006).

The confidence in the health effects database is moderate to high. Data on acute toxicity, repeated-dose toxicity, carcinogenicity, genetic toxicity, and reproductive and developmental toxicity in experimental animals are available, although no chronic oral studies are available. Studies in humans include occupational exposure to inhaled cobalt as well as short-term oral studies on cobalt salts in anaemic patients and longer-term oral exposure to cobalt sulfate in beer drinkers. The database is limited by the small number of subjects in the oral studies on humans, as well as by the absence of healthy controls in those studies. Inhalation studies in humans are limited as most are in occupational exposure scenarios where other substances are present (ie hard metals), and exposures are difficult to quantify.

Characterization of Risk to Human Health

Based principally on the evidence-based assessments of international and other national agencies, a critical effect for the characterization of risk to human health for elemental cobalt, cobalt chloride, and cobalt sulfate is carcinogenicity. Concentration-related increases in lung tumours were observed in both sexes of rats and mice exposed to cobalt sulfate by inhalation; female rats also had an increase in adrenal tumours at the highest test concentration. Epidemiological studies have not shown an increase in lung cancer in humans exposed to cobalt by inhalation. Although no studies of cancer from oral exposure to cobalt in humans or in experimental animals were identified, the available short-term and subchronic data do not provide any indication of carcinogenic potential following oral exposure to cobalt or soluble cobalt (II) salts.

In vitro and *in vivo* genotoxicity data on elemental cobalt and soluble cobalt (II) salts indicate that these substances can cause DNA and chromosome damage. However, these effects are likely mediated by indirect mechanisms including the generation of reactive oxygen species, increased oxidative stress, and inhibition of DNA repair enzymes. As the tumours observed in experimental animals are unlikely to have resulted from direct interaction with genetic material, a margin of exposure approach is used to assess risk to human health.

Due to its capacity to stimulate red blood cell production, cobalt has been used as a treatment for certain types of anaemia. Increased red blood cell numbers and hemoglobin concentration have been observed in volunteers and anaemic patients given cobalt salts orally at daily doses ranging from 0.16 to 1 mg Co/kg-bw, for periods of several weeks to several months.

In the 1960s a number of cases of fatal cardiomyopathy in beer drinkers was linked to the addition of cobalt sulfate to the beer as a foam stabilizer. An estimated human LOAEL of 0.04 mg Co/kg-bw per day has been reported by other international and national

agencies, based on a cobalt sulfate concentration of 1-1.5mg/L and consumption of 8-30 pints daily for several years (ATSDR 2004; IPCS 2006). As the effect level is lower than the doses safely used to treat anaemia, it is suspected that dietary insufficiencies, prior cardiac damage from excessive alcohol consumption, or synergism with concomitant chronic exposure to alcohol may have caused the affected population to be more susceptible to the effects of cobalt. The LOAEL of 0.04 mg Co/kg-bw per day was selected as the critical effect level for the calculation of conservative margins of exposure for the oral route, even though evidence exists of therapeutic use of cobalt at higher doses.

Thyroid abnormalities including hyperplasia were observed in some anaemic patients given cobalt salts at doses of 2.8 to 3.9 mg Co/kg bw per day for several months, as well as in some of the fatal cases of beer drinkers' cardiomyopathy.

The lowest oral LOEL in experimental animals is 0.5 mg/kg-bw per day based on polycythemia in rats treated for up to 7 months with cobalt chloride. There is some evidence for reproductive and developmental toxicity of soluble cobalt (II) salts in rodents, but only at oral doses more than 100 times greater than the critical effect level of 0.04 mg/kg-bw per day in humans. The lowest oral LOEL for developmental toxicity was 5.2 mg Co/kg-bw per day in rats; and the lowest oral LOEL for toxicity to the male reproductive system was 6.4 mg Co/kg-bw per day in mice.

The principle source of exposure to cobalt by the general population is diet, which is consistent with several reports from the United States and other developed nations. Data from outside of Canada are typically reported as total cobalt intake per day, thus for comparison purposes, the intake estimate in Appendix V was multiplied by the appropriate body weight, giving an estimate of total cobalt intake for the 20–59 years age group of 17 µg/day. Iyengar et al. compared the estimated intake of cobalt by the male 25-30 years age group for two diet studies. (Iyengar et al. 2000) The first was the United States Food and Drug Administration (US-FDA) TDS for 1982-1984 which sampled regionally four times per year. The second was from an initiative by the International Atomic Energy Agency (IAEA), where excess portions of food samples collected for the TDS were analyzed by the National Institute of Science and Technology and where food composites were prepared according to USDIETS (US diet composites). The US-FDA TDS reported an average dietary cobalt intake of 11 ug/day and the USDIETS analysis reported 14 ug/day. The 1994 United Kingdom TDS estimated average daily intake for the general population was 12 ug/day and the upper bounding intake estimate by adult consumers was 19 ug/day. (Ysart et al 1999). A study conducted in France estimated an average cobalt intake by adults of 29 ug/day (Biego et al 1998). A study on dietary metal exposure carried out at the University of Valencia in Spain estimated daily cobalt intakes of 26 ug/day for university students eating at the campus cafeteria (Barbera et al. 1993). In Australia, an estimated daily intake of 34.2 ug/day was reported based on the cobalt concentrations measured in 150 food and beverage items. (Hokin et al 2004a,b) The WHO has estimated daily cobalt intakes via food of 5-45 ug/day. (WHO 1994) Based on these data, the daily dietary intake of cobalt by Canadians (17 µg/day) is similar to that reported in other developed nations.

The upper bounding estimate for daily intake of cobalt from ingestion of environmental media and food is 0.64 µg/kg-bw per day (0.00064 mg/kg-bw/day) for breast-fed infants 0 – 6 months of age and for children 0.5 – 4 years of age.

Comparison of the critical effect level for repeated-dose toxicity via the oral route (i.e., the LOAEL of 0.04 mg/kg-bw/day) with the upper bounding estimate of general population exposure (i.e., 0.00064 mg/kg-bw/day) results in a margin of exposure (MOE) of approximately 62.5. The critical effect level selected is very conservative as it is at the lower end of the range of estimates for cobalt exposure in a small group of highly sensitive subjects with cobalt intake associated with use as a beer antifoaming agent, poor diet and lifestyle. In contrast, significantly higher therapeutic doses ranging from 0.16 to 1 mg Co/kg-bw per day have been reported in anemic patients and healthy volunteers (Duckham and Lee 1976; Taylor et al 1977) and in the treatment of haemodialysis patients (Edwards and Curtis 1971)

The target organs of inhalation exposure to cobalt in both experimental animals and humans is the respiratory system, including the lungs. The critical effect level identified from animal and human studies is a LOAEC of 0.0151 mg Co/m^3 in workers in diamond-polishing workshops exposed to cobalt dust. There was a significantly higher prevalence of eye, nose and throat irritation and cough, and reduced lung function in the high exposure group (0.0151 mg Co/m^3) compared to the low exposure group (0.0053 mg Co/m^3) and unexposed control workers. A NOAEC of 0.0053 mg/m^3 was determined in this study (Nemery et al 1992).

In mice and rats, respiratory tract lesions were observed following inhalation exposure to cobalt sulfate at all tested concentrations (0.11 to 1.14 mg Co/m^3) for 2 years. A concentration-dependent increase in lung tumours was also observed (significant at 1.14 mg Co/m^3 in male mice and rats and at 0.38 and 1.14 mg Co/m^3 in female mice and rats). The lowest dose at which tumours were observed in rodents (i.e., 0.38 mg Co/m^3) is 25 times higher than the critical effect level in humans (i.e., 0.0151 mg Co/m^3). Evidence of toxicity to the male reproductive system was observed in a 13-week study in mice exposed to cobalt sulfate at 1.14 to 11.38 mg Co/m^3.

Using the highest 95th percentile cobalt concentration in ambient air reported between 2003 – 2008 as part of the NAPS program (i.e., 6.8×10^{-7} mg/m^3), the maximum daily intake via inhalation is estimated to be <0.001 µg/kg-bw per day (<0.2% of the oral daily intake). Comparison of the critical effect level for repeated-dose inhalation toxicity (i.e., a LOAEC in humans of 0.0151 mg/m^3) with the upper bounding estimate of general population exposure (i.e., 0.68 ng/m^3) results in a margin of exposure of approximately 22,000.

The margins of exposure for oral and inhalation exposure to cobalt are considered adequate to address uncertainties in the health effecs and exposure databases.

As indicated, elemental cobalt, cobalt chloride and cobalt sulfate are primarily used as industrial substances in the manufacture of products such as cobalt containing alloys, cemented carbides, oxides, and other salt forms which where not evaluated in this assessment. Cobalt alloys and cemented carbides are widely used in applications where high strength, temperatures or corrosion resistance are required. Cobalt alloys are also used in medical and dental implants, which are subject to regulatory approval processes. Cobalt oxides and salts are commonly found in batteries and magnetic recording media (e.g. computer hard drives); release of cobalt from these products is considered negligible. Due to the high strength and wear resistance of these materials, exposure by the general population is expected to be negligible, and any available cobalt from these sources is considered to be captured in measurements of environmental media: house dust, soil and air.

Exposure estimates were derived for personal care products, though the actual concentrations and forms of cobalt are not known with precision. The upper-bound estimate of intake from the use of personal care products containing cobalt chloride is 2.1×10^{-5} mg/kg-bw per day from dermal exposure (equivalent to 6.0×10^{-6} mg Co/kg-bw per day). These estimates of systemic exposure to cobalt, assuming 1% absorption by the dermal route, are highly conservative because the amount of cobalt that penetrates human skin is very low (Filon et al 2004, 2009).

Comparison of the critical effect level for repeated-dose toxicity via the oral route (i.e., the LOAEL of 0.04 mg/kg-bw/day) with the upper bounding estimate of cobalt exposure from consumer products containing cobalt chloride (i.e., 6.0×10^{-6} mg/kg-bw/day) results in a margin of exposure of approximately 6700. Dermal sensitization and allergic contact dermatitis to cobalt are also potential hazards however, the exposure levels required to induce sensitization or to cause a reaction in sensitized individuals have not been characterized.

Uncertainties in Evaluation of Risk to Human Health

The mode of action of carcinogenicity has not been fully elucidated; however the available data indicate that key steps through which cobalt induces DNA damage are indirect, such as generation of reactive oxygen species generation and inhibition of DNA repair enzymes. In addition, the only evidence of cobalt carcinogenicity is increased tumours observed at the mid- and high- doses of one rodent study following inhalation exposure to cobalt sulfate. However, the primary route of exposure to cobalt for the general population is oral (inhalation exposure is estimated to be 0.16% of total exposure). There are limited health effects data on the chronic effects of oral exposure to cobalt; however, there is no evidence in the available short-term and subchronic studies that would indicate cancer as a potential endpoint following oral exposure.

There is some uncertainty in the characterization of exposure to cobalt from environmental media and food. Only one Canadian study reporting cobalt concentrations in human milk was identified, but use of the highest reported median concentration provides a conservative exposure estimate. As described in the Exposure Assessment

section, cobalt concentrations in environmental media and food represent all forms of cobalt. Uncertainty exists regarding the extent to which elemental cobalt, cobalt chloride and cobalt sulfate contribute to total cobalt intake. Considering this, deriving an exposure estimate based on total cobalt provides a conservative estimate of daily intake of the substances considered in this assessment from environmental media and food.

Exposure to total cobalt, (i.e. including alloys, carbides oxidic and other salt forms) from the use of consumer products was not evaluated in this assessment. There is uncertainty in the presence, form, and concentrations of cobalt, cobalt chloride and cobalt sulfate in consumer products due to limited information. Therefore, exposure estimates from the use of consumer products containing these substances were based on conservative assumptions.

Conclusion

Based on the information presented in this final screening assessment, it is concluded, at this time, that elemental cobalt, cobalt sulfate and cobalt chloride are not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

On the basis of the adequacy of the margins between upper-bounding estimates of exposure and critical effect levels in humans, it is concluded that elemental cobalt, cobalt chloride, and cobalt sulfate are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore concluded that elemental cobalt, cobalt chloride and cobalt sulfate do not individually meet any of the criteria set out in section 64 of CEPA 1999. Additionally, elemental cobalt, cobalt chloride and cobalt sulfate meet the criteria for persistence but not for bioaccumulation as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

The ecological risks of the total dissolved cobalt moiety and relative importance of these three substances as contributors to the environmental loading and effects of total dissolved cobalt do however warrant further examination. It is proposed that these and other substances contributing to the total loadings of the cobalt moiety in the environment be considered in a future moiety-based assessment.

The three substances will be considered for inclusion in the *Domestic Substances List* inventory update initiative. In addition and where relevant, research and monitoring will support verification of assumptions used during the screening assessment.

References

Adam C, Baudin JP, and Garnier-Laplace J. 2001. Kinetics of 110mAg, 60Co, 137Cs, and 54Mn Bioaccumulation from water and Depuration by the Crustacean Daphnia Magna. Water Air Soil Pollut. 125: 171-188.

Adeyeye EI. 2002. Determination of the chemical composition of the nutritionally valuable parts of male and female common West African fresh water crab *Sudanautes africanus africanus*. Int. J. Food Sci. Nutr. 53:189-196.

Agbayani E, Laxamana EF. 2009. *Microcosmus sulcatus*. SeaLife Base [Internet]. Cited 2010 Mar 3. Available from http://www.sealifebase.org/summary/SpeciesSummary.php?id=83779.

Alberta Environment. 2010. Surface water quality data [database on the Internet]. Edmonton (Alta): Government of Alberta. [Updated in 2010; cited 2010 Jan]. Available from: http://environment.alberta.ca/2024.html.

Alexander CS 1969 Cobalt and the heart. Annals of Internal Medicine. 70:411–413. [cited in IPCS 2006]

Alexander, C.S. 1972 Cobalt-beer cardiomyopathy. A clinical and pathologic study of twentyeight cases. Am. J. Med. 53: 395–417

Allison JD, Allison TL. 2005. Partition Coefficients for Metals in Surface Water, Soil, and Waste. Washington (DC) U.S. Environmental Protection Agency, Office of Research and Development. Report No.:EPA/600/R-05/074. Contract No : 68-C6-0020.

Alvarez-Puebla RA, Valenzuela-Calahorro C, Garrido JJ. 2004. Retention of Co(II), Ni(II), and Cu(II) on a purified brown humic acid. modeling and characterization of the sorption process. Langmuir 20: 3657-3664.

Amacher, D.E., Paillet, S.C. 1980. Induction of trifluorothymidine-resistant mutants by metal ions in L5178Y/TK+/– cells. Mutat. Res. 78: 279–288 [cited in IARC 1991, IARC 2006]

Anard, D., Kirsch-Volders, M., Elhajouji, A., Belpaeme, K., Lison, D. 1997. In vitro genotoxic effects of hard metal particles assessed by alkaline single cell gel and elution assays. Carcinogenesis. 18: 177–184 [cited in IARC 2006]

Andersen, O. 1983 Effects of coal combustion products and metal compounds on sister chromatid exchange (SCE) in a macrophage-like cell line. Environ. Health Perspect. 47: 239–253 [cited in IARC 1991, IARC 2006]

Anderson MB, Pedigo NG, Katz RP, et al. 1992. Histopathology of testes from mice chronically treated with cobalt. Reprod Toxicol 6:41-50.

Anderson MB, Lepak K, Farinas V, George WJ. 1993. Protective action of zinc against cobalt-induced testicular damage in the mouse. Reproductive Toxicology. 7:49–54.

Arlauskas A., Baker RSU, Bonin AM, Tandon RK, Crisp PT, Ellis J. 1985. Mutagenicity of metal ions in bacteria. Environ. Res. 36: 379–388 [cited in IARC 1991, IARC 2006]

Arnot JA, Gobas FAPC. 2006. A review of bioconcentration factor (BCF) and bioaccumulation factor (BAF) assessments for organic chemicals in aquatic organisms. Environ. Rev. 14: 257-297.

Asante KW, Agusa T, Mochizuki H, Ramu K, Inoue S, Kubodera T, Takahashi S, Subramanian A, Tanabe S. 2008. Trace elements and stable isotopes ($\delta^{13}C$ and $\delta^{15}N$) in shallow and deep-water organisms from the East China Sea. Environ. Pollut. 156:862-873.

Ashfaq M, Ali S, and Hanif MA. 2009. Bioaccumulation of cobalt in silkworm (Bombyx mori L.) in relation to mulberry, soil and wastewater metal concentrations. Process Biochem. 44: 1179 -1184.

Asmuss M, Mullenders LH, Hartwig A. 2000. Interference by toxic metal compounds with isolated zinc finger DNA repair proteins. Toxicology Letters, 112–113:227–231.

[ATSDR] Agency for Toxic Substances and Disease Registry. 2004. Toxicological Profile for Cobalt. [Internet]. Atlanta (GA): U.S. Department of Health and Human Services, ATSDR. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp33.html

Balasubramaniam R and Lee SS. 2007. Characteristics of Indoor Aerosols in Residential Homes in Urban Locations: A Case Study in Singapore. Journal of the Air and Waste Management Association. 57:981-990.

Barbant C, Schwikowski M, Döring T, Gäggeler HW, Schotterer U, Tobler L, Van de Velde K, Ferrari C, Cozzi G, Turetta A, Rosman K, Bolshov M, Capodaglio G, Cescon P, Boutron C. 2004. Historical record of European emissions of heavy metals to the atmosphere since de 1650s from alpine snow/ice cores drilled near Mote Rosa. Environ. Sci. Technol. 38:4085-4090

Barbera R, Farré R and Mesado D. 1993. Oral intake of cadmium, cobalt, copper, iron, lead, nickel, manganese and zinc in the University student's diet. Die Nahrung 37(3): 241-245.

Barceloux DG. 1999. Cobalt. Clinical Toxicology 37(2): 201-216.

Batley, GE, Gardner D.. 1977. Sampling and storage of natural waters for trace metal analysis. Water Res. 11: 745-756.

Baudin JP, Fritsch AF. 1989. Relative contributions of food and water in the accumulation of ^{60}Co by a freshwater fish. Water Res. 23(7):817-823.

Behrens T, Muller J, Diepenbrock W. 2006. Utilization of canopy reflectance to predict properties of oilseed rape (*Brassica napus* L.) and barley (*Hordeum vulgare* L.) during ontogenesis. European Journal of Agronomy vol. 25, no 4, p. 345-355.

Bencko V, Wagner V, Wagnerova M, Reichrtova E. 1983. Immuno-biochemical findings in groups of individuals occupationally and non-occupationally exposed to emissions containing nickel and cobalt. Journal of Hygiene, Epidemiology, Microbiology and Immunology, 27(4):387–394. [cited in IPCS 2006]

Beneš P, Steinnes E. 1974. *In situ* dialysis for the determination of the state of trace elements in natural waters. Water Res. 8: 947-953.

Beyersmann D, Hartwig A. 2008. Carcinogenic metal compounds: recent insight into molecular and cellular mechanisms. Arch Toxicol. 82: 493-512

[BGS] British Geological Survey [Internet]. 2009. Cobalt Commodity Profile. Nottingham (UK): British Geological Survey. [Accessed 24 Sept 2009] Available from: http://www.bgs.ac.uk/mineralsuk/industry/2009/09aug.html#cobalt

Biego GH, Joyeux M, Hartemann P, Debry. 1998. Daily intake of essential minerals and metallic micropollutants from foods in France. The Science of the Total Environment 217: 37-36.

Bird GA, Hesslein RH, Mills KH, Schwartz WJ, Turner MA. 1998. Bioaccumulation of radionuclides in fertilized Canadian Shield lake basins. Sci. Tot. Environ. 218:67-83.

Bonenfant JL, Auger C, Miller G, Chenard J, Roy PE. 1969. Quebec beer-drinkers' myocardosis: pathological aspects. Ann N Y Acad Sci. 156(1):577-582.

Borgmann U, Norwood WP. 1995. Kinetics of excess background copper and zinc in Hyalella azteca and their relationship to chronic toxicity. Can. J. Fish. Aquat. Sci. 52: 864-874.

Borgmann U, Couillard Y, Doyle P, Dixon G. 2005. Toxicity of sixty-three metals and metalloids to Hyalella azteca at two levels of water hardness. Environ. Toxicol. Chem. 24: 641-652.

Borgmann U, Norwood WP, Dixon DG. 2004. Re-evaluation of metal bioaccumulation and chronic toxicity in Hyalella azteca using saturation curves and the biotic ligand model. Environ. Pollut. 131: 469-484.

Bourg WJ, Nation JR, Clark DE. 1985. The effects of chronic cobalt exposure on passive-avoidance performance in the adult rat. Bulletin of the Psychonomic Society 23(6):527-530. [cited in ATSDR 2004]

Brewitz E, Larsson CM and Larsson M. 1996. Responses of nitrate assimilation and N translocation in tomato (Lycopersicon esculentum Mill) to reduced ambient air humidity. J. Exp. Bot. 47 (300): 855-861.

Brookins DG. 1988. Eh–pH diagrams for geochemistry. Berlin, Heidelberg: Springer-Verlag. 175 p.

