GLOSSARY AND ACRONYMS

Relative bioavailability	A comparative fraction which predicts bioavailability in one medium or form in relation to the medium for which the TRV was derived.
RfC	Reference Concentration. The RfC is an estimate of lifetime daily exposure to a non-carcinogen in air for the general human population that appears to be without appreciable risk of deleterious effects expressed in mg chemical/kg body weight-day.
RfD	Reference Dose. The RfD is an estimate of lifetime daily exposure to a non-carcinogen for the general human population that appears to be without appreciable risk of deleterious effects expressed in mg chemical/kg body weight-day.
SF	Slope factor. The SF is a plausible upper bound estimate of the probability of a response per unit intake of a chemical over a lifetime expressed as (mg chemical/kg body weight-day)$^{-1}$ and is used to express carcinogenic effects.
STSC	Superfund Health Risk Technical Support Center
TC	Tolerable Concentration. A term used by Health Canada to describe concentrations in air that a person may be continuously exposed to over a lifetime without adverse effects. The TC is used to derive the TDI.
TC_{05}	Tumorigenic concentration that will induce a 5% increase in the incidence of tumors or deaths due to tumors following exposure to that chemical in air.
TD	Tumorigenic Dose. A term used to describe a dose that will induce an increase in the incidence of tumors or deaths due to tumours as calculated from a non-threshold dose-response curve.
TD_{05}	Tumorigenic Dose that will induce a 5% increase in the incidence of tumors or deaths due to tumors
TDI	Tolerable Daily Intake. A term used by Health Canada in place of RfD.
TEF	Toxic Equivalency Factor
TEQ	Toxic Equivalent
TRV	Toxicity Reference Value

GLOSSARY AND ACRONYMS

UF	Uncertainty Factor. A factor that is applied to NOAELs or LOAELs to yield a RfC or RfD. For example, the UF can be used to account for intra-species and inter-species extrapolations
UL	Tolerable upper intake level. A term used by the IOM to describe the highest daily nutrient intake that will not result in adverse health effects.
Unit Risk	Units risks estimate the upper bound probability of an individual developing cancer following exposure to a particular level (usually as 1 µg/L in water or 1 µg/m^3) of a potential carcinogen. For example, if the unit risk is 1.2×10^{-6} µg/L then it is expected that 1.2 excess tumours are expected to occur per 1,000,000 people exposed to 1 µg of that chemical in 1 L of drinking water.
US EPA	United States Environmental Protection Agency
WHO	World Health Organization

1. INTRODUCTION

For the purpose of this assessment, toxicity reference values (TRVs) were obtained for each of the identified contaminants of potential concern (COPC). Toxicological information was obtained, as necessary, from various sources including Health Canada, the US EPA Integrated Risk Information System (IRIS) database, the Agency for Toxic Substances and Disease Registry (ATSDR).

TRVs are values used to describe maximum acceptable doses of chemicals that will not result in the development of adverse health effects. TRVs can be used to describe non-carcinogenic and carcinogenic effects and can express effects in different terms based on magnitude of the dose, length of exposure and route of exposure.

1.1 Non-Carcinogenic TRVs

Non-carcinogenic chemicals exhibit threshold effects following exposure. Threshold effects are defined by the observation of adverse effects at a given dose or concentration. Given these threshold effects, two measures of interest can describe the dose-response curve: the no-adverse-effects-level (NOAEL) and lowest-adverse-effects-level (LOAEL). The NOAEL is the benchmark at which the highest dose does not result in observed adverse effects. The LOAEL may be used when a NOAEL is not available and is the lowest dose at which adverse effects are observed.

The reference dose (RfD) is used for the assessment of non-carcinogenic endpoints. The RfD is the estimate of lifetime daily exposure to a non-carcinogenic substance for the general human population that appears to be without appreciable risk of deleterious effects. It is expressed as mg chemical/kg body weight/day (e.g., mg/kg-day). The RfD is derived from either the NOAEL or the LOAEL determined in a laboratory study. Uncertainty factors (UF) are applied to the NOAEL or LOAEL to account for interspecies variability and intraspecies variability (e.g., sensitive sub-populations). Additionally, uncertainty factors are applied to extrapolate from subchronic exposure to chronic exposure or where there is a paucity of data available for a chemical (e.g., no data regarding effects on reproduction).

Other regulatory agencies have substituted the term RfD to be reflective of objectives and toxicological endpoints. Health Canada replaces the term RfD with tolerable daily intake (TDI), also expressed in mg/kg-day. Health Canada also uses a tolerable concentration (TC) to express concentrations in air that a person can be continuously exposed to over their lifetime without adverse effects. The Institute of Medicine (IOM) uses the tolerable upper intake level (UL)

expressed as mg chemical/day to describe the highest daily nutrient intake that will not result in adverse health effects. The ATSDR uses a minimal risk level (MRL) similar to the IOM's UL, that estimates daily human exposure to a substance that, over a specified duration, will not cause an appreciable risk of adverse effects.

The reference concentration (RfC) is also used as a non-carcinogenic endpoint specific to inhalation exposure. The RfC is typically reported as a concentration in air which can be converted to a RfD for inhaled dose expressed as mg/kg-day.

1.2 Carcinogenic TRVs

Carcinogenic chemicals exhibit non-threshold effects following exposure. Non-threshold effects are defined by the observation of adverse effects regardless of concentration and length of exposure. Primarily, two TRVs are used to describe carcinogenic effects: the slope factor and unit risk.

A slope factor (SF) is used for assessment of carcinogenic effects of a chemical. The SF is a plausible upper-bound estimate of the probability of a response per unit intake of a chemical over a lifetime, expressed as $(mg/kg\ body\ weight/day)^{-1}$. It is used to estimate an upper bound probability of an individual developing cancer as a result of exposure to a particular level of a potential carcinogen.

Unit risks are used to estimate an upper bound probability of an individual developing cancer as a result of exposure to a particular level (usually as 1 µg/L in water, or 1 $\mu g/m^3$ in air) of a potential carcinogen. Unit risks are calculated by dividing the SF by body weight and multiplying that product by the inhalation or drinking rate as applicable.

Health Canada uses tumorigenic doses and concentrations for substances that are considered to have non-threshold or carcinogenic effects. The potency is expressed as a dose or concentration that will induce a 5% increase in the incidence of tumours or deaths due to tumours as calculated from a dose-response curve. The TRVs that defined the 5% increased are tumorigenic concentration 05 (TC_{05}) primarily used as a benchmark for exposure to a certain chemical in air or tumorigenic dose 05 (TD_{05}).

1.3 Bioavailability

The definition of bioavailability varies with the source and context in which the term is used. The simplest and broadest definition of bioavailability describes the extent or rate that a chemical

enters a receptor or is made available at the target site (e.g., blood). The importance of bioavailability in risk assessment is illustrated by comparison TRVs as toxicity measures that are usually defined by laboratory studies. The fraction of a dose which is absorbed during an animal study may differ from the fraction that is available to a receptor in the environment due to several factors including weathering.

There are two specific types of bioavailability that are applicable to risk assessment: absolute and relative bioavailability. Absolute bioavailability is the fraction or percentage of an administered dose that reaches systemic circulation (blood) irrespective of via the gastrointestinal tract, skin or lungs. Relative bioavailability is the absolute bioavailability in one medium divided by the absolute bioavailability of the chemical under the conditions used to derive the TRV. Therefore, the relative bioavailability is a comparative fraction which predicts bioavailability in one medium or form in relation to the medium for which the TRV was derived. Relative bioavailability can be expressed as a relative absorption fraction (RAF).

In the following toxicity profiles, both absolute and relative bioavailabilities have been provided, where applicable, with the relative bioavailability selected for use in the assessment.