Brügmann L. 1981. Heavy metals in the Baltic Sea. Mar. Pollut. Bull. 12(6):214-218.

Bucher, J.R., Elwell, M.R., Thompson, M.B., Chou, B.J., Renne, R., Ragan, H.A. 1990 Inhalation toxicity studies of cobalt sulfate in F344/N rats and B6C3F1 mice. Fundam. Appl. Toxicol. 15: 357–372.

Bucher, J.R., Hailey, J.R., Roycroft, J.R., Haseman, J.K., Sills, R.C., Grumbein, S.L., Mellick, P.W., Chou, B.J. 1999. Inhalation toxicity and carcinogenicity studies of cobalt sulfate. Toxicol. Sci. 49: 56–67.

Buchter B, Davidoff B, Amacher MC, Hinz C, Iskandar IK, Selim HM. 1989. Correlation of Freundlich Kd and n retention parameters with soils and elements. Soil Science, Vol. 148, No 5

Buchter B, Davidoff B, Amacher MC, Hinz C, Iskandar IK, Selim HM. 1989. Correlation of Freundlich Kd and n retention parameters with soils and elements. Soil Science, Vol. 148, No 5

Buffle J. 1988. Complexation reactions in aquatic systems. An analytical approach. Chichester (England): John Wiley & Sons.

Buikema AL, Cairns J, Sullivan GW. 1974. Evaluation of *Philodina acuticornis* (Rotifera) as a bioassay organism for heavy metals. Water Resources Bulletin 10 (4): 648-661.

Calgary. 2004. Drinking Water Quality Summary, Glenmore Water Treatment Plant. Unpublished Report. Calgary (AB): The City of Calgary Waterworks.

Camner, P., Boman, A., Johansson, A., Lundborg, M., Wahlberg, J.E. 1993 Inhalation of cobalt by sensitised guinea pigs: Effects on the lungs. Br. J. ind. Med. 50: 753–757.

Campbell LM, Norstrom RJ, Hobson KA, Muir DCG, Backus S, and Fisk AT. 2005 Mercury and other trace elements in a pelagic Arctic marine food web (Northwater Polynya, Baffin Bay). Sci. Total Environ. 351-352: 247-263.

Campbell PGC. 1995. Interactions between trace metals and aquatic organisms: A critique of the free-ion activity model. In: Tessier A, Turner Dr (eds.) Metal speciation and bioavailability in aquatic systems. Chichester (England): John Wiley and Sons Ltd. p 45-102.

Canada. 1999. Canadian Environmental Protection Act, 1999. S.C., 1999, c. 33, Canada Gazette. Part III, vol. 22, no. 3. Available from: http://www.gazette.gc.ca/archives/p3/1999/g3-02203.pdf

Canada. 2000. Canadian Environmental Protection Act: Persistence and Bioaccumulation Regulations, P.C. 2000-348, 23 March 2000, SOR/2000-107. Available from: http://www.gazette.gc.ca/archives/p2/2000/2000-03-29/pdf/g2-13407.pdf

Canada, Dept. of the Environment, Dept. of Health. 2006. Canadian Environmental Protection Act, 1999: Notice of intent to develop and implement measures to assess and manage the risks posed by certain substances to the health of Canadians and their environment. Canada Gazette, Part I, vol. 140, no. 49, p. 4109–4117. Available from: http://www.gazette.gc.ca/archives/p1/2006/2006-12-09/pdf/g1-14049.pdf

Canada, Dept. of the Environment, Dept. of Health. 2009a. Canadian Environmental Protection Act, 1999: Notice of tenth release of technical information relevant to substances identified in the Challenge. Canada Gazette, Part I, vol. 143, no. 25, p. 1791–1795. Available from: http://gazette.gc.ca/rp-pr/p1/2009/2009-06-20/pdf/g1-14325.pdf#page=7

Canada, Dept. of the Environment. 2009b. Canadian Environmental Protection Act, 1999: Notice with respect to Batch 10 Challenge substances. Canada Gazette, Part I, vol. 143, no. 25, p. 1796–1810. Available from: http://gazette.gc.ca/rp-pr/p1/2009/2009-06-20/pdf/g1-14325.pdf#page=7

Canada. 2009c. Food and Drugs Act [Internet]. Ottawa (ON): Health Canada. [cited: 2010 March]. Available from http://www.hc-sc.gc.ca/fn-an/legislation/acts-lois/index-eng.php

Canada. 2009d. Medical Devices Regulations [Internet]. Ottawa (ON): Health Canada. [cited: 2010 March]. Available from http://www.hc-sc.gc.ca/dhp-mps/md-im/index-eng.php

Capomazza C, Botta A. 1991. Cobalt chloride induces micronuclei in human lymphocytes. Med Sci Res 19:219-220.[cited in IPCS 2006]

Carvalho RA, Benfield MC, Santschi PH. 1999. Comparative bioaccumulation studies of colloidally complexed and free-ionic heavy metals in juvenile brown shrimp Penaeus aztecus (Crustacea: Decapoda: Penaeidae). Limnol. Oceanogr. 44: 403-414.

[CAS] Chemical Abstracts Services. 2010. Facsimile from Chemical Abstracts Services, Columbus, OH: received 17-March-2010 by Library Services Health Canada.

Casto, B.C., Meyers, J., DiPaolo, J.A. 1979. Enhancement of viral transformation for evaluation of the carcinogenic or mutagenic potential of inorganic metal salts. Cancer Res. 39: 193–198 [cited in IARC 1991, IARC 2006]

[CCME] Canadian Council of Ministers of the Environment. 2007. A protocol for the derivation of water quality guidelines for the protection of aquatic life 2007. In: Canadian environmental quality guidelines, 1999, Canadian Council of Ministers of the Environment, 1999.

[CDI] The Cobalt Development Institute. 2005. Short-term Chronic Toxicity of Cobalt to *Ceriodaphnia dubia*. Testing laboratory: Parametrix Environmental Research Laboratory. Report no.: 4248-43. A report to the Cobalt Development Institute. Guildford, Surrey, United Kingdom.

[CDI] The Cobalt Development Institute. 2006a. Cobalt Fact Sheet 8: Electronics. Surrey, United Kingdom, [cited on February 5, 2010] Available from: http://www.thecdi.com/cobaltfacts.php

[CDI] The Cobalt Development Institute. 2006b. Cobalt Fact Sheet 6: Chemicals. Surrey, United Kingdom, [cited on February 5, 2010] Available from: http://www.thecdi.com/cobaltfacts.php

[CDI] The Cobalt Development Institute. 2008a. Cobalt News July 2008. Surrey, United Kingdom, [cited on February 5, 2010]. Published by The Cobalt Development Institute. Available from: http://www.thecdi.com/cobaltnews.php

[CDI] The Cobalt Development Institute. 2008b.. Evaluation of chronic toxicity of cobalt to the aquatic oligochaete, *Aeolosoma sp.* Testing laboratory: Parametrix Environmental Research Laboratory. Report no.: 4248-1170R. A report to the Cobalt Development Institute. Guildford, Surrey, United Kingdom.

[CDI] The Cobalt Development Institute. 2009a. Cobalt Fact Sheet 10: Supply and Demand. Surrey, United Kingdom, [cited on February 5, 2010] Available from: http://www.thecdi.com/cobaltfacts.phpChen B, Huang Q, Lin X, Shi Q, Wu S. 1998. Accumulation of Ag, Cd, Co, Cu, Hg, Ni and Pb in *Pavlova viridis* Tseng (Haptophyceae). J. Appl. Phycol. 10:371-376.

[CDI] The Cobalt Development Institute 2009b. Early life-stage toxicity of cobalt to zebrafish (*Danio rerio*) under flow-through conditions. Testing laboratory: Parametrix Environmental Research Laboratory. Report no.: 4248-396. A report to the Cobalt Development Institute. Guildford, Surrey, United Kingdom.

[CDI] The Cobalt Development Institute 2009c. Early life-stage toxicity of cobalt to the fathead minnow (*Pimephales promelas*) under flow-through conditions. Testing laboratory: Parametrix Environmental Research Laboratory. Report no.: 4248-71. A report to the Cobalt Development Institute. Guildford, Surrey, United Kingdom.

[CDI] The Cobalt Development Institute 2009d. Early life-stage toxicity of cobalt to the rainbow trout (*Oncorhynchus mykiss*) under flow-through conditions. Testing laboratory: Parametrix Environmental Research Laboratory. Report no.: 4248-73. A report to the Cobalt Development Institute. Guildford, Surrey, United Kingdom.

[CDI] The Cobalt Development Institute 2009e. Heijerick D, Ghekiere A, Van Sprang P, De Schamphelaere K, Deleebeeck N, Janssen C. 2007. Effect of cobalt (CoCl2.6H2O) on freshwater organisms. Testing laboratory: EURAS & Laboratory of Environmental Toxicology, Ghent University. A report to the Cobalt Development Institute. Guildford, Surrey, United Kingdom.

[CDI] The Cobalt Development Institute 2010a. Summary of Transformation/Dissolution Protocol (OECD 29) Test Results for Cobalt Substances and Cobalt Metal Powders - Data in preparation. Aquatic Research Program. The Cobalt Development Institute. Guildford, Surrey, United Kingdom.

[CDI] Cobalt Development Institute: About Cobalt [Internet]. 2010b. Guildford (UK): Cobalt Development Institute. [cited 9 Feb 2010]. Available from: http://www.thecdi.com/about-cobalt

Cherry DS and Guthrie RK. 1977. Toxic metals in surface water from coal ash. Water Res. Bull. 13(6): 1227-1236.

Cherry DS, Guthrie RK, Sherberger FF, Larrick SR. 1979. The influence of coal ash and thermal discharges upon the distribution and bioaccumulation of aquatic invertebrates. Hydrobiologia. 62(3):257-267.

Chen B, Huang Q, Lin X, Shi Q, Wu S. 1998. Accumulation of Ag, Cd, Co, Cu, Hg, Ni and Pb in Pavlova viridis Tseng (Haptophyceae). J. Appl. Phycol. 10:371-376.

Chetty KN, Rao DSVS, Drummond L, Desaiah, D., 1979. Cobalt induced changes in immune response and adenosine triphosphatase activities in rats. J Environ Sci Health B 14(5):525-544.

Chiffoleau JF, Cossa D, Auger D, Truquet I. 1994. Trace metal distribution in the Seine estuary (France) in low discharge regime. Marine Chemistry 47 (2):145-158.

City of Greater Sudbury. 2001. City of Greater Sudbury's 2001 Lake Water Quality Initiative. Living with Lakes initiative. Available from:
http://www.city.greatersudbury.on.ca/cms/index.cfm?app=div_lakewaterquality&lang=en&currid=720

City of Greater Sudbury. 2004. Lake Water Quality Program 2004 Annual Report. City of Lakes initiative. Available from:
http://www.city.greatersudbury.on.ca/cms/index.cfm?app=div_lakewaterquality&lang=en&currid=720

Clyne N, Hofman-Bang C, Haga Y, Hatori N, Marklund SL,Pehrsson SK, Wibom R. 2001. Chronic cobalt exposure affects antioxidants and ATPproduction in rat myocardium. Scand J Clin Lab Invest 61(8):609-614.

[CNS] Cosmetic Notification System [Proprietary Database]. 2009. Available from Health Canada, Cosmetics Division.

Coakley JP, Nagy E, Serodes JB. 1993. Spatial and vertical trends in sediments-phase contaminants in the upper estuary of the St-Lawrence River. Estuaries. 16(3B):653-669.

Colognato R, Bonelli A, Ponti J, Farina M, Bergamaschi E, Sabbioni E, Migliore L. 2008. Comparative genotoxicity of cobalt nanoparticles and ions on human peripheral leukocytes in vitro. Mutagenesis . 23(5):377-82.

Conestoga-Rovers & Associates. 2008. *Potential releases of chemical management plan challenge substances to the environment from waste sector.* Prepared for Environment Canada. 199p.

[ConsExpo] Consumer Exposure Model [Internet]. 2006. Version 4.1. Bilthoven (NL): Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment). Available from: http://www.rivm.nl/en/healthanddisease/productsafety/ConsExpo.jsp#tcm:13–42840

Corisco JAG, Carreiro MCV. 1999. Co-60 transfer from water to the freshwater planktonic algae *Selenastrum capricornutum* Prinz. In: Anagnostoopoulos P, Brebbia CA, eds. *Water pollution V: Modeling, measuring, and prediction*. Boston, MA, WIT Press, pp. 427–436 (Progress in Water Resources, Vol. 1).

Corrier DE, Mollenhauer HH, Clark DE, Hare MF, Elissalde MH. 1985. Testicular degeneration and necrosis induced by dietary cobalt. Vet Pathol 22:610-616.

Cotton FA, Wilkinson G. 1988. Advanced inorganic chemistry, 5th edition. Toronto (ON): John Wiley and Sons. 1455 p.

Couillard Y, Grapentine LC, Borgmann U, Doyle P, Masson S. 2008. The amphipod Hyalella azteca as a biomonitor in field deployment studies for metal mining. Environ. Pollut. 156: 1314-1324.

[CRC] The Chemical Rubber Company. 1965. Handbook of chemistry and physics. 46th Edition (1965-1966). Published by The Chemical Rubber Co. Ohio. p. E93.

Dabeka RW and McKenzie AD. 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): 897-909.

Dabeka RW. 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. The Science of the Total Environment 89: 279-289.

Dave G, Xiu R. 1991. Toxicity of mercury, copper, nickel, lead, and cobalt to embryos and larvae of zebrafish, *Brachydanio rerio*. Archives of Environmental Contamination and Toxicology 21: 126-134.

Davies J. 2007. Material Safety Data Sheet for Cobalt-Based Alloys. Prepared by Deloro Stellite.Belleville, ON [c2008, cited on 01 february 2010]. Available from: http://stellite.com/Technical/MaterialSafetyDataSheets/tabid/280/Default.aspx

Davis A, Sellstone C, Clough S, Barrick R, Yare B. 1996. Bioaccumulation of arsenic, chromium and lead by fish: constraints imposed by sediment geochemistry. Appl Geochem 11 (3):409-423.

Davis JE, Fields JP. 1958. Experimental production of polycythemia in humans by administration of cobalt chloride. Proc Soc Exp Biol Med 99:493-495. [cited in IPCS 2006]

De Boeck M, Lardao S, Buchet J, Kirsch-Volders M, Lison D. 2000. Absence of significant genotoxicity in lymphocytes and urine from workers exposed to moderate levels of cobalt-containing dust: a cross-sectional study. Environ Mol Mutagen 36(2):151-60. [cited in IARC 2006, IPCS 2006]

De Boeck, M., Lison, D., Kirsch-Volders, M. 1998. Evaluation of the in vitro direct and indirect genotoxic effects of cobalt compounds using the alkaline comet assay. Influence of interdonor and interexperimental variability. Carcinogenesis. 19: 2021–2029 [cited in IARC 2006]

De Boeck, M., Kirsch-Volders, M., Lison, D. 2003a. Cobalt and antimony: Genotoxicity and carcinogenicity. Mutat. Res. 533: 135–152 [cited in IARC 2006]

De Boeck M, Lombaert N, De Backer S, Finsy R, Lison D, Kirsch-Volders M. 2003b. In vitro genotoxic effects of different combinations of cobalt and metallic carbide particles. Mutagenesis. 18: 177–186 [cited in IARC 2006]

De Schamphelaere KAC, Koene JM, Heijerick DG, and Janssen CR. 2008. Reduction of growth and haemolymph Ca levels in the freshwater snail *Lymnaea stagnalis* chronically exposed to cobalt. Ecotoxicology and Environmental Safety 71: 65-70.

Dean JA. 2004. Handbook of organic chemistry. New York, NY: McGraw-Hill Book Co, p. 2-12.

DeForest, DK, Brix KV, and Adams WJ. 2007. Assessing metal accumulation in aquatic environments: the inverse relationship between bioaccumulation factors, trophic transfer factors and exposure concentration. Aquat. Toxicol. 84: 236-246.

Degryse F, Smolders E, Parker DR. 2009. Partitioning of metals (Cd, Co, Cu, Ni, Pb, Zn) in soils: concepts, methodologies, prediction and applications – a review. Eur. J. Soil Sci. 60: 590-612.

Diamond ML, Mackay D, Cornett RJ, Chant LA. 1990. A model of the exchange of inorganic chemicals between water and sediments. Environ. Sci. Technol. 24: 713-722.

Diamond ML, Mackay D, Welbourn PM. 1992. Models of multi-media partitioning of multi-species chemicals: the fugacity/aquivalence approach. Chemosphere 25 (12): 91907-21.

Di Toro DM, Mahony JD, Hansen DJ, Scott KJ, Carlson A, Ankley GT. 1992 Acid volatile sulphide predicts the acute toxicityof cadmium and nickel in sediments. Environ. Sci. Technol. 26, 96–101.

Domingo JL, Llobet JM, Bernat R. 1984. A study of the effects of cobalt administered orally to rats. Arch Farmacol Toxicol 10:13-20. [cited in ATSDR 2004, IPCS 2006]

Domingo JL, Llobet JM. 1984. Treatment of acute cobalt intoxication in rats with L-methionine. Rev Esp Fisiol 40:443-448. [cited in ATSDR 2004]

Domingo JL, Paternain JL, Llobet JM, Corbella J. 1985. Effects of cobalt on postnatal development and late gestation in rats upon oral administration. Rev Esp Fisiol 41:293-298.

Donaldson JD and Beyersmann J. 2005. Cobalt and Cobalt Compounds [Internet]. Ullmann's Encyclopedia of Industrial Chemistry, online version. Available from: http://mrw.interscience.wiley.com/emrw/9783527306732/ueic/article/a07_281/current/pdf [restricted access.]

Doran, A., Law, F.C., Allen, M.J., Rushton, N. 1998. Neoplastic transformation of cells by soluble but not particulate forms of metals used in orthopaedic implants. Biomaterials. 19: 751–759 [cited in IARC 2006]

[DPD] Drug Products Database [Internet]. 2009. Ottawa (ON): Health Canada. [cited 2010 February]. Available from: http://webprod.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp

Duckham JM, Lee HA. 1976. The treatment of refractory anaemia of chronic renal failure with cobalt chloride. Q J Med 178:277-294.

Duggan MJ. 1983. Contribution of lead in dust to children's blood lead. Environmental Health Perspectives 50: 371-381.

Edwards, M.S. and Curtis, J.R. 1971. Use of cobaltous chloride in anæmia of maintenance-hæmodialysis patients. Lancet. 298(7724): 582-583.

Egilsson, V., Evans, I.H., Wilkie, D. 1979. Toxic and mutagenic effects of carcinogens on the mitochondria of Saccharomyces cerevisiae. Mol. gen. Genet. 174: 39–46 [cited in IARC 1991, IARC 2006]

Elbetieha, A., Al-Thani, A.S., Al-Thani, R.K., Darmani, H., Owais, W. 2008. Effects of Chronic Exposure to Cobalt Chloride on the Fertility and Testes in Mice. J. Appl Biol Sci. 2(1):01-06.

Eleftheriadis K, Colbeck I. 2001. Coarse atmospheric aerosol: size distributions of trace elements. Atmos. Environ. 35: 5321-5330.

El-Shenawy NS. 2004. Heavy-Metal and Microbial Depuration of the Clam Ruditapes decussatus and Its Effect on Bivalve Behavior and Physiology. Environ. Toxicol. 19: 143–153.

Environment Canada. 1988. Data relating to the Domestic Substance List (DSL) 1984-1986, collected under CEPA, 1988, s. 25(1). Based on Reporting for the Domestic Substances List [guide] 1988. Data prepared by: Environment Canada.

Environment Canada. 2003. Guidance Manual for the Ecological Categorization of Organic and Inorganic Substances on Canada's Domestic Substances List (DSL): determining persistence, bioaccumulation potential, and inherent toxicity to non-human organisms. Gatineau (QC): Environment Canada, Existing Substances Division.

Environment Canada. 2008. National Pollutant Release Inventory [database on the Internet]. Gatineau (QC): Environment Canada. [cited 2010 mar 19]. Available from: http://www.ec.gc.ca/pdb/querysite/query_e.cfm

Environment Canada. 2009. Data for Batch 10 substances collected under the Canadian Environmental Protection Act, 1999, Section 71: Notice with respect to certain Batch 10 Challenge substances. Data prepared by: Environment Canada, Existing Substances Program.

Environment Canada. 2010a. Data for Batch 10 Substances collected under Canadian Environmental Protection Act, 1999, Section 71 and voluntary data submission: Notices with respect to Batch 10 Challenge substances. Data prepared by: Environment Canada, Existing Substances Program.

Environment Canada. 2010b. Battery recycling in Canada 2009 update -executive summary. Pollution and Waste Department. Available From: http://www.ec.gc.ca/gdd-mw/default.asp?lang=En&n=52DF915F-1&offset=4&toc=show

Ephraim JH, Marinsky JA, Cramer SJ. 1989. Complex-forming properties of natural organic acids – fulving acid complexes with cobalt, zinc and europium. Talanta 36(4): 437-443.