2. ANTIMONY

Antimony is a silvery-white metal that is found in the earth's crust. Exposure to antimony at high levels can result in a variety of adverse health effects. Chronic inhalation of high levels of antimony can irritate the eyes and lungs as well as cause heart and lung problems as well as digestive problems. Ingesting large doses of antimony can cause vomiting. Chronic animal studies have reported that ingesting antimony can cause liver damage and blood changes. (ATSDR, 1992)

2.1 Assessment of Carcinogenicity

The US EPA's IRIS program has not evaluated the carcinogenicity of antimony. The Agency for Toxic Substances and Disease Registry (ATSDR, 1992) state that no information is available on the carcinogenic potential of antimony. The International Agency for Research on Cancer (IARC, 1989) found that there is insufficient supporting evidence to list antimony trioxide or antimony trisulphide as carcinogenic agents at this time.

2.2 Susceptible Populations

Individuals with existing chronic respiratory or cardiovascular disease or problems would probably be at special risk, since antimony probably exacerbates one or both types of health problems. Because antimony is excreted in the urine, individuals with kidney dysfunction may be unusually susceptible (ATSDR, 1992).

2.3 Selection of Toxicity Values

2.3.1 Non-Cancer Oral Toxicity Reference Values

An oral reference dose (RfD) of 0.0004 mg/kg/day was provided for antimony by the U.S. EPA (1987) based on a chronic study examining ingestion by rats. The main endpoints of concern were a decrease in longevity, a decrease in blood glucose levels and an alteration in cholesterol levels. The U.S. EPA (1987) reported a lowest observable adverse effect limit (LOAEL)(of 0.35 mg/kg-day, and applied an uncertainty factor of 1000 (10 for interspecies conversion, 10 to protect sensitive individuals, and 10 because the effect level was a LOAEL and there wasn't a no observable adverse effects level [NOAEL] established) to the LOAEL to derive the RfD.

2.3.2 Cancer Oral Toxicity Reference Values

The lack of suitable positive carcinogenic data precludes the derivation of an oral slope factor or unit risk for antimony.

2.3.3 Non-Cancer Inhalation Toxicity Reference Values

Inhalation toxicity values for antimony have not been developed by the US EPA or Health Canada and therefore, due to insufficient data, a non-cancer inhalation TRV has not been selected for this assessment.

2.3.4 Cancer Inhalation Toxicity Reference Values

The lack of suitable positive carcinogenic data precludes the derivation of an inhalation slope factor or unit risk for antimony.

2.4 Bioavailability

The following section describes the bioavailabilities of antimony.

2.4.1 Oral Bioavailability

The relative oral absorption factor for antimony has been conservatively assumed to be 1.0.

2.4.2 Inhalation Bioavailability

The relative inhalation absorption factor for antimony has been conservatively assumed to be 1.0.

2.4.3 Dermal Bioavailability

Health Canada (2003) also recommends a relative dermal absorption factor of 0.1 for antimony. Therefore, a relative dermal bioavailability of 0.1 was adopted for this assessment.

2.5 Conclusion

The following tables present the TRV and bioavailability summaries for antimony.

Table 1: Selected Toxicity Reference Values for Antimony

Route of Exposure	TRV	TRV Type	Source Agency
Non-Cancer Effects			
Ingestion	4.0×10^{-4} mg/kg-day	RfD	US EPA, 1987
Inhalation	NA	NA	NA
Cancer Effects			
Ingestion	NA	NA	NA
Inhalation	NA	NA	NA

NA – Not Applicable

Table 2: Selected Bioavailabilities for Antimony

Route of Exposure	Relative Bioavailability	Reference
Ingestion	1.0	Assumed
Inhalation	1.0	Assumed
Dermal	0.1	Health Canada, 2003

2.6 References

ATSDR (Agency for Toxic Substances and Disease Registry), 1992. Toxicological Profile for Antimony. September 1992.

Health Canada, 2003. Federal Contaminated Site Risk Assessment in Canada, Part I: Guidance on Human Health Screening Level Risk Assessment (SLRA). October 3, 2003.

International Agency for Research on Cancer (IARC). 1989. "Antimony Trioxide And Antimony Trisulfide". *Monographs.* Vol. 47, p. 291. World Health Organization.