[ESIS] European Chemical Substances Information System [database on the Internet]. 2006. Version 4.5. European Chemical Bureau (ECB). Available from: http://ecb.jrc.it/esis

European Commission. 2003. Technical guidance document on risk assessment part II, Chapter 3: Environmental risk assessment. Commission Directive 93/67/EEEC on Risk Assessment for new notified substances, commission regulation (EC) No 1488/94 on risk assessment for existing substances and directive 98/8/EC of the European Parliement and of the Council concerning the placing of biocidal products on the market. European Commission, Joint Research Centre, Institute for Health and Consumer Production, European Chemicals Bureau [cited 2010 may]. Available from: http://ecb.jrc.ec.europa.eu/tgd/

European Commission. 2004a. Summary Record Meeting of the Technical Committee C&L on the Classification and Labelling of Dangerous Substances. Meeting at Riga, 12-14 May 2004. European Commission Directorate General JRC. Joint Research Centre. Institute for Health and Consumer Protection. European Chemicals Bureau. ECBI/147/04 – Rev. 3. Available from: http://ecb.jrc.ec.europa.eu/documents/Classification-Labelling/ADOPTED_SUMMARY_RECORDS/14704r3_sr_TC_C&L_HEALTH_0504.pdf

European Commission. 2004b. Cobalt sulphate. Commission Directive 2004/73/EC of 29 April 2004. Annex IA. Official Journal of the European Union. 16.6.2004. L216/20. European Commission. 29th ATP. Available from: http://ecb.jrc.it/

European Commission. 2008. Council Directive of 27 July 1976 (76/768/EEC). Brussels (BE): European Commission Enterprise and Industry Cosmetics Directive. Available from: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1976L0768:20080424:en:PDF

European Commission 2009. Risk Assessment Report on nickel and its compounds: Environmental part. Health and Consumer protection Directorate General, Brussels. Available from: http://ec.europa.eu/health/ph_risk/committees/04_scher/docs/scher_o_112.pdf

Farah, S.B. 1983 The in vivo effect of cobalt chloride on chromosomes. Rev. Brasil. Genet. 6:433–442 [cited in IARC 1991, IARC 2006]

FDRL. 1984a. Acute oral LD50 study of cobalt sulphate lot no. S88336/A in Sprague-Dawley rats. FDRL study no. 8005D. Food and Drug Research Laboratories, Inc., Waverly, NY. April 11, 1984. [cited in ATSDR 2004]

Filon FL, Maina G, Adami G, Venier M, Coceani N, Bussani R, Massiccio M, Barbieri P, Spinelli P. 2004. In vitro percutaneous absorption of cobalt. Int Arch Occup Environ Health. 77: 85–89.

Filon FL, D'Agostin F, Crosera M, Adami G, Bovenzi M, Maina G. 2009. In vitro absorption of metal powders through intact and damaged human skin. Toxicol In Vitro. 23(4):574-9.

Fletcher T, Stephenson GL, Wang J, and Wren CD, for the Standards Development Branch of the Ontario Ministry of Environment and Energy. 1996. Scientific criteria document for the development of a provincial water quality objective for cobalt (stable isotope). Guelph (ON): Ecological Services for Planning Ltd. p. 18-19.

Förstner U, Wittmann GTW. 1981. Metal pollution in the aquatic environment, 2nd ed. Berlin: Springer. 532 pp.

Fowler SW, Teyssié, Cotret O, Danis B, Rouleau C, Warnau M. 2004. Applied radiotracer techniques for studying pollutant bioaccumulation in selected marine organisms (jellyfish, crabs and sea stars). Nukleonika 49(3):97-100.

Fraysse B, Baudin JP, Garnier-Laplace J, Adam C, and Boudou A. 2002. Effects of Cd and Zn waterborne exposure on the uptake and depuration of 57Co, 110mAg and 134Cs by the Asiatic clam (Corbicula fluminea) and the zebra mussel (Dreissena polymorpha)—whole organism study. Environ. Pollut. 118 : 297-306.

Friel JK, Andrews WL, Jackson SE, Longerich HP, Mercer C, McDonald A, Dawson B, Sutradhar B. 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: 225-247.

Fukunaga, M., Kurachi, Y. & Mizuguchi, Y. 1982. Action of some metal ions on yeast chromosomes.Chem. pharm. Bull. 30: 3017–3019 [cited in IARC 1991, IARC 2006]

Gál J, Hursthouse A, Tatner P, Stewart F and Welton R. 2008. Cobalt and secondary poisoning in the terrestrial food chain: Data review and research gaps to support risk assessment. Environ. Int. 34: 821-838.

Garrett RG. 2005. Natural distribution and abundance of elements. In: Selinus O (ed.). The essentials of medical geology. Amsterdam (The Netherlands): Elsevier Academic Press. p. 17-41.

Gaur JP, Noraho N, Chauhan YS. 1994. Relationship between heavy metal accumulation and toxicity in *Spirodela polyrhiza* (L.) Schleid and *Azolla pinnata* (R.Br.) Aquatic Botany 49: 183-192.

Gobeil C, Rondeau B, Beaudin L. 2005. Contribution of municipal effluents to metal fluxes in the St. Lawrence River. Environ Sci Technol 39 (2):456-464.

Gobeil C, Rondeau B, Beaudin L. 2005. Contribution of municipal effluents to metal fluxes in the St. Lawrence River. Environ Sci Technol 39 (2):456-464.

Greiner EOC, Gubler R and Yokose K. 2003. CEH Marketing Research Report: Animals: Chemical Inputs for Nutrition and Health – Overview. Menlo Park (CA): SRI Consulting. Available from: http://www.sriconsulting.com/CEH/Public/Reports/index.html [restricted access].

Grice HC, Goodman T, Munro IC, Wiberg GS, Morrison AB. 1969. Myocardial toxicity of cobalt in the rat. Ann Acad Sci NY 156:189-194.

Gross RT, Kriss JP, Spaet TH. 1955. The hematopoietic and goitrogenic effects of cobaltous chloride in patients with sickle cell anaemia. Pediatrics 15:284-290.

Guo L, Hunt BJ, Santschi PH, Ray SM. 2001. Effect of dissolved organic matter on the uptake of trace metals by American oysters. Environ. Sci. Technol. 35: 885-893.

Haga Y, Clyne N, Hatori N, Hoffman-Bang, C., Pehrsson, S.K., Ryden, L. 1996. Impaired myocardial function following chronic cobalt exposure in an isolated rat heart model. Trace Elem Electrolytes 13(2):69-74.

Hamilton-Koch, W., Snyder, R.D. & Lavelle, J.M. 1986. Metal-induced DNA damage and repair in human diploid fibroblasts and Chinese hamster ovary cells. Chem.-biol. Interact. 59: 17–28 [cited in IARC 2006]

Hamilton-Taylor J, Postill AS, Tipping E, Harper MP. 2002. Laboratory measurements and modeling of metal–humic interactions under estuarine conditions. Geochim. Cosmochim. Acta 66(3): 403-415.

Hamilton-Taylor JM and CS Willis. 1984. Reynolds Depositional fluxes of metals and phytoplankton in Windemere as measured by sediment traps. Limnology and Oceanography 29(4): 695-710.

Hanna PM, Kadiiska MB and Mason RP. 1992. Oxygen-derived free radical and active oxygen complex formation from Cobalt(II) chelates in vitro. Chemical Research in Toxicology. 5:109–115.

Harris LE. 1975. Guide for estimating toxic residues in animal feeds or diets. U.S. Environmental Protection Agency. EPA-540/9-75-019.

Hartwig, A., Kasten, U., Boakye-Dankwa, K., Schlepegrell, R., Beyersmann, D. 1990. Uptake and genotoxicity of micromolar concentrations of cobalt chloride in mammalian cells. Toxicol. environ. Chem. 28: 205–215 [cited in IARC 1991, 2006]

Harvey C, MacKay D and Webster E. 2007. Can the unit world model concept be applied to hazard assessment of both organic chemicals and metal ions. Environmental Toxicology and Chemistry, Vol 26. No. 10 pp. 2129-2142.

Harvey C, MacKay D and Webster E. 2007. Can the unit world model concept be applied to hazard assessment of both organic chemicals and metal ions. Environmental Toxicology and Chemistry, Vol 26. No. 10 pp. 2129-2142.

Hatch. 2000. Review of environmental releases for the base metals smelting sector. Appendix A. Prepared for Environment Canada.

Health Canada 1998. Exposure factors for assessing total daily intake of priority substances by the general population of Canada. Unpublished report. Ottawa (ON): Health Canada, Environmental Health Directorate.

Health Canada. 2007. Multi-vitamin/mineral supplement monograph [Internet]. Ottawa (ON) : Health Canada. Available from : http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodnatur/multivit_min_mono-eng.pdf

Health Canada. 2008. Guidelines for Canadian Drinking Water Summary Table [Internet]. Ottawa (ON): Federal-Provincial-Territorial Committee on Drinking Water. Available from: http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/pubs/water-eau/sum_guide-res_recom/summary-sommaire-eng.pdf

Health Canada. 2009a. Cosmetic Ingredient Hotlist [Internet]. Ottawa (ON): Health Canada. [cited 2010 February]. Available from: http://www.hc-sc.gc.ca/cps-spc/person/cosmet/info-ind-prof/_hot-list-critique/hotlist-liste-eng.php

Health Canada. 2009b. Canadian Total Diet Study [Internet]. Ottawa (ON): Health Canada. [cited: 2010 February]. Available from: http://www.hc-sc.gc.ca/fn-an/surveill/total-diet/index-eng.php

Hodge FG and Dominey L. 2001. Cobalt and cobalt alloys [Internet]. Kirk-Othmer Encyclopedia of Chemical Technology, online version. Available from: http://mrw.interscience.wiley.com/emrw/9780471238966/kirk/article/cobahodg.a01/current/pdf [restricted access].

Hoet PMH, Roesems G, Demedts MG, Nemery B 2002. Activation of the hexose monophosphate shunt in rat type II pneumocytes as an early marker of oxidative stress caused by cobalt particles. *Archives of Toxicology*, 76(1):1–7. [Cited in IPCS 2006]

Hokin B, Adams M, Ashton J, Louie H. 2004a. Analysis of the cobalt content in Australian foods. Asia Pacific Journal of Clinical Nutrition 13(3): 284–288.

Hokin B, Adams M, Ashton J, Louie H. 2004b. Comparison of the dietary cobalt intake in three different Australian diets. Asia Pacific Journal of Clinical Nutrition 13(3): 289–291.

Holly RG. 1955. Studies on iron and cobalt metabolism. JAMA. 158:1349-1352.

Hopke PK, Lamb RE and Natusch DFS. 1980. Multielemental characterization of urban roadway dust. Environmental Science and Technology 14(2): 164-172.

Hume, DN 1973. Pitfalls in the determination of environmental trace metals. In: Ahuja S., E. M. Cohen, T. J. Kniep, J. L. Lambert & G. Zweign (eds.). Chemical analysis of the environment and other modern techniques. New York (NY): Plenum Press. p. 3-16.

IARC (International Agency for Research on Cancer). 1991. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 52. Chlorinated drinking water; chlorinated by-products; some other halogenated compounds; cobalt and cobalt compounds.

IARC (International Agency for Research on Cancer). 2006. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 86. Cobalt in hard metals and cobalt sulphate, gallium arsenide, indium phosphide and vanadium pentoxide.

Ikarashi Y, Ohno K, Tsuchiya T, Nakamura A. 1992a. Differences of draining lymph node cell proliferation among mice, rats and guinea pigs following exposure to metal allergens. Toxicology. 76:283-292.

Ikarashi Y, Tsuchiya T, Nakamura A. 1992b. Detection of contact sensitivity of metal salts using the murine local lymph node assay. Toxicol Lett. 62:53-61.

Ikemoto T, Tu NPC, Okuda N, Iwata A, Omori K, Tanabe S, Tuyen BC and Takeuchi I. 2008. Biomagnification of trace elements in the aqautic food web in the Mekong delta, South Vietnam using stable carbon and nitrogen isotope analysis. Arch. Environ. Contam. Toxicol. 54: 504-515.

Inoue T, Ohta Y, Sadaie Y, Kada, T. 1981. Effect of cobaltous chloride on spontaneous mutation induction in a Bacillus subtilis mutator strain. Mutat Res 91:41-45. [cited in IARC 1991, IARC 2006]

[IPCS] International Programme on Chemical Safety. 2006. Cobalt and inorganic cobalt compounds. Geneva (CH): World Health Organization. (Concise International Chemical Assessment Document 69). Jointly sponsored by the United Nations Environment Programme, the International Labour Organization, and the World Health Organization, and produced within the framework of the Inter-Organization Programme for the Sound Management of Chemicals. Available from: http://www.inchem.org/documents/cicads/cicads/cicad69.htm.

Ishii T, Suzuki H, Koyanagi T. 1978. Determination of trace elements in marine organisms. I. Factors for variation of concentration of trace element. Nippon Suisan Gakkaishi. 44(2):155-162.

Ivancsits S, Diem E, Pilger A, Rudiger HW 2002. Induction of 8-hydroxy-2'-deoxyguanosine by cobalt(II) and hydrogen peroxide in vitro. *Journal of Toxicology and Environmental Health, Part A*, 65(9):665–676.

Iyengar GV, Wolf WR, Tanner, JT and Morris ER. 2000. Content of minor and trace elements, organic nutrients in representative mixed total diet composites from the USA. The Science of the Total Environment 256: 215-226.

Johansson, A., Lundborg, M., Hellström, P.-Å., Camner, P., Keyser, T.R., Kirton, S.E., Natusch, D.F. 1980. Effect of iron, cobalt, and chromium dust on rabbit alveolar macrophages: A comparison with the effects of nickel dust. Environ. Res. 21: 165–176.

Johansson, A., Camner, P., Jarstrand, C., Wiernik, A. 1983. Rabbit alveolar macrophages after inhalation of soluble cadmium, cobalt, and copper: A comparison with the effects of soluble nickel. Environ. Res. 31: 340–354.

Johansson A, Curstedt T, Robertson B, Camner P. 1984. Lung morphology and phospholipids after experimental inhalation of soluble cadmium, copper, and cobalt. Environ Res. 34:295-309.

Johansson, A., Lundborg, M., Wiernik, A., Jarstrand, C., Camner, P. 1986. Rabbit alveolar macrophages after long-term inhalation of soluble cobalt. Environ. Res. 41: 488–496.

Johansson A, Robertson B, Camner P. 1987. Nodular accumulation of type II cells and inflammatory lesions caused by inhalation of low cobalt concentrations. Environ Res. 43:227-243.

Johansson A, Curstedt T, Camner P. 1991. Lung lesions after combined inhalation of cobalt and nickel. Environ Res 54:24-38.

Johansson A, Curstedt T, Rasool O, Jarstrand C, Camner P. 1992. Rabbit lung after combined exposure to soluble cobalt and trivalent chromium. Environ Res. 58:80-96.

Kada, T. and Kanematsu, N. 1978. Reduction of N -methyl-N'-nitrosoguanidine-induced mutations by cobalt chloride in Escherichia coli. Proc. Jpn. Acad. 54B: 234–237 [cited in IARC 1991, IARC 2006]

Kadiiska MB, Maples KR, Mason RP (1989) A comparison of cobalt(II) and iron(II) hydroxyl and superoxide free radical formation. *Archives of Biochemistry and Biophysics*, 275(1):98–111. [Cited in IPCS 2006]

Kanematsu N, Hara M, Kada T. 1980. Rec assay and mutagenicity studies on metal compounds. Mutat Res 77:109-116. [cited in IARC 1991, IARC 2006]

Kasprzak KS, Zastawny TH, North SL, Riggs CW, Diwan BA, Rice JM, Dizdaroglu M. 1994. Oxidative DNA base damage in renal, hepatic, and pulmonary chromatin of rats after intraperitoneal injection of cobalt(II) acetate. Chem Res Toxicol 7:329-335.[cited in IPCS 2006]

Kasten U, Mullenders LH, Hartwig A. 1997. Cobalt(II) inhibits the incision and the polymerization step of nucleotide excision repair in human fibroblasts. Mutat Res 383:81-90. [cited in IARC 2006]

Kawanishi S, Inoue S, Yamamoto K (1994) Active oxygen species in DNA damage induced by carcinogenic metal compounds. *Environmental Health Perspectives*, 102(Suppl. 3):17–20. [cited in IPCS 2006]

Kelly BC, Ikonomou MG, Higgs DA, Oakes J, and Dubetz C. 2008. Mercury and other trace elements in farmed and wild salmon from British Columbia, Canada. Environ. Toxicol. Chem. 27: 1361-1370.

Kerckaert, G.A., LeBoeuf, R.A., Isfort, R.J. 1996. Use of the Syrian hamster embryo cell transformation assay for determining the carcinogenic potential of heavy metal compounds. Fundam. appl. Toxicol. 34: 67–72 [cited in IARC 2006]

Kerfoot EJ. 1975. Semi-chronic inhalation study on cobalt. Diss Abstr Int B 35:6054-6055.

Kesteloot H, Roelandt J, Willems J, Claes JH, Joosens JV. 1968. An enquiry into the role of cobalt in the heart disease of chronic beer drinkers. Circulation 37:854-864. [cited in IPCS 2006]

Khangarot, BS, Rathore, RS, Singh, BB 2003. pH-dependent toxicity of heavy metals to a freshwater sludgeworm *Tubifex tubifex* Muller.. Bull. Environ. Contam. Toxicol. 71: 283- 289.

Kharab P, Singh I. 1985. Genotoxic effects of potassium dichromate, sodium arsenite, cobalt chloride and lead nitrate in diploid yeast. Mutat Res 155:117-120. [cited in IARC 1991, IARC 2006]

Kharab, P., Singh, I. 1987. Induction of respiratory deficiency in yeast by salts of chromium, arsenic, cobalt and lead. Indian J. exp. Biol. 25: 141–142 [cited in IARC 1991, IARC 2006]

Kimball G. 1978. The effects of lesser known metals and one organic to fathead minnows (*Pimephales promelas*) and *Daphnia magna*. Department of Entomology, Fisheries and Wildlife, University of Minnesota.

Kimura Y, and Honda Y. 1977. Uptake and elimination of some radionuclides by eggs and fry of rainbow trout (I). J. Radiat. Res. 18:170-181.

Kitahara, J., Yamanaka, K., Kato, K., Lee, Y.-W., Klein, C.B., Costa, M. 1996. Mutagenicity of cobalt and reactive oxygen producers. Mutat. Res. 370: 133–140 [cited in IARC 2006]

Kopera E, Schwerdtle T, Hartwig A, Bal W. 2004. Co(II) and Cd(II) Substitute for Zn(II) in the Zinc Finger Derived from the DNA Repair Protein XPA, Demonstrating a Variety of Potential Mechanisms of Toxicity. Chem. Res. Toxicol. 17:1452-1458.

Krachler M, Prohaska T, Koellensperger G, Rossipal E, Stingeder G. 2000. Concentrations of selected trace elements in human milk and in infant formulas determined by magnetic sector field inductively coupled plasma-mass spectrometry. Biological Trace Element Research 76: 97-112.

Krasovskii GN, Fridlyand SA. 1971. Experimental data for the validation of the maximum permissible concentration of cobalt in water bodies. Hyg Sanit 26:277-279.

Kriss JP, Carnes WH, Ross RT. 1955. Hypothyroidism and thyroid hypoplasia in patients treated with cobalt. JAMA 157(2):117-121.

Kurk DN, Choppin GR. 2000. Determination of Co(II) and Ni(II)-humate stability constants at high ionic strength NaCl solutions. Radiochim. Acta 88: 583-586.

Kyono H, Kusaka Y, Homma K, Kubota H, Endo-Ichikawa Y. 1992. Reversible lung lesions in rats due to short-term exposure to ultrafine cobalt particles. Ind Health 30:103-118.

Lee J, Joansson JL. 1983. Contribution of organic complexation to Ni, Co and Cu speciation in surface waters: implications for hydrogeochemical surveys. J. Geochem. Explor. 18: 25-48.

Lee Y, Tebo BM. 1994. Cobalt oxidation by the marine manganese (II) oxidizing Bacillus sp. Strain SG-1. Applied and Environmental Microbiology, 60(8): 2949-2957

Leitão, A.C., Soares, R.A., Cardoso, J.S., Guillobel, H.C., Caldas, L.R. 1993. Inhibition and induction of SOS response in Escherichia coli by cobaltous chloride. Mutat. Res. 286: 173–180 [cited in IARC 2006]

Leonard S, Gannett PM, Rojanasakul Y, Schwegler-Berry D, Castranova V, Vallyathan V, and Shi X. 2006. Cobalt mediated generation of reactive oxygen species and its possible mechanism. Journal of Inorganic Biochemistry. 70:239–244.