US EPA (Environmental Protection Agency). 1987. Integrated Risk Information System (IRIS) Database – Antimony. Confirmed current as of December 2004. Available on-line at: http://www.epa.gov/iris/

3. BARIUM

Barium is a silvery-white metal found in nature. Health effects of barium compounds depend on how well the compound dissolves in water. Compounds that do not dissolve well in water are not generally harmful. However, barium compounds that dissolve well in water may cause harmful effects in people. Ingestion of barium compounds that readily dissolve in water can lead to difficulties in breathing, increased blood pressure, changes in heart rhythm, stomach irritation, brain swelling, muscle weakness and damage to the liver, kidney, heart and spleen. (ATSDR, 1992).

3.1 Assessment of Carcinogenicity

The oral database of information suggests that barium is unlikely to be carcinogenic to humans, and the inhalation database is inadequate to assess carcinogenicity (US EPA, 1998). Barium would be classified as Group D - not classifiable as to human carcinogenicity, under the United States Environmental Protection Agency's (US EPA) 1986 Guidelines for Carcinogen Risk Assessment. Under the Proposed Guidelines for Carcinogenic Risk Assessment (US EPA, 1999), barium is considered not likely to be carcinogenic to humans following oral exposure and its carcinogenic potential cannot be determined for inhalation exposure.

3.2 Susceptible Populations

Gastrointestinal absorption data suggest that barium absorption may be higher in children than in adults (US EPA, 1998). No other studies were located regarding unusual susceptibility of any human sub-population to barium (ATSDR, 1992).

3.3 Selection of Toxicity Values

3.3.1 Non-Cancer Oral Toxicity Reference Values

An oral reference dose (RfD) of 0.07 mg/kg/day was provided for barium by the U.S. EPA (1999) based on several different studies. The main endpoint of concern was increased kidney weights. The U.S. EPA (1998) reported an adjusted no observable adverse effects level (NOAEL) of 0.21 mg/kg-day, and applied an uncertainty factor of 3 to the NOAEL to derive the RfD.

Health Canada (2003) provides a tolerable daily intake (TDI) of 0.016 mg/kg-day, which was used in this assessment.

3.3.2 Cancer Oral Toxicity Reference Values

The lack of suitable positive carcinogenic data precludes the derivation of an oral slope factor or unit risk for barium.

3.3.3 Non-Cancer Inhalation Toxicity Reference Values

Inhalation toxicity values for barium have not been developed by the US EPA or Health Canada and therefore, due to insufficient data, a non-cancer inhalation TRV has not been selected for this assessment.

3.3.4 Cancer Inhalation Toxicity Reference Values

The lack of suitable positive carcinogenic data precludes the derivation of an inhalation slope factor or unit risk for barium.

3.4 Bioavailability

The following section describes the bioavailabilities of barium.

3.4.1 Oral Bioavailability

Like other metals, barium is poorly absorbed from the gastrointestinal tract, with studies suggesting that absorption in humans is less than 5% (ATSDR, 1992). The range of reported oral absorption factors for all animal studies was 0.7 to 85% (US EPA, 1998). The oral bioavailability of barium was reported to be 0.07 by the Oak Ridge National Laboratory (ORNL, 2004). For the purpose of this assessment, the relative oral bioavailability from soil exposure was assumed to be 100% or 1.0.

3.4.2 Inhalation Bioavailability

No data are available on inhalation absorption of barium in humans; however, animal studies provide evidence that barium compounds are absorbed from the respiratory tract (US EPA, 1998). The inhalation bioavailability factor used in this assessment was 1.0.

3.4.3 Dermal Bioavailability

Health Canada (2003) also recommends a relative dermal absorption factor of 0.1 for barium. Therefore, a relative dermal bioavailability of 0.1 was adopted for this assessment.

3.5 Conclusion

The following tables present the TRV and bioavailability summaries for barium.

Table 3: Selected Toxicity Reference Values for Barium

Route of Exposure	TRV	TRV Type	Source Agency
Non-Cancer Effects			
Ingestion	1.60×10^{-2} mg/kg-day	TDI	Health Canada, 2003
Inhalation	NA	NA	NA
Cancer Effects			
Ingestion	NA	NA	NA
Inhalation	NA	NA	NA

NA – Not Applicable

Table 4: Selected Bioavailabilities for Barium

Route of Exposure	Relative Bioavailability	Reference
Ingestion	1.0	Assumed
Inhalation	1.0	Assumed
Dermal	0.1	Health Canada, 2003

3.6 References

ATSDR (Agency for Toxic Substances and Disease Registry). 1992. Toxicological Profile for Barium. Available on-line at: http://www.atsdr.cdc.gov/toxprofiles/

Health Canada, 2003. Federal Contaminated Site Risk Assessment in Canada, Part I: Guidance on Human Health Screening Level Risk Assessment (SLRA). October 3, 2003.

ORNL (Oak Ridge National Laboratory). 2004. Risk Assessment Program. Risk Assessment Information System. Toxicity and Chemical-specific Factors Data Base Search. Available on-line at: http://risk.lsd.ornl.gov/

US EPA (Environmental Protection Agency). 1998. Toxicological Review of Barium and Compounds (CAS No. 7440-39-3). In support of Summary Information on the Integrated Risk Information System (IRIS). March 1998. Available on-line at: http://www.epa.gov/iris/toxreviews/

US EPA (Environmental Protection Agency). 1999. Integrated Risk Information System (IRIS) Database – Barium and compounds. Confirmed current as of December 2004. Available on-line at: http://www.epa.gov/iris/

4. BERYLLIUM

According to the ATSDR (2002), beryllium is a hard, grayish metal naturally found in mineral rocks, coal, soil, and volcanic dust. Beryllium compounds are commercially mined, and the beryllium is purified for use in nuclear weapons and reactors, aircraft and space vehicle structures, instruments, x-ray machines, and mirrors. Beryllium ores are used to make speciality ceramics for electrical and high-technology applications. Beryllium alloys are used in automobiles, computers, sports equipment (golf clubs and bicycle frames), and dental bridges.

4.1 Assessment of Carcinogenicity

The Department of Health and Human Services (DHHS) and the International Agency for Research on Cancer (IARC) have determined that beryllium is a human carcinogen. The U.S. EPA has determined that beryllium is a probable human carcinogen.

4.2 Susceptible Populations

There are no studies on the health effects of children exposed to beryllium. It is likely that the health effects seen in children exposed to beryllium will be similar to the effects seen in adults. We do not know whether children differ from adults in their susceptibility to beryllium (ATSDR, 2002).

It is not known if exposure to beryllium will result in birth defects or other developmental effects in people: the studies on developmental effects in animals are not conclusive.

4.3 Selection of Toxicity Values

4.3.1 Non-Cancer Oral Toxicity Reference Values

The oral reference dose (RfD) for beryllium published by the US EPA (1998) is 0.002 mg/kg-d. The US EPA oral RfD is based on a long-term study of dogs fed diets containing beryllium by Morgareidge, *et al* (1976). The oral RfD is based on the development of intestinal lesions. A BMD_{10} (the lower 95% confidence limit on the dose from the maximum likelihood estimate [MLE] of a 10% relative change) of 0.46 mg/kg-day (MLE = 1.4 mg/kg-day) was derived for the lesions and used for further quantitation in this assessment in the US EPA's assessment. (U.S. EPA, 1995). An uncertainty factor of 300 was applied: 10 for extrapolation for interspecies differences, 10 for consideration of intraspecies variation, and 3 for database deficiencies. The USEPA has low to medium confidence in this RfD.

An oral RfD of 0.002 mg/kg-day has been adopted in this assessment based on the US EPA's recommended oral RfD.

4.3.2 Cancer Oral Toxicity Reference Values

The lack of suitable positive carcinogenic data precludes the derivation of an oral slope factor or unit risk for beryllium.