Lewis CPL, Demedts M, Nemery B (1991) Indices of oxidative stress in hamster lung following exposure to cobalt(II) ions: In vivo and in vitro studies. *American Journal of Respiratory Cell and Molecular Biology*, 5:163–169. [cited in IPCS 2006]

Li HF, Gray C, Mico C, Zhao FJ, and McGrath SP. 2009. Phytotoxicity and bioavailability of cobalt to plants in a range of soils. Chemosphere 75: 979-986.

Lide DR (editor). 2007-2008. CRC Handbook of Chemistry and Physics. 88rd ed. Boca Raton (FL): CRC Press Inc. 2640 p.

Lindegren, C.C., Nagai, S. & Nagai, H. 1958. Induction of respiratory deficiency in yeast by manganese, copper, cobalt and nickel. Nature. 182: 446–448 [cited in IARC 1991, IARC 2006]

Linna A, Oksa P, Palmroos P, Roto P, Laippala P, Uitti J. 2003. Respiratory health of cobalt production workers. American Journal of Industrial Medicine. 44:124–132.

Linna, A., P. Oksa, K. Groundstroem, M. Halkosaari, P. Palmroos, S. Huikko, J. Uitti. 2004. Exposure to cobalt in the production of cobalt and cobalt compounds and its effect on the heart. Occup. envir. Med. 61(11): 877-85.

Lithner G, Holm K, Borg H. 1995. Bioconcentration factors for metals in humic waters at different pH in the Rönnskär area (N. Sweden). Water Air Soil Pollut. 85:785-790.

Lloyd DR, Phillips DH, Carmichael PL (1997) Generation of putative intrastrand cross-links and strand breaks in DNA by transition metal ion-mediated oxygen radical attack. *Chemical Research in Toxicology*, 10:393–400. [Cited in IPCS 2006]

[LNHPD] Licensed Natural Health Products Database [Internet]. 2010. Ottawa (ON): Health Canada. [cited: 2010 February]. Available from: http://webprod.hc-sc.gc.ca/lnhpd-bdpsnh/start-debuter.do?language-langage=english

Lock K, De Schamphelaere KAC, Becaus S, Criel P, Van Eeckhout H, Janssen CR. 2006. Development and validation of an acute biotic ligand model (BLM) predicting cobalt toxicity in soil to the potworm Enchytraeus albidus. Soil Biol. Biochem. 38: 1924-1932.

Lock K, De Schamphelaere KAC, Becaus S, Criel P, Van Eeckhout H, Janssen CR. 2007. Development and validation of a terrestrial biotic ligand model predicting the effect of cobalt on root growth of barley (Hordeum vulgare). Environ. Pollut. 147: 626-633.

Lofts S, Tipping E. 2000. Solid-solution metal partitioning in the Humber Rivers: application of WHAM and SCAMP. Science of the Total Environment 251/252: 381-399.

Lofts S, Tipping E. 2000. Solid-solution metal partitioning in the Humber Rivers: application of WHAM and SCAMP. Science of the Total Environment 251/252: 381-399.

London. 2006. City of London 2005 Annual Drinking Water Compliance Report [Internet]. London (ON): City of London Distribution System. Available from: http://www.london.ca/Water/PDFs/WaterWorks2005.pdf

London. 2009. City of London 2008 Annual Drinking Water Compliance Report [Internet]. London (ON): City of London Distribution System. Available from: http://www.london.ca/Water/PDFs/2008_Annual_Compliance_Report_Final.pdf

Loretz et al. 2005. Exposure data for cosmetic products: lipstick, body lotion, and face cream. Food and Chemical Toxicology 43: 279-291.

Macfie SM, Tarmohamed Y, Welbourn PM. 1994. Effects of cadmium, cobalt, copper, and nickel on growth of the green alga *Chlamydomonas reinhardtii*: The influences of the cell wall and pH. Archives of Environmental Contamination and Toxicology 27: 454-458.

MacLean RS, Borgmann U, Dixon DG. 1996. Bioaccumulation kinetics and toxicity of lead in *Hyalella azteca* (Crustacea, Amphipoda). Can. J. Fish. Aquat. Sci. 53: 2212-2220.

Maeda S, Fukuyama H, Yokohama E, Kuroiwa T, Ohki A and Naka K. 1997. Bioaccumulation of antimony by Chlorella vulgaris and the association mode of antimony in the cell. Appl. Organometal Chem. 11: 393-396.

Malinowska E, Szefer P, and Falandysz J. 2004. Metals bioaccumulation by bay bolete, Xerocomus badius, from selected sites in Poland. Food Chem. 84: 405-416.

Markert, B. 1994. The biological system of the elements (BSE) for terrestrial plants (Glycophytes). Sci. Total Environ. 155: 221-228.

Marks, J.G., Jr, D.V. Belsito, V.A. DeLeo, J.F. Fowler Jr, A.F. Fransway, H.I. Maibach, C.G. Mathias, M.D. Pratt, R.L. Rietschel, E.F. Sherertz, F.J. Storrs and J.S. Taylor; North American Contact Dermatitis Group. 2003. North American Contact Dermatitis Group patch-test results, 1998 to 2000. Am. J. Contact Derm. 14: 59-62.

Mateuca, R., Aka, P.V., De Boeck, M., Hauspie, R., Kirsch-Volders, M., Lison, D. 2005. Influence of *hOGG1*, *XRCC1* and *XRCC3* genotypes on biomarkers of genotoxicity in workers exposed to cobalt or hard metal dusts. Toxicology Lett. 156: 277-288.

Mathews T, Fisher NS, Jeffree RA and Teyssié JL. 2008. Assimilation and retention of metals in teleost and elasmobranch fishes following dietary exposure. Mar. Ecol. Prog. Ser. 360: 1-12.

McGeer JC, Brix KV, Skeaff JM, DeForest DK, Brigham SI, Adams WJ, and Green A. 2003. Inverse relationship between bioconcentration factor and exposure concentration for metals: implications for hazard assessment of metals in the aquatic environment. Environ. Toxicol. Chem. 22(5): 1017–1037.

McLean, J.R., McWilliams, R.S., Kaplan, J.G., Birnboim, H.C. 1982. Rapid detection of DNA strand breaks in human peripheral blood cells and animal organs following treatment with physical and chemical agents. In: Bora, K.C., Douglas, G.R. & Nestmann, E.R., eds, Progress in Mutation Research, Vol. 3, Amsterdam, Elsevier Biomedical Press, pp. 137–141 [cited in IARC 1991, IARC 2006]

Mead DJ, Cornforth IS. 1995. Proceedings of the Trees and Soil Workshop, Lincoln university 28 February-2 March 1994. Agronomy Society of New Zealand Special Publication No. 10 Lincoln University Press, Canterbury.

Vangheluwe M, Van Sprang P, Verdonck F, Heijerick D, Versonnen B, Vandenbroele M, Van Hyfte A. 2007. Metals Environmental Risk Assessment Guidance. [Internet]. London (UK): International Council of Mining and Metals [ICMN]. 32 p. Available from: http://www.icmm.com/page/1185/metals-environmental-risk-assessment-guidance-merag

Mermut AR, Jain JC, Song, L, Kerrich R, Kozak L and Jana S. 1996. Trace element concentrations of selected soils and fertilizers in Saskatchewan, Canada. Journal of Environmental Quality 25: 845-853.

Mesjasz-Przbylowicz J, Przybylowicz W, Ostachowicz B, Augustyniak M, Nakonieczny M, Migula P. 2002. Trace elements in the chrysomelid beetle (*Chrysolina pardalina*) and its Ni-hyperaccumulating host-plant (*Berkheya coddii*). Fresenius Environ. Bull. 11(2):78-84.

Metian M, Warnau M, Hédouin L, and Busamante P. 2009. Bioaccumulation of essential metals (Co, Mn and Zn) in the king scallop Pecten maximus: seawater, food and sediment exposures. Mar. Biol. 156: 2063–2075.

Mielke HW, Reagan PL. 1998. Soil is an important pathway of human lead exposure. Environmental Health Perspectives 106(s1): 217-229.

Miller, A.C., Mog, S., McKinney, L., Luo, L., Allen, J., Xu, J., Page, N. 2001. Neoplastic transformation of human osteoblast cells to the tumorigenic phenotype by heavy metal-tungsten alloy particles: Induction of genotoxic effects. Carcinogenesis. 22: 115–125 [cited in IARC 2006]

Miyaki, M., Akamatsu, N., Ono, T., Koyama, H. 1979. Mutagenicity of metal cations in cultured cells from Chinese hamster. Mutat. Res. 68: 259–263 [cited in IARC 1991, IARC 2006]

Mochizuki, H., Kada, T. 1982. Antimutagenic action of cobaltous chloride on Trp-P-1-induced mutations in Salmonella typhimurium TA98 and TA1538. Mutat. Res. 95: 145–157 [cited in IARC 1991, IARC 2006]

Mohiuddin SM, Taskar PK, Rheault M, Roy P-E, Chenard J, Morin Y. 1970. Experimental cobalt cardiomyopathy. Am Heart J. 80(4):532-543. [cited in ATSDR 2004]

Mollenhauer HH, Corrier DE, Clark DE, Hare MF, Elissalde MH. 1985. Effects of dietary cobalt on testicular structure. Virchows Arch B 49:241-248.

Montreal. 2000. Qualité de l'eau potable produite par la ville de Montréal. Montréal (QC): la ville de Montréal.

Montreal. 2004. Municipal Drinking Water Produced by Atwater and Charles-J.-des-Baillets Water Plants. Montréal (QC): la ville de Montréal.

Montreal. 2005. Municipal Drinking Water Produced by Atwater and Charles-J.-des-Baillets Water Plants. Montréal (QC): la ville de Montréal. Available from: http://www2.ville.montreal.qc.ca/pls/portal/docs/page/eau_potable_en/media/documents/annual_report_2005.pdf

Montreal. 2006. Municipal Drinking Water Produced by Atwater and Charles-J.-des-Baillets Water Plants. Montréal (QC): la ville de Montréal. Available from: http://www2.ville.montreal.qc.ca/pls/portal/docs/page/eau_potable_en/media/documents/rapport_annuel_2006_en.pdf

Moorhouse CP, Halliwell B, Grootveld M, Gutteridge JM 1985. Cobalt(II) ion as a promoter of hydroxyl radical and possible "crypto-hydroxyl" radical formation under physiological conditions. Differential effects of hydroxyl radical scavengers. *Biochimica et Biophysica Acta*, 843(3):261–268. [Cited in IPCS 2006]

Morin Y, Daniel P. 1967. Quebec beer-drinkers' cardiomyopathy: etiological considerations. Can Med Assoc J 97:926-928. [cited in IPCS 2006]

Morin Y, Tetu A, Mercier G. 1971. Cobalt cardiomyopathy: Clinical Aspects. Br Heart J 33:175-178. [cited in IPCS 2006]

Morvai V, Szakmary E, Tatrai E, Ungvary G, Folly G. 1993. The effects of simultaneous alcohol and cobalt chloride administration on the cardiovascular system of rats. Acta Physiol Hung 81(3):253-261.[cited in IPCS 2006, ATSDR 2004]

Murdock HR 1959. Studies on the pharmacology of cobalt chloride. Journal of the American Pharmaceutical Association. 48:140–142.

Nagpal NK. 2004. Technical report - Water quality guidelines for cobalt. Water Protection Section, Water, Air and Climate Change Branch, Ministry of Water, Land and Air Protection. 61p.

Nakahara M, Cross FA. 1978. Transfer of cobalt-60 from phytoplankton to the clam *Mercenaria mercenaria*. Mipopn Suisan Gakkaishi 44(5):419-425.

[NAPS] National Air Pollutants Surveillance Network. 2003 – 2008. [Prepublication NAPS data on Excel spreadsheet] Environment Canada. Air Monitoring Data.

Nation JR, Bourgeois AE, Clark DE, Hare, MF. 1983. The effects of chronic cobalt exposure on behaviour and metallothionein levels in the adult rat. Neurobehav Toxicol Teratol 5:9-15.

Natural Resources Canada and Statistics Canada. 2003. Canadian Mineral Yearbook Chapter 38: Nickel. [Modified on 12 January 2010, cited on 10 February 2010] Available from: http://www.nrcan.gc.ca/mms-smm/busi-indu/cmy-amc/com-eng.htm

Natural Resources Canada and Statistics Canada. 2003. Canadian Mineral Yearbook Chapter 38: Nickel. [Modified on 12 January 2010, cited on 10 February 2010] Available from: http://www.nrcan.gc.ca/mms-smm/busi-indu/cmy-amc/com-eng.htm

Natural Resources Canada, [GSC] Geological Survey Canada (Kliza, D., and Telmer, K.). 2001. Phase I: Lake sediment studies in the vicinity of the Horne smelter in Rouyn-Noranda, Quebec, GSC-Openfile 2952.

Nautilus Environmental (2009) Environmental. Summary of ecotoxicity data for the purpose of developing a species sensitivity distribution (SSD) for cobalt and its compounds Final Report, Available upon request.

[NCI] National Chemical Inventories [database on CD-ROM]. 2007. Issue 1. Columbus (OH): American Chemical Society. [cited 2010 Jan 11]. Available from: http://www.cas.org/products/cd/nci/index.html

Nemery B, Casier P, Roosels D, Lahaye D, Demedts M. 1992. Survey of cobalt exposure and respiratory health in diamond polishers. Am Rev Respir Dis 145:610-616.

Nfon E, Cousins IT, Jarvinen O, Mukherjee AB, Verta M, and Broman D. 2009. Trophodynamics of mercury and other trace elements in a pelagic food chain from the Baltic Sea. Sci. Total Environ. 407: 6267-6274.

Nguyen HL, Leermakers M, Elskens M, De Ridders F, Hoa Doan T, Baeyens W. 2005. Correlations , partitioning and bioaccumulation of heavy metals between different compartments of Lake Balaton. Science of the Total Environment, Vol 341, 211– 226.

Nguyen HL, Leermakers M, Elskens M, DeRidder F, Doan TH, and Baeyens W. 2005. Correlations, partitioning and bioaccumulation of heavy metals between different compartments of Lake Balaton. Sci. Total Environ. 341: 211- 226.

[NHPID] Natural Health Products Ingredients Database [Internet]. 2010. Ottawa (ON): Health Canada. [cited: 2010 March]. Available from: http://www.hc-sc.gc.ca/dhp-mps/prodnatur/applications/online-enligne/nhpid-bipsn-eng.php

Nielsen NH, Kristiansen J, Borg L, Christensen JM, Poulsen LK, Menne T. 2000. Repeated exposures to cobalt or chromate on the hands of patients with hand eczema and contact allergy to that metal. *Contact Dermatitis*, 43(4):212–215. [cited in IPCS, 2006]

Nishikawa K, Tominaga N. 2001. Isolation, growth, ultrastruture, and metal tolerance of the green alga, *Chlamydomonas acidophila* (Chlorophyta). Bioscience, Biotechnology, Biochemistry 65 (12): 2650-2656.

Nishioka, H. 1975. Mutagenic activities of metal compounds in bacteria. Mutat. Res. 31:185–189 [cited in IARC 1991, IARC 2006]

Norwood WP, Borgmann U, Dixon DG. 2006. Saturation models of arsenic, cobalt, chromium and manganese bioacccumulation by *Hyalella azteca*. Environ. Pollut. 143:519-528.

Norwood WP, Borgmann U, Dixon DG. 2007. Chronic toxicity of arsenic, cobalt, chromium and manganese to Hyalella azteca in relation to exposure and bioaccumulation. Environ. Poll. 147: 262-272.

Nriagu, JO. 1989. A global assessment of natural sources of atmospheric trace metals. Nature 338: 47–49.

NTP (National Toxicology Program). 1991. Toxicity studies of cobalt sulfate heptahydrate (CAS No. 10026-24-1) in F344/N rats and B6C3F1 mice (inhalation studies). Research Triangle Park, NC, United States Department of Health and Human Services, National Institutes of Health, (NIH Publication No. 91-3124) [cited in IARC, 2006 and IPCS, 2006].

NTP (National Toxicology Program). 1998. Toxicology and carcinogenesis studies of cobalt sulfate heptahydrate (CAS No. 10026-24-1) in F344/N rats and B6C3F1 mice (inhalation studies). (NTP Technical Report 471), Research Triangle Park, NC, pp. 1-268 and pp. 233-239.

[NTP] National Toxicology Program. 2002. Report on Carcinogens Background Document for Cobalt Sulfate. Research Triangle Park (NC): U.S. Department of Health and Human Services. Available from: http://ntp.niehs.nih.gov/ntp/newhomeroc/roc11/CoSO4Pub.pdf

NTP (National Toxicology Program). 2005a. Micronucleus test in mice Study ID A57655 http://ntp-server.niehs.nih.gov/

NTP [National Toxicology Program]. 2005b. 11th Report on carcinogens. Substance Profile: Cobalt Sulfate CAS No. 10124-43-3.

Nucho R, Rambaud A, Foulquier L, Baudin JP. 1988. Bioaccumulation du ^{60}Co par une algue planctonique, *Scenedesmus obliquus*. Influence du stade de développement de la culture sur la fixation du radionucléide. Acta Oecologica Oecologia Applicata, 9(2):111–125.

[NWRI] National Water Research Institute. Received in 2009. EC data collection program for Prairies provinces and North-West territories.

[OECD] Organisation for Economic Co-operation and Development. 1993. Bioaccumulation: sequential static fish test. OECD Guidelines for the Testing of Chemicals No. 305A. Organisation for Economic Co-operation and Development, Paris, France. 13 p.

[OECD] Organisation for Economic Co-operation and Development. 1996. Bioconcentration: flow-through fish test. OECD guidelines for the testing chemicals No. 305E. Organization for Economic Co-operation and Development, Paris, France. 23 p.

[OECD] Organisation for Economic Co-operation and Development. 2001. Guidance Document on Transformation/Dissolution of Metals and Metal Compounds in Aqueous Media. Method 29. Organization for Economic Co-Operation and Development. Paris, France.

[OECD] Organisation for Economic Co-operation and Development. 2004. Draft emission scenario on textile manufacturing wool mills [Internet]. Paris (FR): OECD, Environment Directorate. Report No.: ENV/JM/EEA(2004)8/1/REV, JT00175156. [cited 2010 03 25]. Available from: http://www.oecd.org/dataoecd/2/47/34003719.pdf

Ogawa HI, Sakata K, Inouye T, Jyosui S, Niyitani Y, Kakimoto K, Morishita M, Tsuruta S, Kato Y. 1986. Combined mutagenicity of cobalt(II) salt and heteroaromatic compounds in Salmonella typhimurium. Mutat Res 172:97-104. [cited in IARC 1991, IARC 2006]

Ogawa HI, Shibahara T, Iwata H, Okada T, Tsuruta S, Kakimoto K, Sakata K, Kato Y, Ryo H, Itoh T, Fujikawa K. 1994. Genotoxic activities in vivo of cobaltous chloride and other metal chlorides as assayed in the drosophila wing spot test. Mutat Res 320:133-140. [cited in IARC 2006]

Ogawa HI, Ohyama Y, Ohsumi Y, Kakimoto K, Kato Y, Shirai Y, Nunoshibaand T, Yamamoto K. 1999. Cobaltous chloride-induced mutagenesis in the supF tRNA gene of Escherichia coli. Mutagenesis 14(2):249-253. [cited in IARC 2006]

Olivero S, Villani P, Botta A. 1995. Genotoxic effects of cobalt chloride, sulfate and nitrate on cultured human lymphocytes. Med Sci Res 23:339-341. [cited in IPCS 2006]

[OMOE] Ontario Ministry of the Environment. 2002a. Soil Investigation and Human Health Risk Assessment for the Rodney Street Comminity, Port Colborne, Part B – Human Health Risk Assessment Main Document [Internet]. Toronto (ON): Ontario Ministry of the Environment. [Accessed 15 Jan 2010]. Available from: http://www.ene.gov.on.ca/envision/land/portcolborne/4255e.htm

[OMOE] Ontario Ministry of the Environment. 2002b. Soil Investigation and Human Health Risk Assessment for the Rodney Street Comminity, Port Colborne, Part B – Human Health Risk Assessment: Appendix 1 – Environmental Monitoring of Metals in the Rodney Street Community and Port Colborne [Internet]. Toronto (ON): Ontario Ministry of the Environment. [Accessed 9 Sept 2009]. Available from: http://www.ene.gov.on.ca/envision/land/portcolborne/4255e.htm

[OMOE] Ontario Ministry of the Environment. 2002c. Soil Investigation and Human Health Risk Assessment for the Rodney Street Comminity, Port Colborne, Part B – Human Health Risk Assessment: Appendix 3 – Detailed Estimates of Daily Intakes of Metals [Internet]. Toronto (ON): Ontario Ministry of the Environment. [Accessed 9 Sept 2009]. Available from: http://www.ene.gov.on.ca/envision/land/portcolborne/4255e.htm

[OMOE] Ontario Ministry of the Environment, Environmental Monitoring and Reporting Branch, Water Monitoring Section. 2004. Great Lakes reconnaissance survey; water and sediment quality monitoring survey, harbours and embayments, Lake Superior and the Spanish River. Available From: http://www.ene.gov.on.ca/en/publications/water/index.php

[OMOE] Ontario Ministry of the Environment. 2009. Data downloads (databases for Provincial Water Quality Monitoring Network, years 2003-2007 were downloaded). Available at: http://www.ene.gov.on.ca/en/publications/dataproducts/2Water/PWQMN_by_year/index4.php

Pacific Ecorisk . 2005. An Evaluation of the Acute Toxicity of Cobalt in Panther Creek Water to Three Resident Invertebrate Species (*Brachycentrus americanus*, *Centroptilum conturbatum*, and *Serratella tibialis*) and the Acute and Chronic Toxicity of Cobalt in Panther Creek Water to *Chironomus tentans* and *Oncorhynchus mykiss*. Testing laboratory: Pacific Ecorisk, Martinez, CA. A report to the Blackbird Mine Site Group.

Pagano, D.A. & Zeiger, E. 1992. Conditions for detecting the mutagenicity of divalent metals in *Salmonella typhimurium*. Environ. mol. Mutag. 19:139–146 [cited in IARC 2006]

Painter RB, Howard R. 1982. The hela DNA-synthesis inhibition test as a rapid screen for mutagenic carcinogens. Mutat Res 92:427-437.

Palit S, Ghosh AK, Sharma A, Talukder G. 1991a. Modification of the clastogenic effects of cobalt by calcium in bone marrow cells of mice in vivo. Cytologia 56:373-377. [cited in IPCS 2006]

Palit S, Sharma A, Talukder G. 1991b. Chromosomal aberrations induced by cobaltous chloride in mice in vivo. Biol Trace Elem Res 29:139-145. [cited in IPCS 2006]

Palit S, Sharma A, Talukder G. 1991c. Cytotoxic effects of cobalt chloride on mouse bone marrow cells in vivo. Cytobios 65:85-89. [cited in IPCS 2006]

Palit S, Sharma A, Talukder G. 1991d. Protection by chlorophyllin against induction of chromosomal aberrations by cobalt in bone marrow cells of mice in vivo. Fitoterapia 62:(5)425-428. [cited in IPCS 2006]

Pandey AK, Pandey SD, Misra V. 2000. Stability constants of metal-humic acid complexes and its role in environmental detoxification. Ecotoxicol. Environ. Safety 47: 195-200.

Papadopoulou C, Kanias GD. 1977. Tunicate species as marine pollution indicators. Mar. Pollut. Bull. 8(1):229-231.

Paquin PR, Gorsuch JW, Apte S, Batley GE, Bowles KC, Campbell PGC, Delos CG, Di Toro DM, Dwyer RL, Galvez F, Gensemer RW, Goss GG, Hogstrand C, Janssen CR, McGeer JC, Naddy RB, Playle RC, Santore RC, Schneider U, Stubblefield WA, Wood CM, Wu KB. 2002. The biotic ligand model: a historical overview. Comp. Biochem. Physiol. Part C 133, 3–35.

Paternain JL, Domingo JL, Corbella J. 1988. Developmental toxicity of cobalt in the rat. J Toxicol Environ Health 24:193-200.

Paton, G.R., Allison, A.C. 1972 Chromosome damage in human cell cultures induced by metal salts. Mutat. Res. 16: 332–336 [cited in IARC 1991]

Pavageau M-P, Morin A, Seby F, Guimon C, Krupp E, Pécheyran C, Poulleau J, Donard AFO. 2004. Partitioning of metal species during an enriched fuel combustion experiment, speciation in the gaseous and particulate phases. Environmental Science & Technology. 38(7):2252-2263.

Pedigo NG, George WJ, Anderson MB. 1988. Effects of acute and chronic exposure to cobalt in male reproduction in mice. Reprod Toxicol 2:45-53.

Pedigo NG, Vernon MW. 1993. Embryonic losses after 10-week administration of cobalt to male mice. Reprod Toxicol 7:111-116.

Pehrsson SK, Hatori N, Clyne N, Koch, J., Lins, L-E, Ryden, L. 1991. The effect of chronic cobalt exposure on cardiac function in rats. Trace Elem Med 8(4):195-198. [cited in ATSDR 2004]

Pennington JAT and Church HN. 1985. Food Values of Portions Commonly Used. 14th edition. Harper and Row, New York.

Percival JB, Dumaresq CG, Kwong YTJ, Hendry KB, Michel FA. 1996. Arsenic in surface waters, Cobalt, Ontario. Current Research; Geological Survey of Canada. p. 137-146.

Perdue EM, Ritchie JD. 2003. Dissolved organic matter in freshwaters. In: Drever JI (ed.), Surface and ground water, weathering, and soils. Amsterdam: Elsevier. pp. 273-318.

Periera R, Marques CR, Silva Ferreira MJ, Neves MFJV, Caetano AL, Antunes SC, Mendo S, and Gonçalvecs F. 2009. Phytotoxicity and genotoxicity of soils from an abandoned uranium mine area. Appl. Soil Ecol. 42: 209-220.

Perry RH, Green D. 1984. Perry's Chemical Engineers' Handbook. Sixth Edition. McGraw-Hill Publishing Company. ISBN 0-07-049479-7. p. 2336.

Pham M, Garnier J-M. 1998. Distribution of trace elements associated with dissolved compounds (<0.45 µm - 1 nm) in freshwater using coupled (frontal cascade) ultrafiltration and chromatographic separations. Environ. Sci. Technol. 32(4): 440-449.

Ponti J, Sabbioni E, Munaro B, Broggi F, Marmorato P, Franchini F, Colognato R, Rossi F. 2009. Genotoxicity and morphological transformation induced by cobalt nanoparticles and cobalt chloride: an *in vitro* study in Balb/3T3 mouse fibroblasts. Mutagenesis. 24: 439 - 445.

Prado AGS, Airoldi C. 2003. Humic acid-divalent cation interactions. Thermochim. Acta 405: 287-292.

Pratt MD, Belsito DV, DeLeo VA, Fowler Jr JF, Fransway AF, Maibach HI, Marks JG, Mathias CG, Rietschel RL, Sasseville D, Sherertz EF, Storrs FJ, Taylor JS, Zug K. 2004. North American contact dermatitis group patch-test results, 2001-2002 study period. Dermatitis 15: 176-183.

Prazmo W, Balbin E, Baranowska H, Ejchart A, Putrament A. 1975 Manganese mutagenesis in yeast. II. Conditions of induction and characteristics of mitochondrial respiratory deficient *Saccharomyces cerevisiae* mutants induced with manganese and cobalt. Genet. Res. Camb. 26: 21–29 [cited in IARC 1991, IARC 2006]

Proctor PD, Sinha B. Cobalt-nickel-cadmium mobilization, transportation, and fixation in surface waters, stream sediments and selected aquatic life in Fredericktown Co-Ni metallogenic province, Southeast Missouri. In: Trace substances in environmental health XII. Hemphill DD, editors. Proceedings of the university of Missouri's 12th annual conference on trace substances in environmental health. Columbia, Missouri. June 6-8, 1978. University of Missouri, Columbia, Missouri, 1979 pp 119-128.

Putrament A, Baranowska H, Ejchart, A, Jachymczyk W. 1977 Manganese mutagenesis in yeast. VI. Mn2+ uptake, mitDNA replication and ER induction: Comparison with other divalent cations. Mol. gen. Genet., 151: 69–76 [cited in IARC 2006]

Qian J, Xue HB, Sigg L, Albrecht A. 1998. Complexation of cobalt by natural ligands in freshwater. Environ. Sci. Technol. 32: 2043-2050.

Queneau PE, Marcuson, SW. 1996. Oxygen Pyrometallurgy at Copper Cliff—A Half Century of Progress. JOM (The Minerals, Metals & Material Society) 48 (1): 14-21.

RACA journal 2010. Kitwe Mining Exhibition. Published by Intereact Media Defined. Bedfordview, Republic of South Africa. Available from: http://www.refrigerationandaircon.co.za/index.php?option=com_content&view=section&layout=blog&id=37&Itemid=150

Rasmussen PE, Subramanian KS, and Jessiman BJ. 2001. A multi-element profile of housedust in relation to exterior dust and soils in the city of Ottawa, Canada. The Science of the Total Environment. 267: 125-140.

Reagan EL. 1992. Acute oral LD[-50] study in rats with cobalt powder. J Am Coll Toxicol 11(6):686.

Reimann C, de Caritat P. 1998. Chemical elements in the environment. Berlin (Germany): Springer-Verlag. 398 p.

Resende de Souza Nazareth, H. (1976) Efeito do cloreto de cobalto em não-disjunção. Cie. Cult.28, 1472–1475 [cited in IARC 1991, IARC 2006]

Richardson HW. 2003. Cobalt compounds [Internet]. Kirk-Othmer Encyclopedia of Chemical Technology, online version. Available from: http://mrw.interscience.wiley.com/emrw/9780471238966/kirk/article/cobarich.a01/current/pdf [restricted access].

[RIVM] Rijksinstituut voor Volksgezondheid en Milieu. 2006. Cosmetics fact sheet: To assess the risks for the consumer. Updated version for ConsExpo 4 [Internet]. [cited 2010 Feb]. Bilthoven (NL): RIVM

(National Institute for Public Health and the Environment). RIVM Report 320104001/2006. Available from: http://www.rivm.nl/bibliotheek/rapporten/320104001.pdf

Roditi HA, Fisher NS, Sañudo-Wilhelmy SA. 2000. Uptake of dissolved organic carbon and trace elements by zebra mussels. Nature 407: 78-80.

Rodriguez P, Dell'amico J, Morales D, Sánchez Blanco MJ and Alarcón JJ. Effects of salinity on growth, shoot water relations and root hydraulic conductivity in tomato plants. 1997. J. Agric. Sci. 128: 439-444.

Rondeau B, Cossa D, Gagnon P, Pham TT, Surette C. 2005. Hydrological and biogeochemical dynamics of the minor and trace elements in the St. Lawrence River. Applied Geochemistry 20 (7): 1391-1408.

Rossman, T.G., Molina, M., Meyer, L.W. 1984. The genetic toxicology of metal compounds: I. Induction of λ prophage in *E. coli* WP2s(λ). Environ. Mutag. 6: 59–69 [cited in IARC 1991, IARC 2006]

Rossman R, Barres J. 1988. Trace element concentrations in near-surface waters of the Great Lakes and methods of collection, storage and analysis. J. Great Lakes Res. 14(2): 188-204.

Santschi PH. 1984. Particle flux and trace metal residence time in natural waters. Limnol. Oceanogr. 29: 1100-1108.

Schladot JD, Backhaus F, Ostapczuk P, Emons H. 1997. Eel-pout (*Zoarces viviparus* L.) as a marine bioindicator. Chemosphere. 34(9-10):2133-2142.

Schlekat CE, McGeer JC, Blust R, Borgmann U, Brix KV, Bury N, Couillard Y, Dwyer RL, Luoma SN, Robertson S, Sappington KG, Schoeters I, and Sijm DTHM. 2007. Bioaccumulation; hazard identification of metals and inorganic metal substances. In: Adams WJ, Chapman PM, editors. Assessing the hazard of metals and inorganic metal substances in aquatic and terrestrial systems. Pensacola (FL): SETAC Publications, CRC Press. Chap 4: 55-87.

Sheppard MI, Sheppard SC, and Grant CA. 2007. Solid/liquid partition coefficients to model trace element critical loads for agricultural soils in Canada. Canadian Journal of Soil Science, 87(2): 189-201.

Sheppard, M.I., Sheppard, S.C., and Grant, C.A. 2007. Solid/liquid partition coefficients to model trace element critical loads for agricultural soils in Canada. Canadian Journal of Soil Science, 87(2): pp. 189-201.

Shi X, Dala NS and Kasprzak KS. 1993. Generation of free radicals from model lipid hydrpoeroxides and H2O2 by Co(II) in the presence of cysteinyl and histidyl chelators. Chemical Research in Toxicology. 6:277–283.

Shirakawa T, Kusaka Y, Fujimura N, Goto S, Kato M, Heki S, Morimoto K. 1989 Occupational asthma from cobalt sensitivity in workers exposed to hard metal dust. *Chest*. 95(1):29–37.

Shirakawa T, Kusaka Y, Fujimura N, Goto S, Morimoto K. 1988. The existence of specific antibodies to cobalt in hard metal asthma. *Clinical Allergy*, 18:451–460.

Shrivastava VK, David CV, Khare N, et al. 1996. Cobalt chloride induced histopathological changes in thyroid gland of female mice, Mus musculus (P.). Pollut Res 15(3):307-309. [cited in ATSDR 2004]

Shuman MS, Smock LA, Haynie CL. 1977. Metals in the water, sediment and biota of the Haw and New Hope Rivers, North Carolina. Department of Environmental Sciences and Engineering, School of Public Health, University of North Carolina at Chapel Hill. Project No. A-070-NC.

Sibly RM. 1981. Strategies of digestion and defecation. In: Physiological Ecology, Townsend CR, Colon P, editors. Blackwell Publishing.

Singh I. 1983. Induction of reverse mutation and mitotic gene conversion by some metal compounds in Saccharomyces cerevisiae. Mutat Res 117:149-152. [cited in IARC 1991, IARC 2006]

Singh PP, Junnarkar AY. 1991. Behavioral and toxic profile of some essential trace metal salts in mice and rats. Indian J Pharmacol 23:153-159.

Skeaff JM, Hardy DJ, King P. 2008. A new approach to the hazard classification of alloys based on transformation/dissolution. Integr. Environ. Assess. Manage. 4(1): 75-93.

Smith IC, Carson BL. 1981. Trace metals in the environment. Ann Arbor, MI: Ann Arbor Publishers. Volume 6: Cobalt. 1202p.

Smith IC, Carson BL. 1981. Trace metals in the environment. Ann Arbor, MI: Ann Arbor Publishers. Volume 6: Cobalt. 1202 p.

Smith RM, Martell AE. 2004. Critical constants for metal complexes [database on a CD-ROM]. NIST Standard Reference database 46 Version 8. Gaithersburgh (MD): U.S. Department of Commerce, National Institute of Standards and Technology. [updated 2004]. Available from: http://www.nist.gov/srd/nist46.htm

Smolders E, McGrath S, Fairbrother A, Hale BA, Lombi E, McLaughlin M, Rutgers M, Van der Vliet L. 2007. In: Adams WJ, Chapman PM (eds.). Hazard identification approaches for metals and inorganic metal substances. Pensacola (FL): SETAC Press. p. 113-133.

Smolders E, Oorts K, Van Sprang P, Schoeters I, Janssen CR, McGrath SP, McLaughlin MJ. 2009. Toxicity of trace metals in soil as affected by soil type and aging after contamination: using calibrated bioavailability models to set ecological soil standards. Environ. Toxicol. Chem. 28(8): 1633-1642.

Snyder, R.D., Davis, G.F., Lachmann, P.J. 1989. Inhibition by metals of X-ray and ultraviolet induced DNA repair in human cells. Biol. trace Elem. Res. 21: 389–398 [cited in IARC 2006]

Speijers GJA, Krajnc EI, Berkvens JM, van Logten MJ. 1982. Acute oral toxicity of inorganic cobalt compounds in rats. Food Chem Toxicol 20:311-314.

[SSD Master] Determination of Hazardous Concentrations with Species Sensitivity Distributions [Computer Model]. 2008. Version 2. Ottawa (ON): Intrinsikscience.

Stanley AJ, Hopps HC, Shideler AM. 1947. Cobalt polycythemia. II. Relative effects of oral and subcutaneous administration of cobaltous chloride. Proc Soc Exp Biol Med 66:19-20.

Statistics Canada. 2000. Sound recording survey 2000. Catalogue no. 87F0008XIE Available from: http://publications.gc.ca/control/publicHomePage?lang=English

Statistics Canada. 2007. Sound recording and music publishing service bulletin 2007. Catalogue no. 87F0008X Available from: http://publications.gc.ca/control/publicHomePage?lang=English

Statistics Canada. 2008. Metal ore mining NAICS 2122 for 2006, Catalogue no. 26-223-X, Available from: http://www.statcan.gc.ca/bsolc/olc-cel/olc-cel?lang=eng&catno=26-223-X

Stevenson, CD 1985. Analytical advances and changing perceptions of environmental heavy metals. J. Royal. Soc. New Zealand 15(4): 355-362.

Stockdale A, Davison W, Zhang H, Hamilton-Taylor J. 2010. The association of cobalt with iron and manganese (oxyhydr)oxides in marine sediment. Aquat. Geochem. DOI 10.1007/s10498-010-9092-1.

[STN] STN on the web. [database on the Internet]. 1984. Chemical Abstracts Services, Columbus:OH. Available from: https://stnweb.cas.org/ (restricted access).

Sullivan JF, Egan JD, George RP. 1969. A distinctive myocardiopathy occurring in Omaha, Nebraska: Clinical aspects. Ann N Y Acad Sci 156(1):526-543 [cited in IPCS 2006]

Suttle NF, Bell J, Thornton I, Agyriaki A. 2003. Predicting the risk of cobalt deprivation in grazing livestock from soil composition data. Environ. Geochem. Health 25(1): 33-39.

Suzuki Y, Shimizu H, Nagae Y, Fukumoto M, Okonogi H, Kadokura M. 1993. Micronucleus test and erythropoiesis: Effect of cobalt on the induction of micronuclei by mutagens. Environ Mol Mutagen 22:101-106. [cited in IARC 2006, IPCS 2006]

Swennen B, Buchet J-P, Stanescu D, Lison D, Lauwerys R. 1993. Epidemiological survey of workers exposed to cobalt oxides, cobalt salts, and cobalt metal. Br J Ind Med 50:835-842.

Szakmary E, Ungvary G, Hudak A, Tatrai E, Naray M, Morvai V. 2001. Effects of cobalt sulfate on prenatal development of mice, rats, and rabbits, and on early postnatal development of rats. J Toxicol Environ Health A 62:367-386.

Szefer P, Falandysz J. 1985. Trace metals in muscle tissue of fish taken from the Southern Baltic. Z. Lebensm. Unters. Forsch. 181:217-220.

Szefer P, Falandysz J. 1983. Investigations of trace metals in Long-tailed duck (*Clangula hyemalis* L.) from the Gdańsk Bay. Sci. Tot. Environ. 29:269-276.

Szefer P, Skwarzec B, Koszteyn J. 1985. The Occurrence of some Metals in Mesozooplankton Taken From the Southern Baltic. Mar. Chem. 17:237-253.

Szefer P, Szefer K. 1985. Occurrence of ten metals in *Mytilus edulis* L. and *Cardium glaucum* L. from the Gdańsk Bay. Mar. Pollut. Bull. 16(11): 446-450.

Szefer P. 1991. Interphase and trophic relationships of metals in a Southern Baltic ecosystem. Sci. Total Environ. 101:210-215.

Takeno N. 2005. Atlas of Eh-pH diagrams. Geological Survey of Japan Open File Report No. 419. National Institute of Advanced Industrial Science and Technology. 285 p. Available from: http://www.gsj.jp/GDB/openfile/files/no0419/openfile419e.pdf.

Taylor A, Marks V, Shabaan AA, et al. 1977. Cobalt induced lipaemia and erthropoiesis. Dev Toxicol Environ Sci 1:105-108. [cited in ATSDR 2004]

Tessier A, Campbell PGC, Bisson M. 1979. Sequential extraction procedure for the speciation of particulate trace metals. Anal. Chem. 51(7): 844-850.

Tewari A, Joshi HV, Raghunathan C, Sravan Kumar VG, Kotiwar OS. 2000. New record of *Mytilus viridis* Linn., its density, growth and accumulation of heavy metals on Saurashtra coast, Arabian Sea. Current Sci. 78(1): 97-101.

Thibault DH, Sheppard MI, Smith PA. 1990. A Critical Compilation and Review of Default Soil Solid/Liquid Partition Coefficients, Kd, for use in Environmental Assessments: Report Number 10125. Pinawa (MB.) Atomic Energy of Canada Limited.

Thibault DH, Sheppard MI, Smith PA. 1990. A Critical Compilation and Review of Default Soil Solid/Liquid Partition Coefficients, Kd, for use in Environmental Assessments: Report Number 10125. Pinawa (MB.) Atomic Energy of Canada Limited.

Tipping E, Lofts S, Lawlor AJ. 1998. Modelling the chemical speciation of trace metals in the surface waters of the Humber system. Sci. Total Environ. 210/211: 63-77.

Tipping E. 2002. Cation binding by humic substances. Cambridge (UK): Cambridge University Press. 434 p.

Tong SSC, Gutenmann WH, Lisk DJ, Burdick GE, and Harris EJ. 1972. Trace metals on New York State fish. New York Fish Game J. 19(2):123-131.

Tong SSC, Youngs WD, Gutenmann WH, and Lisk DJ. 1974. Trace metals in lake Cayuga lake trout (*Salevinus namaycush*) in relation to age. J. Fish. Res. Board Can. 31(2):238-239.

Tso W-W, Fung W-P. 1981. Mutagenicity of metallic cations. Toxicol Lett 8:195-200. [cited in IARC 1991, IARC 2006]

[US EPA] US Environmental Protection Agency. 1998. Compilation of air pollutant emission factors, Volume 1: Stationary Point and Area Sources, Fifth Edition, AP 42 Supplement E.