4.3.3 Non-Cancer Inhalation Toxicity Reference Values

The inhalation reference concentration (RfC) for beryllium published by the US EPA (1998) is 2E-2 $\mu g/m^3$. The RfC is based on beryllium sensitization and progression to chronic beryllium disease (CBD) identified in the co-principal studies by Kreiss, *et al.* (1996) and Eisenbud, *et al.* (1949). The Kreiss, *et al.* (1996) occupational exposure study identified a lowest observed adverse effects level (LOAEL) for beryllium sensitization in workers exposed to 0.55 $\mu g/m^3$ (median of average concentrations). The Eisenbud, *et al.* (1949) study, using relatively insensitive screening methods, suggests a no observed adverse effects level (NOAEL) of 0.01-0.1 $\mu g/m^3$ in community residents living near a beryllium plant. The LOAEL from the Kreiss, *et al.* study was used for the operational derivation of the RfC because the screening method used in the Eisenbud, *et al.* (1949) study was less sensitive than the method used in the Kreiss, *et al.* (1996) study.

Because individuals developing beryllium sensitization and CBD are the most sensitive subpopulation, an uncertainty factor of 1 was used to account for human variability. An uncertainty factor of 1 was also used to adjust for the less-than-chronic exposure duration of the Kreiss, *et al.* (1996) study; use of this uncertainty factor is supported by the evidence that the occurrence of CBD does not appear to be related to exposure duration. A database uncertainty factor of 3 was used to account for the poor quality of exposure monitoring in the co-principal studies and other epidemiology studies that assessed the incidence of beryllium sensitization and CBD among exposed workers and community residents. The US EPA has medium confidence in this RfD.

An RfD of 4.47E-6 mg/kg-d was then calculated based on the US EPA RfC, by dividing by an adult body weight of 70.7 kg and multiplying by an adult inhalation rate of 15.8 m^3/d, which was then used in this assessment.

4.3.4 Cancer Inhalation Toxicity Reference Values

The US EPA (1998) has published an inhalation unit risk for beryllium of 2.4E-3 $(\mu g/m^3)^{-1}$. The unit risk value is based on an occupational exposure epidemiological study by Wagoner, *et al.* (1980) which was used to estimate the lifetime cancer risk from exposure to beryllium oxide based on the estimated lower and upper bounds of exposure estimated by the National Institute of Occupational Safety and Health (NIOSH); namely, 100 and 1,000 $\mu g/m^3$.

An inhalation slope factor of 10.9 $(mg/kg\text{-}d)^{-1}$ was then calculated by multiplying the US EPA inhalation unit risk, by an adult body weight of 70.7 kg and dividing by an adult inhalation rate of 15.8 m^3/d, which was then used in this assessment.

4.4 Bioavailability

The following section describes the bioavailabilities of beryllium.

4.4.1 Oral Bioavailability

The relative oral absorption factor for beryllium has been conservatively assumed to be 1.0.

4.4.2 Inhalation Bioavailability

The relative inhalation absorption factor for beryllium has been conservatively assumed to be 1.0.

4.4.3 Dermal Bioavailability

Health Canada (2003) recommends a relative dermal absorption factor of 0.03 for beryllium. Therefore, a relative dermal bioavailability of 0.03 was adopted for this assessment.

4.5 Conclusion

The following tables present the TRV and bioavailability summaries for beryllium.

Table 5: Selected Toxicity Reference Values for Beryllium

Route of Exposure	TRV	TRV Type	Source Agency
Non-Cancer Effects			
Ingestion	2.00E-03 mg/kg-day	RfD	US EPA, 1998
Inhalation	4.47E-06 mg/kg-day	RfC	US EPA, 1998
Cancer Effects			
Ingestion	NA	NA	NA
Inhalation	10.7 $(mg/kg\text{-}day)^{-1}$	Slope Factor	US EPA, 1998

NA – Not Applicable

Table 6: Selected Bioavailabilities for Beryllium

Route of Exposure	Relative Bioavailability	Reference
Ingestion	1.0	Assumed
Inhalation	1.0	Assumed
Dermal	0.03	Health Canada, 2003

4.6 References

ATSDR (Agency for Toxic Substances and Disease Registry), 2002. Toxicological Profile for Beryllium. September 2002. Available on-line at: http://www.atsdr.cdc.gov/toxpro2.html.