Uter, W., Hegewald J., Aberer W., Ayala F., Bircher A.J., Brasch J., Coenraads P.J., Schuttelaar M.L., Elsner P., Fartasch M., Mahler V., Belloni Fortina A., Frosch P.J., Fuchs T., Johansen J.D., Menne T., Jolanki R., Krecisz B., Kiec-Swierczynska M., Larese F., Orton D., Peserico A., Rantanen T. and Schnuch A. 2005. The European standard series in 9 European countries, 2002/2003 – first results of the European Surveillance System on Contact Allergies. Contact Dermatitis 53: 136-145.

Vaganov PA, Kulikov VD, Shtangeeva IV. 1978. Biogeochemical characteristics of Barents Sea algae (based on results of neutron-activation analysis). Geokhimiya 11:1740-1745.

Van de Velde K, Ferrari C, Barbante C, Moret I, Bellomi T, Hong S, Boutron C. 1999. A 200 year record of atmospheric cobalt, chromium, molybdenum and antimony in high altitude alpine firn and ice. Environmental science and technology. 33(20): 3495-3501

Van Goethem F, Lison D, Kirsch-Volders M. 1997. Comparative evaluation of the in vitromicronucleus test and the alkaline single cell gel electrophoresis assay for the detection of DNA metallic cobalt particles 154 damaging agents: Genotoxic effects of cobalt powder, tungsten carbide and cobalt-tungstencarbide. Mutattion Research. 392: 31–43.

Vancouver. 2009. Drinking Water Quality 2008 Annual Report. Vancouver (BC): City of Vancouver. Available from: http://vancouver.ca/engsvcs/watersewers/water/pdf/WQReport_2008.pdf

Victoria. 2009. 2008 Treated Water Quality below Japan Gulch Plant. Victoria (BC): CRD Water Servies. Available from: http://www.crd.bc.ca/water/waterquality/documents/Table2.pdf

Voroshilin, S.I., Plotko, E.G., Fink, T.V., Nikiforova, V.J. 1978. [Cytogenetic effect of inorganic compounds of tungsten, zinc, cadmium and cobalt on animal and human somatic cells]. Tsitol.Genet. 12 241–243 (in Russian) [cited in IARC 1991, IARC 2006]

Wang W-X, Guo L. 2000. Bioavailability of colloid-bound Cd, Cr, and Zn to marine plankton. Mar. Ecol. Prog. Ser. 202: 41-49.

Wappelhorst O, Kükn I, Heidenreich H, and Markert B. 2002. Transfer of selected elements from food into human milk. Nutrition 18: 316-322.

Warshaw,E.M.; Ahmed,R.L.; Belsito,D.V.; Deleo,V.A.; Fowler,J.F.,Jr.; Maibach,H.I.; Marks,J.G.,Jr.; Toby Mathias,C.G.; Pratt,M.D.; Rietschel,R.L.; Sasseville,D.; Storrs,F.J.; Taylor,J.S.; Zug,K.A. 2007. Contact dermatitis of the hands: cross-sectional analyses of North American Contact Dermatitis Group Data, 1994-2004. J Am Acad Dermatol. 57(2): 301-314.

Watmough SA, Dillon PJ, Epova EN 2005. Metal partitioning and uptake in central Ontario forests. Environmental Pollution 134, p 493-502.

Watmough SA, Dillon PJ, Epova EN 2005. Metal partitioning and uptake in central Ontario forests. Environmental Pollution 134, p 493-502.

Wedrychowski, A., Schmidt, W.N., Hnilica, L.S. 1986 DNA-protein crosslinking by heavy metals in Novikoff hepatoma. Arch. Biochem. Biophys. 251 397–402 [cited in IARC 1991, IARC 2006]

Winnipeg. 2002. 2001 Drinking Water Quality Test Results. Winnipeg (MB): Winnipeg Water and Waste Department. Available from: http://www.winnipeg.ca/waterandwaste/pdfs/water/2001_water/winnipeg.pdf

Winnipeg. 2003. 2002 Drinking Water Quality Test Results. Winnipeg (MB): Winnipeg Water and Waste Department. Available from: http://www.winnipeg.ca/waterandwaste/pdfs/water/2002_water/winnipeg.pdf

[WHO] World Health Organization. 1989. Minor and trace elements in breast milk. Geneva (CH): World Health Organization / International Atomic Energy Association. http://whqlibdoc.who.int/publications/1989/9241561211.pdf

[WHO] World Health Organization. 1994. Biological Monitoring of Metals. Geneva (CH): http://whqlibdoc.who.int/hq/1994/WHO_EHG_94.2.pdf

Wong, P.K. 1988. Mutagenicity of heavy metals. Bull. environ. Contam. Toxicol. 40: 597–603 [cited in IARC 1991, IARC 2006]

Wren CD, Maccrimmon HR, Loescher BR. 1983. Examination of bioaccumulation and biomagnification of metals in a Precambrian shield lake. Water Air Soil Pollut. 19:277-291.

Yasuda H, Uchida S, Murumatsu Y, Yoshida S. 1995. Sorption of manganese, cobalt, zinc, strontium and cesium onto agricultural soils: statistical analysis on effects of soil properties. Water, air, and soil Pollution, vol 83, 85-96.

Yesilada, E. 2001. Genotoxicity testing of some metals in the *Drosophila* wing somatic mutation and recombination test. Bull. environ. Contam. Toxicol. 66: 464–469 [cited in IARC 2006]

Yokoiyama, A., Kada, T., Kuroda, Y. 1990. Antimutagenic action of cobaltous chloride on radiation-induced mutations in cultured Chinese hamster cells. Mutat. Res. 245: 99–105 [cited in IARC 2006]

Ysart G, Miller P, Crews H, Robb P, Baxter M, De L'Argy C, Lofthouse S, Sargent C and Harrison N. 1999. Dietary exposure estimates of 30 elements from the UK Total Diet Study. Food Additives and Contaminants. 19(9): 391-403.

Zeiger, E., Anderson, B., Haworth, S., Lawlor, T., Mortelmans, K. 1992 Salmonella mutagenicity tests: V. Results from the testing of 311 chemicals. Environ mol. Mutagen. 19 (Suppl. 21): 2–141 [cited in IARC 2006]

Appendix I - Details of the modeling with WHAM VI and descriptions of water types used

Speciation of metals in the dissolved phase was determined with the help of the Windermere Humic Aqueous Model (WHAM Model 6.0.7: Tipping 2002).

- Metal complexes most likely to occur in selected water types were determined from Eh–pH diagrams (Brookins 1988).
- Thermodynamic constants for metal–inorganic ligand interactions were obtained from NIST (National Institute of Standards and Technology) Standard Reference database 46 (Smith and Martell 2004).
- When needed, constants were corrected for an ionic strength of 0 using the Extended Dubye–Hückel equation in order to produce a thermodynamic database usable by WHAM.
- All chemical concentrations were converted as moles/L before entering them in WHAM spreadsheet.
- To convert DOC concentrations (mg C/L) to humic (HA) and fulvic (FA) concentrations (mg/L), it was assumed that (i) the ratio of DOM:DOC is 2:1 (Buffle 1988; DOM is dissolved organic matter) and (ii) 60% of DOM is composed of humic substances (i.e., HA and FA) with a ratio 1 HA:3 FA (Perdue and Ritchie 2003).
- Dissolved inorganic carbon or HCO_3^- concentrations were entered in the spreadsheet as CO_3^{2-} concentrations.

Table A.1. Physico-chemical characteristics of surface waters used to model speciation of cobalt in solution. *

Water body/location	**N** (water samples)	**Dissolved Inorganic Carbon**	**NO_3^{2-}**	**Cl^-**	**SO_4^{2-}**	**pH**	**Ca**	**Mg**	**Na**	**K**
		Means in moles/L								
Clear Lake, Alberta Prairie [a]	35	4.63×10^{-3}	1.51×10^{-6}	7.79×10^{-4}	2.92×10^{-3}	8.6	1.23×10^{-3}	1.51×10^{-3}	7.52×10^{-3}	6.14×10^{-4}
Lake Ontario [b]	17 to 85	1.71×10^{-3}	--	7.02×10^{-4}	3.21×10^{-4}	8.2	9.22×10^{-4}	3.55×10^{-4}	5.70×10^{-4}	4.22×10^{-5}
Allard River, Station 12	3	Rivers of the Canadian Precambrian Shield, Abitibi-James Bay, Quebec [c]								
		5.28×10^{-4}	5.27×10^{-6}	2.77×10^{-5}	5.99×10^{-5}	6.97	2.33×10^{-4}	1.36×10^{-4}	1.04×10^{-4}	4.14×10^{-5}
Colombière River, Station 1		2.13×10^{-4}	1.08×10^{-7}	1.30×10^{-5}	2.41×10^{-5}	6.36	1.17×10^{-4}	2.65×10^{-5}	3.78×10^{-5}	8.78×10^{-6}
10% Lake Ontario [d]	17 to 85	1.71×10^{-4}	--	7.02×10^{-5}	3.21×10^{-5}	7.30	9.22×10^{-5}	3.55×10^{-5}	5.70×10^{-5}	4.22×10^{-6}

(Continued)

Water body/location	**Al**	**Fe**	**Mn**	**DOC** (mg C/L)	**Co**
	Means in moles/L				
Clear Lake	2.21×10^{-6}	1.13×10^{-6}	1.30×10^{-7}	13.6	6.15×10^{-9}
Lake Ontario	5.46×10^{-7}	4.81×10^{-7}	3.08×10^{-8}	1.91	6.86×10^{-10}
Allard River, Station 12	Rivers of the Canadian Precambrian Shield, Abitibi-James Bay, Quebec				
	7.23×10^{-6}	3.93×10^{-6}	2.68×10^{-7}	18.2	1.53×10^{-9}
Colombière River, Station 1	4.91×10^{-6}	4.79×10^{-6}	3.98×10^{-7}	14.3	8.32×10^{-10}
10% Lake Ontario	5.46×10^{-8}	4.81×10^{-8}	3.08×10^{-9}	1.0	2.73×10^{-7}

* All values are for the dissolved phase.

[a] Alberta Environment (2010). Surface water quality data from Clear Lake in Alberta: averages of chemical concentrations measured from 2001 to 2006 (N=35). Concentrations less than detection limits (DL) were given values of half DL. A PO_4^{3-} concentration of 6.34 µmoles/L was also considered for modelling with this water type.

[b] Borgmann et al. (2005)and Rossman and Barres (1988). Al, Fe, Mn and Co concentrations were obtained from the latter paper.

[c] Couillard et al. (2008). Only stations without perturbations considered. Filtered water samples (0.45 µm poresize). Sampling performed in June 2003.

[d] Borgmann et al. (2005). Element concentrations were approximately the tenth of those of full Lake Ontario water. Chemical speciation determined at the 7-day LC_{50} of cobalt for the freshwater amphipod *Hyalella azteca.*

Appendix II – Criteria and considerations for determining the quality of BCF and BAF values, and other bioaccumulation ratios, for metals and elements

The following criteria and considerations were used to determine the reliability of BCF and BAF studies used in this screening assessment:

1. Evidence is provided to the effect that steady state (SS) is reached between chemical concentrations in the test organism and those of its surrounding medium (BCFs and BAFs are required to be obtained at SS). Calculation methods may be based on kinetic rate constants or on concentrations obtained at SS.
2. BAFs measured under field exposures defined in time (e.g., transplantation of organisms) are preferred over laboratory-derived BCFs because they provide information about the element's actual bioaccumulation behaviour in the environment and because they comprise a bioaccumulation measure that includes all routes of chemical uptake and elimination.
3. Reports of samplings in natural environments offer advantages similar to the above, but assumption of SS is to be judged on a case-by-case basis.
4. Metal concentrations in test organism and water are measured simultaneously.
5. Metal concentrations in water are low in order to (1) minimize BCF/BAF decreases with increases in exposure concentrations, (2) be well below levels causing chronic toxicity (e.g., OECD 1993, 1996) and (3) water concentrations and tissue concentrations must be significantly above detection limits.
6. Methodological details are provided (e.g., organism weights, replication, use of controls, method of chemical analysis, water quality).
7. Quality assurance and quality control (QA/QC) checks are reported, allowing one to judge whether or not good laboratory practices were followed.
8. To the extent possible, BCFs and BAFs are expressed on a wet weight basis. When published information permits, body concentrations are corrected for metal concentrations in gut contents, and bioaccumulation ratios are corrected for background metal concentrations in test organism and water.
9. Consideration is given to degree of essentiality of the metal entity. For example, BCFs and BAFs are expected to be of little usefulness for macroelements. Elements known by science to be macronutrients include H, C, N, O, P, S, Cl, Ca, Mg, Na, K, and Fe (Markert 1994). They may however have some relevance for micronutrients. In this context, a micronutrient can be defined as any non-macronutrient element for which there is some evidence of nutritional essentiality.
10. Consideration is given to detoxification mechanisms. For example, BCFs and BAFs are less meaningful for organisms that store large quantities of metals in inert forms or for organisms that regulate metals to a constant tissue level regardless of exposure concentration.
11. Studies reporting metal concentrations in water and tissues measured before 1977–1978 are generally considered of uncertain quality and potentially of low reliability because of numerous analytical difficulties, at that time, brought about notably by sources of inadvertent contamination, poor reproducibility and

problems associated with filtration and separation of metals in water (e.g., Hume 1973; Beneš and Steinnes 1974; Batley and Gardner 1977; Stevenson 1985).

Considerations in the evaluation of BSAF-soil, BSAF-sediment, BMF and TTF:

12. All the criteria above, except No. 8, can be transposed to the evaluation of the present bioaccumulation ratios. Criterion No. 8 is replaced by the criteria below.
13. To the extent possible, BSAF-soil, BSAF-sediment, BMF and TTF are expressed on a whole-body wet weight basis. Bioaccumulation ratios are corrected for background metal concentrations in test organism and in abiotic compartment.
14. To the extent possible, gut cleared tissue concentrations are needed for organism exposed to contaminated sediments and soils.
15. To the extent possible, non gut cleared tissue concentrations are needed for trophic transfer calculations.

Studies selected in the present context may not meet all of the above criteria and may be attributed high to moderate confidence scores; those with low confidence scores are not generally retained. These critical evaluations are made with the help of robust study summaries developed for bioaccumulation data. These robust study summaries are available upon request.

Appendix III: Complete summary of experimental data selected for estimating the bioaccumulation potential of cobalt*,**

Organism	Study Type		Evidence of SS	Water conc. meas.	End-point	Mean value (wet wt)	Reliability[1]	Reference
Marine Invertebrate								
Ruditapes decussatus (Grooved carpet shell clam)	Field	Su	N	Y	BAF	366	H	El-Shenawy 2004
Ruditapes decussatus (Grooved carpet shell clam)	Field	Su	N	Y	BAF	227	H	El-Shenawy 2004
Pecten maximus (King scallop)	Lab	SS	Y	Y	BCF	40	H	Metian et al. 2009
Pecten maximus (King scallop)	Lab	SS	Y	Y	BSAF-sed.	0.067	H	Metian et al. 2009
Marine Fish								
Sparus auratus (Gilt-head bream)	Lab	SS	N	Y	BCF	20.4	H	Mathews et al. 2008
Freshwater Algae								
Selenastrum capricornutum (Green algae)	Lab	SS	N	Y	BCF	1750	S	Corisco and Carreiro 1999
Phytoplankton	Field	Su	N	Y	BAF	456	S	Ikemoto et al. 2008
Marine Algae								
Pavlova viridis (Flagellate algae)	Lab	SS	Y	N	BCF	720	S	Chen et al. 1998
Freshwater Invertebrate								
Macrobrachium equidens (Rough river prawn)	Field	Su	N	Y	BAF	2280	S	Ikemoto et al. 2008
Macrobrachium rosenbergii (Giant river prawn)	Field	Su	N	Y	BAF	1710	S	Ikemoto et al. 2008
Macrobrachium sp.4	Field	Su	N	Y	BAF	1630	S	Ikemoto et al. 2008
Metapenaeus tenuis	Field	Su	N	Y	BAF	1470	S	Ikemoto et al. 2008
Macrobrachium sp.3	Field	Su	N	Y	BAF	1220	S	Ikemoto et al. 2008
Dreissena polymorpha (Zebra mussel)	Lab	Ki	Y	Y	BCF	1100	S	Fraysse et al. 2002
Corbicula fluminea (Asian clam)	Lab	Ki	Y	Y	BCF	530	S	Fraysse et al. 2002
Hyallela azteca (Freshwater amphipod)	Lab	Ki	Y	Y	BCF (ww)	515	H	Norwood et al. 2006

Daphnia magna (Water flea)	Lab	Ki	Y	Y	BCF	265	H	Adam et al. 2001
Chironomidae (Lake flies)	Field	Su	N	Y	BAF	148	S	Cherry et al. 1979
Enallagma sp. (Bluets)	Field	Su	N	Y	BAF	29.3	S	Cherry et al. 1979
Libellula sp. (Dragonflies)	Field	Su	N	Y	BAF	24.5	S	Cherry et al. 1979
Procambarus sp. (crayfish)	Field	Su	N	Y	BAF	21.8	S	Cherry et al. 1979
Chironomidae (Lake flies)	Field	Su	N	Y	BSAF-sed.	0.645	S	Cherry et al. 1979
Enallagma sp. (Bluets)	Field	Su	N	Y	BSAF-sed	0.221	S	Cherry et al. 1979
Libellula sp. (Dragonflies)	Field	Su	N	Y	BSAF-sed	0.138	S	Cherry et al. 1979
Procambarus sp. (crayfish)	Field	Su	N	Y	BSAF-sed	0.091	S	Cherry et al. 1979
Freshwater fish								
Pisodonophis boro (Estuary snake eel)	Field	Su	N	Y	BAF	3110	S	Ikemoto et al. 2008
Cyclocheilichthys armatus (Carp)	Field	Su	N	Y	BAF	1490	S	Ikemoto et al. 2008
Glossogobius aureus (Golden goby)	Field	Su	N	Y	BAF	1420	S	Ikemoto et al. 2008
Polynemus paradiseus (Paradise threadfin)	Field	Su	N	Y	BAF	1200	S	Ikemoto et al. 2008
Cynoglossus sp.2 (Tonguesole)	Field	Su	N	Y	BAF	991	S	Ikemoto et al. 2008
Eleotris melanosoma (Ebony sleeper)	Field	Su	N	Y	BAF	849	S	Ikemoto et al. 2008
Punitioplites proctozysron	Field	Su	N	Y	BAF	778	S	Ikemoto et al. 2008
Clupeoides sp.	Field	Su	N	Y	BAF	708	S	Ikemoto et al. 2008
Parambassis wolfii (Duskyfin glassy perchlet)	Field	Su	N	Y	BAF	559	S	Ikemoto et al. 2008
Salmo gairdneri irideus (Rainbow trout) eggs	Lab	Ki	Y	Y	BAF	7.4	S	Kimura and Honda 1977
Freshwater Zooplankton								
Zooplankton (including *Eudiaptomus gracilis, Cyclops vicinus* and *Mesocyclops leukarti*)	Field	Su	N	Y	BAF	1590	S	Nguyen et al. 2005
Soil – Fungi								

Xerocomus badius (Bay bolete)	Field	Su	Y	Y	BSAF soil - Cap only	0.15 (0.009 - 0.81) [0.95 (0.06 - 5.26)]	n/a	Malinowska et al. 2004
Xerocomus badius (Bay bolete)	Field	Su	Y	Y	BSAF soil - Stalk only	0.11 (0.007 - 0.81) [0.7 (0.05- 5.26)]	n/a	Malinowska et al. 2004
Soil - Plant								
Morus alba (White mulberry)	Field	Tr	N	Y	BSAF-soil	0.28 [0.92]	n/a	Ashfaq et al. 2009
Brassica napus (Oilseed rape)	Lab	SS	N	Y	BAF soil - Shoot only	0.146 [0.729]	n/a	Li et al. 2009
Lycopersicon esculentum (Tomato)	Lab	SS	N	Y	BAF soil - Shoot only	0.100 [0.668]	n/a	Li et al. 2009
Hordeum vulgare (Barley)	Lab	SS	N	Y	BAF soil - Shoot only	0.121 [0.605]	n/a	Li et al. 2009
Morus alba (White mulberry)	Field	Tr	N	Y	BSAF-soil	0.078 [0.26]	n/a	Ashfaq et al. 2009

* BCFs, BAFs and BSAFs expressed on a dry weight basis have been converted to a wet weight basis using the following conversions: per one gram of wet material, assume 0.2 g dry for invertebrates and fish (e.g., Ikemoto et al. 2008; Campbell et al. 2005); 0.1g dry for mushrooms (Pennington and Church, 1985); 0.65g dry for forest soils; 0.2g dry for agricultural soils; 0.2 g dry for oilseed rape shoots and barley shoots (Behrens et al. 2006); 0.15g dry for tomato shoots (Brewitz et al. 1996; Rodriguez et al. 1997); 0.24g for mulberry leaves (likened to the aerial part of grass plants, from Harris 1975 and Sibly 1981). In the study done by Pereira et al. (2009), plant and soil moisture content was directly reported, facilitating conversions.

** **Abbreviations**: SS: Steady state & Steady state study; Su: Field survey of organisms, water, sediment etc.; Ki: Study of kinetics of uptake and depuration; Steady state study coupled with transplantation or deployment; Y/N: Yes and No; S: Satisfactory; H: High confidence; BAF: Bioaccumulation factor expressed in litres per kilogram; BCF: Bioconcentration factor, expressed in litres per kilogram; BSAF-sed: Biota- sediment accumulation factor; BSAF-soil: Biota-soil accumulation factor; n/a: Not applicable

[1] Reliability score considered not applicable for soil data, as Robust Study Summary (RSS) grading scheme has not yet been developed for soil experiments for comparison to aquatic RSS outcomes. Soil studies were nonetheless reviewed for quality assurance.

Appendix IV: Summary of Studies Rejected for Use in Estimating the Bioaccumulation Potential of Cobalt*,**

Reference	End Point	Maximum Value Observed	Organism	Reason for Rejection
Adeyeye 2002	BAF	1900[1] L/kg	*Sudananautes africanus africanus* (West African crab)	Test conditions not adequately reported.
Bird et al. 1998	K_u	1400 d^{-1} in tadpoles	*Semotilus margarita* (Pearl dace), *Cottus cognatus* (Slimy sculpin), *Pimephales promelas* (Fathead minnow), *Rana catesbeiana* (Tadpoles) and *Coregonusclupeaformis* (Lake whitefish)	Study measured uptake of radiotracers; water concentrations and BAFs not reported.
Brugmann 1981	BAF	none	Fish, mussels, and macrophytes of the Baltic Sea	Study only reported measurements of other papers (no new data); organism concentrations of cobalt were not reported.
				.
Cherry and Guthrie 1977	BCF, BSAF-sed.	BCF: 28.3 L/kg in invertebrates and plants; BSAF-sed: 0.154 in invertebrates and plants	*Chironomidae* (Midges), *Astacidae* (Crayfish), *Libellula* sp. (Odonates), *Gambusia affinis* (Mosquito fish), *Rana* sp. (Tadpoles), *Oscillatoria* sp., *Lemna perpusilla* (duckweed), *Hydrodictyon* sp., *Pontederia* sp., *Typha latifolia* (Cattail), *Taxodium distichum* (Cypress)	Chemical analysis performed prior to 1977; considered to be of unreliable quality.
Fowler et al 2004	BCF	82 L/kg for *C. andromeda*	*Aurelia aurita* (Pelagic jellyfish) and *Cassiopea andromeda* (Benthic jellyfish)	Review paper; no new data provided.
Lithner et al. 1995	BAF	none	*Fontinalis antipyretica* (Bryophyte), *Asellus aquaticus, Sialis lutaria* and *Libellulidae* (Invertebrates), *Perca fluviatilis* and *Esox lucius* (Fish)	Water and organism samples not taken simultaneously; cobalt measurements in organisms not included in metal analysis.

Mesjasz-Prbylowicz et al. 2002	BMF	none	*Chrysolina pardalina* (Chrysomelid beetle), *Berkheya coddii* (Asteraceae plant)	Cobalt measurements not included in chemical analysis.
Nucho et al. 1988	BCF	4000 L/kg	*Scenedesmus obliquus* (Algae)	Culture medium free of cold cobalt; hyperaccumulator test species used; cobalt is an essential element to this test species.
Papadopoulou and Kanias 1977	BAF	340 L/kg for *M. sulcatus*	*Microcosmus sulcatus, Ciona intestinalis* (Marine tunicates)	Chemical analysis performed prior to 1977; considered to be of unreliable quality. Water and organisms not sampled simultaneously.
Pereira et al. 2009	BSAF-soil	3.50 in lettuce	*Lactuca sativa* (Lettuce), *Zea mays* (Maize)	Cobalt concentrations not directly reported in soil or plant tissue. Cannot correct for background concentrations in soil.
Schladot et al. 1997	CM, CL	None	*Zoarces viviparus* (Eel-pout)	No details provided on water sampling; no organism or water concentration measurements reported.
Shuman et al. 1977	BAF	BAF: 8.88 L/kg in discriminate feeders (including Ephemeroptera, Gastropoda, Decapoda, and Plecoptera)	Sediment-dependent organisms, filter feeders, discriminate feeders, carnivores, and surface feeders of the Haw and New Hope Rivers (NC)	Chemical analysis performed prior to 1977; considered to be of unreliable quality. Organisms not gut-cleared upon anlaysis.

Szefer 1991	BAF	4700 L/kg in soft tissue of the mollusc *Mya arenaria*	Southern Baltic algae, zooplankton, molluscs, crustacea, fish	Chemical analysis performed before 1977; considered to be of unreliable quality. Water and organism samples not taken simultaneously.
Szefer and Falandysz 1983	CT[2]	0.44 µg/g in female heart tissue (dry-weight)	*Clangula hyemalis* (Long-tailed duck)	BAF, BMF not provided; water measurements not taken.
Szefer and Falandysz 1985	CM	0.019 µg/g in Herring (*Clupea harengus*)	11 fish species of the Baltic Sea	BAF, BMF not provided; water measurements not taken.
Szefer and Szefer 1985	CS	4.6 µg/g in *M. edulis*	*Mytilus edulis* and *Cardium glaucum* (Marine molluscs)	BAF, BMF not provided; water measurements not taken.
Tewari et al. 2000	CS	16.39 µg/g	*Mytilus viridis* (Green mussel)	BAF not provided; water measurements not taken.
Wren et al. 1983	CT[3]	5.4 µg/g in clams (*Elliptio dilata*)	Clam, fish, bird, and mammal species of a precambrian shield lake	Water measurements not taken; no BAF provided.

***Abbreviations:** BAF: Bioaccumulation factor, BSAF-soil: Biota-soil accumulation factor, K_u: radionuclide uptake coefficient, BCF: Bioconcentration factor, BMF: Biomagnification factor, CM: Metal concentration in muscle; CL: Metal concentration in liver, CS: Metal concentration in soft tissue, CT: Metal concentration in tissue

**Dry weight values converted to wet weight basis using 0.2 g dry per 1 g wet for zooplankton, crustaceans, fish and molluscs (Ikemoto et al. 2008; Campbell et al. 2005; Szefer et al. 1985; Szefer and Szefer 1985), 0.1 g dry per 1 g wet for algae (Maeda et al. 1997), 0.24g for Mulberry leaves (likened to aerial part of grass plants, Harris 1975 and Sibly 1981), 0.2g for agricultural soils.

[1] Value was observed in thoracic sterna of female crab; values observed for other body compartments ranged from 120 to 310 L/kg.

[2] Tissues sampled were from liver, breast muscle, leg muscle, heart, stomach, and feathers.

[3] Tissue samples were from soft tissue for clams, muscle for larger fish, birds and mammals, and whole skinless fillets for smaller fish.

Appendix V: Upper-bounding estimates of daily intake of cobalt by the general population in Canada by environmental media and food.

Route of exposure	Estimated intake (µg/kg-bw per day) of cobalt by various age groups						
	0–6 months[1, 2]		0.5–4 years[4]	5–11 years[5]	12–19 years[6]	20–59 years[7]	60+ years[8]
	breast fed	not breast fed[3]					
Air[9]	<0.001		<0.001	<0.001	<0.001	<0.001	<0.001
Drinking water[10]	NA[12]	0.04	0.02	0.02	0.01	0.01	0.01
Food and beverages[11]	0.59	0.53	0.54	0.42	0.29	0.23	0.19
Soil[12]	0.05		0.08	0.03	<0.01	<0.01	<0.01
Total intake	0.64	0.62	0.64	0.47	0.30	0.24	0.20

1 Maximum concentration measured in breast milk from 43 mothers in Newfoundland was 6µg/L. (Friel et al 1999)

2 Assumed to weigh 7.5 kg, to breathe 2.1 m^3 of air per day and to ingest 30 mg of soil per day (Health Canada 1998).

3 Assumed to drink 0.2 L of water per day (Health Canada 1998).

4 Assumed to weigh 15.5 kg, to drink 0.2 L of water, to breathe 9.3 m^3 of air per day and to ingest 100 mg of soil per day (Health Canada 1998).

5 Assumed to weigh 31.0 kg, to drink 0.4 L of water, to breathe 14.5 m^3 of air per day, and to ingest 65 mg of soil per day (Health Canada 1998).

6 Assumed to weigh 59.4 kg, to drink 0.4 L of water, to breathe 15.8 m^3 of air per day, and to ingest 30 mg of soil per day (Health Canada 1998).

7 Assumed to weigh 70.9 kg, to drink 0.4 L of water, to breathe 16.2 m^3 of air per day, and to ingest 30 mg of soil per day (Health Canada 1998).

8 Assumed to weigh 72.0 kg, to drink 0.4 L of water, to breathe 14.3 m^3 of air per day, and to ingest 30 mg of soil per day (Health Canada 1998).

9 The maximum concentration, 6.8×10^{-4} µg/m^3, of cobalt in outdoor air represents the 95th percentile collected under NAPS in Halifax, NS between April 2006 and Oct 2008. 135 samples were analyzed (NAPS 2003 – 2008). During the period 2003 – 2008 over 4500 samples were analyzed from eighteen sites across Canada under as part of NAPS; the Halifax data represented the highest concentration reported. Canadian data for indoor air concentrations of cobalt were not identified, however indoor air concentrations are reportedly lower than outdoor concentrations (2010 personal communication from Environmental and Radiation Health Sciences Directorate, Health Canada, to Existing Substances Risk Assessment Bureau, Health Canada; unreferenced and Balasubramaniam and Lee 2007). Therefore, considering Canadians are assumed to spend 3 hours outdoors each day and 21 hours indoors (Health Canada 1998) use of outdoor data is conservative.

10 Maximum concentration of cobalt in kitchen tap water measured in the Canadian TDS was 1.5µg/L. (Health Canada 2009b) The range of cobalt concentrations in tap water were reported to be 0.63 – 1.5 µg/L and includes data reported in the TDS covering the years 1993 – 2002.

11 Estimates of intake from food are the results reported as part of the Canadian TDS for year 2002 (http://www.hc-sc.gc.ca/fn-an/surveill/total-diet/index-eng.php) ; the value presented in the table corresponds to the highest value reported for overlapping age groups: 0-6 months non-breast fed is represented by 2-3 months, 0.5-4 years is represented by 1-4 years, 12-19 years is represented by 12-19 years male, 20-59 years is represented by 20-39 years male and 60+ is represented by 40-64 years

male. Approximately 210 individual food items were purchased from three to four supermarkets, the food samples were then prepared and processed as they would be consumed in the average Canadian household. The processed foods were then mixed to make composites (over 140 different composites) which were analyzed to determine cobalt content. The concentration was then combined with food intake information for Canadians to estimate dietary daily intake. (TDS)

[12] The maximum concentration of cobalt in Ottawa was reported to be 15.18×10^3 µg/kg in garden soil (50 samples), 22.67×10^3 µg/kg in house dust (48 samples) and 12.59×10^3 µg/kg in adjacent street dust (45 samples). The 95th percentile concentrations of cobalt in this study were reported to be 11.58×10^3 µg/kg in garden soil, 13.10×10^3 µg/kg in house dust and 11.15×10^3 µg/kg in adjacent street dust. The highest 95th percentile, house dust, was used to estimate intake. The concentrations are consistent with data obtained in Canadian agricultural land and US studies.

[13] NA – not applicable

Appendix VI. Estimated dermal exposures[1] to cobalt from personal care products containing cobalt chloride (CNS 2009)

Personal Care Product[2]	Maximum Concentration (%)	Use frequency[3] (times per year)	Chronic Exposure[4] (mg/kg-bw per day)	
			$CoCl_2$	Co Equivalent[5]
Face moisturizer[6]	0.005	730	1.7×10^{-5}	4.2×10^{-6}
Hair Conditioner	0.001	104	5.6×10^{-7}	2.5×10^{-7}
Facial Scrub	0.1	104	3.2×10^{-6}	1.5×10^{-6}
Total:			2.1×10^{-5}	6.0×10^{-6}

1 Body weight assumed to be 70.9 kg (Health Canada 1998).

2 The personal care products listed were identified to contain cobalt chloride.

3 (RIVM 2006).

4 See Appendix VII for details of modelling parameters.

5 Chronic exposures to cobalt were derived based on the weight fraction of cobalt in cobalt chloride (0.45) and the estimated chronic exposures to cobalt chloride. Sample calculation for Hair Conditioner: Co equivalent = estimated intake $CoCl_2 \times$ weight fraction cobalt = 5.6×10^{-7} mg/kg-bw per day $\times$ 0.45 = 2.5×10^{-7} mg/kg-bw per day.

6 Product was reported to contain cobalt chloride hexahydrate, which was used in the calculation of weight fraction of cobalt (0.25). Sample calculation for face moisturizer: Co equivalent = estimated intake $CoCl_2 \cdot 6H_2O \times$ weight fraction cobalt = 1.7×10^{-5} mg/kg-bw per day $\times$ 0.25 = 4.2×10^{-6} mg/kg-bw per day.

Appendix VII: Estimated intake of Cobalt Chloride from Personal Care Products

Personal Care Product Scenario	**Assumptions**	**Estimated exposure**
Face Moisturizer	Concentration: 0.005% (CNS 2009) **General assumptions** - Exposure frequency: 730 times/year (RIVM 2006) - Body weight: 70.9 kg (Health Canada 1998) **Dermal route** - Exposure type: direct dermal contact with product: instant application (RIVM 2006) - Exposed area: ½ area head (RIVM 2006): (0.5 × 1275) = 637 cm^2 (Health Canada 1998) - Applied amount: 1.2 g (Loretz et al. 2005) - Dermal absorption fraction[1]: 0.01	**Dermal** Chronic dose = 1.7×10^{-5} mg/kg-bw per day
Hair Conditioner	Concentration: 0.001% (CNS 2009) **General assumptions** - Exposure frequency: 104 times/year (RIVM 2006) - Body weight: 70.9 kg (Health Canada 1998) **Dermal route** - Exposure type: direct dermal contact with product: instant application (RIVM 2006) - Exposed area: area of hands + ½ area head (RIVM 2006): (925+0.5×1275) = 1548 cm^2 (Health Canada 1998) - Applied amount: 14 g (RIVM 2006) - Dermal absorption fraction[1]: 0.01 - Retention factor: 0.1	**Dermal** Chronic dose = 5.6×10^{-7} mg/kg-bw per day
Facial Scrub	Concentration: 0.1% (CNS 2009) **General assumptions** - Exposure frequency: 104 times/year (RIVM 2006) - Body weight: 70.9 kg (Health Canada 1998) **Dermal route** - Exposure type: direct dermal contact with product: instant application (RIVM 2006) - Exposed area: ½ area head (RIVM 2006): (0.5 × 1275) = 638 cm^2 (Health Canada 1998) - Applied amount: 0.8 g (RIVM 2006) - Dermal absorption fraction[1]: 0.01 - Retention factor: 0.1	**Dermal** Chronic dose = 3.2×10^{-6} mg/kg-bw per day

[1] Dermal penetration of cobalt through intact skin is reported to be very low (0.009 to 0.089 in an *in vitro* study) (Filon et al 2004, 2009), therefore absorption fraction of 0.01 is considered conservative.

Appendix VIII. Summary of health effects information for elemental cobalt and soluble cobalt(II) salts

Endpoint	Lowest Effect Levels/Result
Laboratory animals and *in vitro*	
Acute toxicity	**Lowest oral LD_{50}** (rat) = 42.4 mg Co/kg-bw (Singh and Junnarkar 1991) [$CoCl_2$] Note: The original paper does not specify which form of $CoCl_2$ was used. The LD_{50} for $CoCl_2$ was 171 mg/kg in rat and was converted to mg Co/kg-bw assuming the hexahydrate was tested. Additional oral studies: Speijers et al 1982 [$CoCl_2$,$CoSO_4$], Domingo and Llobet 1984 [$CoCl_2$], FDRL 1984a [$CoSO_4$], Reagan 1992 [Cobalt metal] **Lowest inhalation LOEC** (rat) =2.72 mg Co/m^3 based on histopathological changes in the lungs (slight increase in alveolar macrophages in alveolar ducts) 3 days after exposure for 5 hours [ultrafine Co particules (d= 20nm)] (Kyono et al 1992) No additional inhalation studies identified. No dermal studies identified.
Short-term repeated dose toxicity	**Lowest oral LOEL** (rabbit) = 4.2mg Co/kg-bw per day based on maternal toxicity (decreased body weight gain and death due to circulatory failure) in a developmental toxicity study (Szakmary et al 2001) [$CoSO_4$] Pregnant rabbits were dosed by gavage at 0, 20, 100 or 200 mg/kg bw/d of $CoSO_4$-$7H_2O$ from gestation day 6-20 (0, 4.2, 21, or 42 mg Co/kg bw/d). 5/25 low dose, 4/13 mid-dose, and 7/8 high dose dams died. **Additional oral studies:** Chetty et al 1979 [$CoCl_2$]; Pehrsson et al 1991 [$CoSO_4$]; Stanley et al 1947 [$CoCl_2$]; Morvai et al 1993 [$CoCl_2$]; Nation et al 1983 [$CoCl_2$]; Bourg et al 1985 [$CoCl_2$]; Mohiuddin et al 1970 [$CoSO_4$]; Szakmary et al 2001 [$CoSO_4$]; Grice et al 1969 [$CoSO_4$]; Shrivastava et al 1996 [$CoCl_2$] **Lowest inhalation LOEC** (rabbit) = 0.5mg Co/m^3 based on effects in the respiratory system following exposure for 4-6 weeks [$CoCl_2$] (Johansson et al 1983, 1984). Male rabbits (groups of 8) were exposed to $CoCl_2$ for 6 hours/day, 5 days per week for 4-6 weeks at 0 or 0.5mg Co/m^3. Exposed animals had hyperplasia of type II cells in the lung with small nodules formed, interstitial inflammation, and increased number and activity of alveolar macrophages. **Additional inhalation studies:** Johansson et al 1980 [Co particles]; NTP 1991 [$CoSO_4$]; Kyono et al 1992 [Co particles]; Camner et al 1993 [CoCl2] **Lowest dermal LOEL**(rat) = 9.6mg Co/kg bw based on sensitization in the local lymph node assay (LLNA) – 3 day exposure (Ikarashi et al 1992 a, b) [$CoCl_2$] **Additional inhalation studies:** Camner et al 1993 [$CoCl_2$]

Subchronic toxicity	**Lowest oral LOEL** (rat) = 0.5mg Co/kg bw/day based on increased latent period of conditioned reflexes following 7 months of treatment. [$CoCl_2$] (Krasovskii and Fridlyand 1971) Rats (strain and number not specified) were treated with $CoCl_2$ by gavage, 6 days per week for up to 7 months, at 0, 0.05, 0.5 or 2.5 mg Co/kg bw/day. Rats treated at 0.5mg/kg bw/day and up also had decreased phagocytic activity of leukocytes, mild polycythemia (increased haemoglobin and RBC), and an increase in incidence of lost conditioned reflexes. Animals treated with the low dose were not different from controls for the parameters examined. (Krasovskii and Fridlyand 1971) **Additional oral studies:** Clyne et al 2001 [$CoSO_4$]; Haga et al 1996 [$CoSO_4$]; Murdock 1959 [$CoCl_2$]; Holly 1955 [$CoCl_2$]; Corrier et al 1985; Mollenhaur et al 1985 [$CoCl_2$]; Domingo et al 1984 [$CoCl_2$]; Anderson et al 1992, 1993 [$CoCl_2$] **Lowest inhalation LOEC** (mice, rat) = 0.1mg Co/m^3 based on effects in the respiratory sytem (squamous metaplasia of the larynx) following 13 weeks of exposure (NTP 1991, Bucher et al 1990). [$CoSO_4$] F344 rats and B6C3F1 mice (groups of 10 per sex) were exposed to $CoSO_4$-$7H_2O$ by inhalation at 0, 0.3, 1, 3,10 and 30 mg/m^3 (0, 0.11, 0.38, 1.14, 3.8 or 11.38 mg Co/m^3), 6 hours/day, 5 days/week for 13 weeks. In both rat and mouse, all tested concentrations resulted in squamous metaplasia of the larynx (the most sensitive tissue). There were more severe effects in the nose, larynx and lung at higher exposures. Lung weights were increased in rats at 0.38 mg Co/m^3 and above, and in mice at 3.8mgCo/m3 and above. In mice, sperm motility decreased at 1.14mgCo/ m^3 and higher (lower doses were not assessed); and at 11.38mgCo/ m^3, there was hyperplasia of the mediastinal lymph nodes, testicular atrophy, increased estrous cycle length, increased abnormal sperm, and decreased testis and epididymal weights. **Additional inhalation studies:** Johansson et al 1986, 1987, 1992, 1991 [$CoCl_2$] Kerfoot et al 1975 [Co metal] No dermal studies identified.
Chronic toxicity/ carcinogenicity	**2 year inhalation bioassay of $CoSO_4$:** F344 rats and B6C3F1 mice (groups of 50 males and 50 females) were exposed to $CoSO_4$-$7H_2O$ by inhalation at 0, 0.3, 1, or 3 mg/m^3 (0, 0.11, 0.38, or 1.14 mg Co/m^3), 6 hours/day, 5 days/week for 105 weeks. (NTP 1998, Bucher et al 1999) **Non-neoplastic effects:** LOEC (mouse, rat) = 0.11mg Co/m^3 based on effects in the respiratory system (lesions in larynx, lung, and nose) In all treated groups, the incidence of alveoli proteinosis, alveolar epithial metaplasia, granulomatous alveolar inflammation and interstitial fibrosis was greater than in the controls. The severity of the lesions increased at higher exposures. The lesions in the mouse were generally less severe than in rat. **Carcinogenicity:** NTP concluded there was 'clear evidence of carcinogenicity' in male and

	female mice, and in female rats; and 'some evidence of carcinogenicity' in male rats. Mice - a concentration-related increase in benign and malignant alveolar/ bronchiolar neoplasms in both sexes. In the males, the combined incidence of alveolar/ bronchiolar adenomas and carcinomas was 11/50, 14/50, 19/50 and 28/50 in the controls, low-, mid- and high-dose groups respectively. The corresponding incidences in the females were 4/50, 7/50, 13/50 and 18/50. The incidences in both the top dose groups were significantly different ($p \leq 0.01$) from their respective controls. The incidence in the mid dose females was also significantly greater ($p \leq 0.05$) than in the controls. Rats - a concentration-related increase in benign and malignant alveolar/ bronchiolar neoplasms in both sexes. In the males, the combined incidence of alveolar/ bronchiolar adenomas and carcinomas was 1/50, 4/50, 4/50 and 7/50 in the controls, low-, mid- and high-dose groups respectively. The corresponding incidences in the females were 0/50, 3/50, 16/50 and 16/50. The incidences in both the top dose groups were significantly different from their respective controls ($p \leq 0.05$ for the males and $p \leq 0.01$ for the females). The incidence in the mid dose females was also significantly greater ($p \leq 0.01$) than in the controls. There was a concentration-related increase in incidence of benign and malignant pheochromocytomas in the treated females (2/48, 1/49, 4/50, and 10/48 in the controls, low, mid and high dose groups respectively. The incidence in the top dose group was significantly higher ($p \leq 0.05$) than in the concurrent controls. Although common in males, pheochromocytomas are much less commonly seen in untreated females. The investigators considered the increased incidence of this tumour type to be an "uncertain" finding because it was seen only in the top group and was not supported by increased incidence or severity of hyperplasia. No other chronic toxicity / carcinogenicity studies on Cobalt metal or soluble cobalt (II) salts with relevant routes of exposure were identified (other available studies used unusual routes of exposure such as injection and implantation)
Genotoxicity – *In vivo*	**Mutagenicity:** **Positive**: Mutation in wing spot test in *drosophila* [$CoCl_2$] (Ogawa et al 1994) **Positive**: Gene mutations in *drosophila* [Co(II)nitrate] (Yesilada 2001) **DNA damage:** **Positive**: 55% frequency of G to T transversion in mouse lung tumours vs 0% in the lung tumours of the controls [inhalation of $CoSO_4$]. (NTP 1998) **Positive**: Oxidative DNA damage in liver, kidney and lung of rat [intraperitoneal injection of Co(II)acetate] (Kasprzak et al 1994) **Clastogenicity**: **Negative**: Micronuclei in mouse peripheral blood [inhalation of cobalt dust] (NTP 2005b). **Positive**: Micronuclei in bone marrow of mice [intraperitoneal injection of $CoCl_2$] (Suzuki et al., 1993) **Positive**: Chromosome Aberrations in bone marrow of mice [oral dose of $CoCl_2$] (Palit et al., 1991a, b, c, d) **Other:** **Positive**: Aneuploidy , pseudodiploidy and hyperploidy in the bone marrow and

	testes of hamsters [intraperitoneal injection of $CoCl_2$] (Farah, 1983) **Positive**: Mitotic recombination in wing spot test in *drosophila* [$CoCl_2$] (Ogawa et al 1994) **Positive**: Chromosomal deletion, non disjunction or mitotic recombination in *drosophila* [Co(II)nitrate] (Yesilada 2001)
Genotoxicity – *In vitro*	**Mutagenicity in bacteria:** **Negative**: *Salmonella typhimurium* TA100 [$CoSO_4$ with activation] (Zeiger et al 1992) **Negative**: *Salmonella typhimurium* TA100, TA2637 [$CoCl_2$ without activation] (Tso &Fung 1981, Arlauskas et al 1985, Ogawa et al 1986) **Negative**: *Salmonella typhimurium* TA102, TA1535, TA98, TA1538, TA1537 [$CoCl_2$ with and without activation] (Arlauskas et al 1985, Mochizuki&Kada 1982, Ogawa et al 1986, Wong 1988) **Negative**: *Salmonella typhimurium* TA1535, TA98 [$CoSO_4$ with and without activation] (Zeiger et al., 1992) **Negative**: *E.coli* [$CoCl_2$ without activation] (Arlauskas et al 1985, Kada & Kanematsu 1978, Leitao et al 1993) **Negative**: *B.subtilis* [$CoCl_2$ without activation] (Inoue et al 1981) **Positive**: *Salmonella typhimurium* TA100 [CoSO4 without activation] (Zeiger et al., 1992) **Positive**: *Salmonella typhimurium* TA1537, TA98, TA97 [$CoCl_2$without activation] (Wong 1988, Pagano and Zeiger 1992) **Positive**: *E.coli* [$CoCl_2$ without activation] (Ogawa et al 1999) **Mutagenicity in yeast:** **Negative:** *S. cerevisiae* [$CoCl_2$ without activation] (Fukunaga et al 1982, Singh 1983, Putrament et al 1977) **Positive:** *S. cerevisiae* [$CoCl_2$ without activation] (Kharab & Singh 1987 Kharab & Singh 1985, Lindegren et al 1958, Egilsson et al 1979 Prazmo et al 1975 Putrament et al 1977) **Mutagenicity in mammalian cells:** **Negative**: Mutations at Gpt and 8AG locus in Chinese hamster V79 cells [$CoCl_2$] (Kitahara et al 1996; Yokoiyama et al 1990) **Negative**: Mutations at tk locus in mouse lymphoma L5178Y cells [$CoCl_2$] (Amacher and Paillet 1980) **Positive**: Mutations at hprt locus in Chinese hamster V79 cells [$CoCl_2$] (Hartwig et al 1990; Miyaki et al) **Positive**: Mutations at Gpt locus in Chinese hamster transgenic G12 cells [$CoCl_2$] (Kitahara et al 1996) **DNA Damage in bacteria:** **Negative**: Rec assay in Bacillus subtilis [$CoCl_2$ without activation] (Nishioka 1975) **Negative**: Prophage induction in E.coli [$CoCl_2$ without activation] (Rossman et al 1984) **Positive**: Rec assay in Bacillus subtilis [$CoSO_4$without activation, $CoCl_2$ without activation] (Kanematsu et al 1980) **DNA damage and repair in mammalian cells:** **Negative**: DNA strand breaks in human lymphocytes and CHO cells [$CoCl_2$] (Anard et al 1997; Hamilton-Koch et al 1986) **Negative**: Inhibition of nucleotide excision repair (ligation step) in human fibroblasts [$CoCl_2$] (Kasten et al 1997) **Positive**: Strand breaks in human WBC, human fibroblasts, HeLa cells, CHO

	cells [$CoCl_2$] (McLean et al 1982; Hamilton-Koch et al 1986; Hartwig et al 1990) **Positive**: Single strand breaks in human mononuclear leucocytes [Cobalt particles] (De Boeck 1998, 2003b; Anard 1997; Van Goethem et al 1997) **Positive**: Comet assay in mouse fibroblasts and human primary blood leukocytes [Cobalt particles] (Ponti et al 2009; Colognato et al 2008) **Positive**: Comet assay in mouse fibroblasts [$CoCl_2$] (Ponti et al 2009) **Positive**: DNA-protein cross-links (DPC) in rat liver hepatoma cells [$CoCl_2$] (Wedrychowski et al 1986) **Positive**: Decrease in DNA synthesis rate in HeLa cells [$CoCl_2$] (Painter and Howard 1982) **Positive**: Inhibition of nucleotide excision repair (incision and polymerization steps) in human fibroblasts [$CoCl_2$] (Kasten et al 1997) **Positive**: Inhibition of DNA repair in HeLa cells [Co(II)acetate] (Snyder et al 1989) **Clastogenicity:** **Negative**: Chromosome aberrations in human lymphocytes [Co(II)acetate], (Voroshilin et al 1978) **Negative**: Chromosome aberrations in human fibroblasts and human leukocytes [Co(II)nitrate] (Paton and Allison 1972) **Negative**: Micronuclei in mouse bone marrow and mouse fibroblasts [CoCl2] (Ponti et al 2009; Suzuki et al 1993) **Positive**: Micronuclei in human lymphocytes and in mouse fibroblasts [Cobalt particles] (De Boeck et al 2003a,b; Van Goethem et al 1997; Ponti et al 2009) **Positive**: Micronuclei in human peripheral blood leukocytes [CoCl2] (Capomazza 1991, Olivero 1995) **Positive**: Sister Chromatid Exchange (SCE) in mouse macrophage and human lymphocytes [CoCl2] (Andersen 1983) **Other:** **Negative**: Cell transformation in mouse fibroblasts and human non-tumorigenic osteosarcoma osteoblast-like cells [Cobalt particles] (Doran et al 1998, Miller et al 2001) **Negative**: Cell transformation in mouse fibroblasts [CoCl2] (Ponti et al 2009) **Positive**: Cell transformation in SHE cells [Co(II)acetate] (Casto et al 1979) **Positive**: Cell transformation in SHE cells [$CoSO_4$] (Kerckaert *et al.*, 1996) **Positive**: Cell transformation in mouse fibroblasts [Cobalt particles] (Ponti et al 2009) **Positive**: Cell transformation in mouse fibroblasts [CoCl2] (Doran et al 1998) **Positive**: Aneuploidy in human lymphocytes [CoCl2] (Resende de Souza-Nazareth 1976) **Positive:** gene conversion in *S. cerevisiae* [$CoCl_2$] (Fukunaga et al 1982, Singh 1983, Kharab & Singh 1985)
Developmental Toxicity	**Lowest oral LOEL** (rat) = 5.2mg Co/kg-bw per day based on teratogenicity, increased perinatal pup death, stunted growth and and transiently delayed developmental parameters. (Szakmary et al. 2001) [$CoSO_4$] Groups of 14-18 pregnant Sprague-Dawley rats were dosed by gavage at 0, 25, 50 or 100 mg/kg bw/d of $CoSO_4$-$7H_2O$ from gestation day 1-20 (0, 5.2, 10.5, 21 mg Co/kg-bw per day). In all treated groups, there was an increased frequency of skeletal retardation, increased frequency of skeletal and urogenital system malformations, decreased perinatal index (number of live pups at postnatal day 5 per number of live pups born), decreased pup body weight at postnatal days 1 and 7, and delays in postnatal developmental parameters (ear opening, incisor eruption, descending of testes, swimming performance and auditory relex).

	Pup body weight and postnatal developmental parameters returned to control levels by postnatal day 21, and the survival index from day 5 to day 21 was the same as controls. Some maternal toxicity was observed at the high dose (increased relative weight of liver, adrenals and spleen; serum alterations). There was also a dose-dependent increase in the number of dams that died during delivery (0, 1, 5, 12 – no statistics given). **Additional oral studies:** Domingo et al. 1985; Patternain et al. 1988 No inhalation or dermal studies on developmental toxicity were identified.
Reproductive Toxicity	**Lowest oral LOEL** (mice) = 6.4mg Co/kg-bw per day based on decreased implantations, decreased number of viable fetuses, increased number of resorptions, and decreased epididymal sperm count. Male swiss mice (groups of 10) were given $CoCl_2$-$6H_2O$ in the drinking water at 0, 200, 400 or 800ppm (6.4, 11.6, 23.0 mg Co/kg-bw per day) for 12 weeks, then mated with untreated females. At all doses, there was decreased body weight gain, decreased implantations, decreased number of viable fetuses, increased number of resorptions, decreased absolute testes weight, and decreased epididymal sperm count. At the 2 higher doses, there were also decreased pregnancies, increased relative seminal vesicle weight, decreased relative testes weight, decreased testes sperm count, and testes necrosis, cellular hypertrophy and degeneration. At the high dose, the absolute epididymal weight decreased. (Elbetieha et al 2008) **Additional oral studies:** Pedigo and Vernon 1993; Pedigo et al 1988 No inhalation or dermal studies on reproductive toxicity were identified.
Sensitization	Dermal: Dermal sensitization in the local lymph node assay (LLNA) following 3 days of dermal exposure to $CoCl_2$ at 9.6mg Co/kg-bw in rat, 10.8mgCo/kg bw in mice and 14.7mg Co/kg bw in guinea pigs. (Ikarashi et al 1992 a, b) Guinea pigs were also sensitized by contact with $CoCl_2$ for 24 hours (occluded), for 4 applications over 9 days. (Camner et al 1993) Inhalation: Groups of 5 minipigs were sensitized to Co for 5 days and following a 10-day waiting period, were exposed for 6 hours per day, 5 days per week to Co metal aerosols at 0.1 or 1.0mg/m3, for 3 months. Changes in lung compliance were reversed following 2 months with no exposure. Treated animals also had transient polycythemia (increased red and white blood cells) – noticeable at 3 weeks but not from 6 weeks to the end of the experiment. (Kerfoot et al 1975)
Epidemiological Studies	
Genotoxicity	35 workers exposed to cobalt dust compared to 27 unexposed workers in a cobalt refinery. There was no indication of increased DNA strand breaks (Comet assay) or micronuclei in blood lymphocytes (De Boeck et al 2000)

	21 workers exposed to cobalt dust, 26 unexposed matched controls in a cobalt refinery. Individuals with hOGG1, XRCC1 variant genotypes (genes involved in base-excision) showed significantly higher micronuclei frequencies in the peripheral blood lymphocytes (Matueca et al 2005)
Short-term repeated dose toxicity	<u>Oral Studies:</u> Volunteer clinical study in 6 healthy males aged 20-47 Daily oral dose of cobalt chloride [about 1 mg Co/kg bw/day] for up to 22 days Red blood cell numbers increased 16–20%. Haemoglobin levels increased, by 6–11% (transient effect) Based on these study findings ATSDR (2004) derived an oral health criteria value (Minimal Risk Level) for "cobalt" pertinent to human exposures of up to 1 year (Davis and Fields, 1958) Study in anephric, anaemic patients 0.16 to 0.32 mgCo/kg/day as CoCl2 (25 or 50 mg per day)*. Patients were treated for 12 to 47 consecutive weeks, followed by a break of at least 12 weeks, and some patients had second and third rounds of treatment. Significant increase in haemoglobin and red cell volume in most patients. (Duckham and Lee 1976; Taylor et al 1977) *Treatment levels used for MOE derivation Pregnant women 0.45 to 0.64 mg Co/kg-bw per day as cobalt chloride (75 or 100 mg per day) daily for 90 days (third trimester) Haemoglobin levels and red blood cells were not increased (Holly 1955). Patients receiving cobalt salts to treat anaemia. Doses of 2.8-3.9mg Co/kg bw per day for 3 to 8 months. Goiter, enlarged thyroid, microscopic changes in thyroid Kriss et al 1955; Gross et al 1955
Subchronic toxicity	<u>Oral Studies</u>: Case reports of consumers of large quantities (approximately 8-30 pints/day) of beer containing cobalt sulfate as a foam stabilizer Possible influences on the victims' susceptibility included a protein-poor diet and cardiac damage from alcohol abuse Estimates of the cobalt exposures leading to death ranged from 0.04 to 0.14 mg/kg bw/day ("for several years")* Lethal cardiomyopathy (Alexander, 1969, 1972; Bonenfant et al., 1969; Kesteloot et al., 1968; Morin and Daniel, 1967; Morin et al., 1971; Sullivan et al., 1969; reviewed in ATSDR 2004; IPCS 2006) *Low end of range for intake estimate used for MOE derivation
Chronic toxicity	<u>Inhalation studies:</u> Cross-sectional study on 194 workers (166 men and 28 women) from 10 diamond-polishing workshops and 59 workers from three other workshops in the diamond industry (controls – 46 men and 13 women) Workers divided into three exposure categories according to airborne cobalt

	measurements: controls (0.0004 +/- 0.0006 mg/m^3), low (0.0053+/- 0.0032 mg/m^3 and high exposure (0.0151 +/- 0.0117 mg/m^3). Exposure was also confirmed by measurement of cobalt in urine. The duration of employment in each exposure group was not discussed; the exposure categories represent air concentrations only at the time of the study. The high exposure group was more likely to complain about respiratory symptoms and had significantly higher prevalence of eye, nose, and throat irritation and cough. The prevalence of some symptoms (e.g. cough, phlegm) was elevated in the low exposure group compared with the control group, but the magnitude of the increase (over that seen in controls) did not achieve statistical significance (at $P < 0.05$). Lung function, assessed by FVC, FEV1, MMEF (forced expiratory flow between 25% and 75% of the FVC), and mean PEFR, was significantly reduced in workers in the high exposure group compared with workers in the lower exposure and control groups. Lung function was not decreased in the low exposure group compared with the control group. LOAEC = 0.0151 mg/m^3 * NOAEC = 0.0053 mg/m^3 IPCS noted that the effects seen in the cross-sectional study "may be a reflection of recent, not chronic, exposure" (Nemery et al., 1992) *Effect level used for MOE derivation Cross sectional occupational; 203 male workers with at least one year of exposure to cobalt and 94 unexposed controls. The exposure range was 0.01- 1.0 mgCo/m3, depending on department. The workers were exposed mainly to a mixture of cobalt(0) and cobalt(II) salts. Mean (and Standard Deviation) exposure time 15.0 (11.6) years. Mean Co exposure 0.40 (0.47) mg-years In the "most highly exposed" group, mean exposure time was 21.2 (9.9) years and mean Co exposure 0.58 (0.51) mg-years. The echocardiographic results were analysed with respect to exposures to cobalt of >0.47 mg-year (55 men), <0.47 mg-year (54 men) and 57 unexposed controls No significant differences between 203 exposed and 94 controls in the electrocardiographic findings and measurements of blood pressure, heart rate and clinical chemistry Two of the echocardiography parameters (out the 16 that were measured) were associated with cobalt exposure. In the higher exposure group the left ventricular isovolumic relaxation time (mean 53.3, 49.1, and 49.7 ms in the high exposure, low exposure, and control groups respectively) and the deceleration time of the velocity of the early rapid filling wave (mean 194.3, 180.5, and 171.7 ms for those in the high exposure, low exposure, and control groups respectively) were prolonged, indicating altered left ventricular relaxation and early filling (Linna et al., 2004) Cross-sectional study of 82 workers in a cobalt refinery exposed to cobalt metal, salts and oxides for 0.3 to 39 years (mean 8 years) at an average concentration of 0.125mg Co/m3 (range 0.001–7.7 mg/m3) Significant increase in dyspnoea and wheezing, lung function (FEV1), and skin lesions such as eczema and erythema compared to controls. Suggests that a high airborne concentration of Co alone can cause asthma but is not sufficient to cause pulmonary fibrosis. (Swennen et al 1993)

	Cross-sectional survey of 110 current and former cobalt refinery workers and 140 control workers in a cobalt plant Workers were potentially exposed to elemental cobalt and cobalt sulfates, carbonates, oxides and hydroxides. Workers had been in the industry for at least 10 years Cumulative exposure was calculated in mg-years for each worker using ambient air measurements and records of exposure hours. Asthma symptoms more prevalent in exposed workers. No cases of hard metal disease or fibrosing alveolitis were found. (Linna et al., 2003).
Sensitization	Cobalt chloride at 1% in petrolatum (24 or 48 hour covered contact) has been used in patch tests to detect the cobalt sensitized state. In large studies (over 4000 subjects), a positive sensitization response was detected in 1 to 10% of patients, and cobalt was often described as one of the most common allergens. (including: Pratt *et al.*, 2004; Marks *et al.*, 2003; Uter *et al.*, 2005; Warshaw et al 2007.) As daily repeated exposure to aqueous cobalt salts did not result in hand eczema in patients known to have cobalt allergy, it has been suggested that the allergic properties of cobalt result mainly from exposure to the metal itself, rather than to a cobalt salt (Nielsen *et al.*, 2000). Inhalation of cobalt chloride aerosols can produce an asthmatic response in sensitized individuals (Shirakawa 1989) IgE and IgA antibodies specific to cobalt have been detected in humans (Bencko et al 1983; Shirakawa et al 1988, 1989)