Eisenbud, M; Wanta, RC; Dustan, C; *et al.*, 1949. Non-occupational berylliosis. J Ind Hyg Toxicol 31:282-294. Cited In: US EPA, 1998.

Kreiss, K; Mroz, MM; Newman, LS; *et al*,. 1996. Machining risk of beryllium disease and sensitization with median exposures below 2 MU-G/M(3). Am J Ind Med 30(1):16-25 Cited In: US EPA, 1998.

Morgareidge, K; Cox, GE; Gallo, MA. 1976. Chronic feeding studies with beryllium in dogs. Food and Drug Research Laboratories, Inc. Submitted to the Aluminum Company of America, Alcan Research & Development, Ltd., Kawecki-Berylco Industries, Inc., and Brush-Wellman, Inc. Cited In: US EPA, 1998.

US EPA (United States Environmental Protection Agency), 1998. Integrated Risk Information System (IRIS) Database. Beryllium and compounds (inorganic). Confirmed current as of December 2004. Available on-line at: http://www.epa.gov/iris/

Wagoner, JK; Infante, PF; Bayliss, DL. (1980) Beryllium: an etiologic agent in the induction of lung cancer, nonneoplastic respiratory disease, and heart disease among industrially exposed workers. Environ Res 21:15-34. Cited In: US EPA, 1998.

5. CADMIUM

Cadmium is a naturally occurring element that is commonly found as a mineral combined with other elements. Cadmium has many uses in industry and consumer products, mainly in batteries, pigments, metal coatings, plastics, and some metal alloys (ATSDR, 1999)

5.1 Assessment of Carcinogenicity

Several occupational studies have reported an excess risk of lung cancer in humans from exposure to inhaled cadmium; however, the evidence is limited rather than conclusive due to confounding factors (US EPA, 1994; ATSDR, 1999). Animal studies have reported cancer resulting from inhalation exposure to several forms of cadmium, while animal ingestion studies have not demonstrated carcinogenicity (US EPA, 1994; ATSDR, 1999). The US EPA (1994) considers cadmium to be a probable human carcinogen and has classified it as Group B1. Health Canada (Environment Canada and Health Canada, 1994) has classified cadmium as a Group II carcinogen – probably carcinogenic to humans.

5.2 Susceptible Populations

Populations which may be unusually susceptible to cadmium exposure are those with a genetic predisposition to lower inducibility of metallothionein, the enzyme which sequesters cadmium (ATSDR, 1999). Dietary deficiencies which lead to depleted levels of calcium or iron in individuals may result in increased absorption of cadmium from the gastrointestinal tract (ATSDR, 1999). Infants and children may have increased uptake of cadmium via the gastrointestinal tract and higher concentrations of cadmium in the bone (ATSDR, 1999).

5.3 Selection of Toxicity Values

Chronic inhalation and oral exposure of humans to cadmium results in a build-up of cadmium in the kidneys that can cause kidney disease, including proteinuria, a decrease in glomerular filtration rate, and an increased frequency of kidney stone formation (ATSDR, 1999). The following section describes various studies conducted to establish cadmium toxicity values via ingestion, inhalation and dermal routes of exposure.

5.3.1 Non-Cancer Oral Toxicity Reference Values

Health Canada (2003a) has adopted the value of 0.0008 mg/kg-day as a tolerabe daily intake (TDI). The Health Canada TDI is based upon the Canadian Guidelines for Drinking Water

Quality, Supporting Documentation (2003b). The Canadian drinking water maximum allowable concentration (MAC) of 0.005 mg/L was calculated based on the joint FAO/WHO expert committee's proposed upper limit provisional tolerable weekly intake (PTWI) of 0.5 mg for adults (WHO, 1992; Health Canada, 2003b). The PTWI was based on the estimation that a daily intake of 0.05 mg would lead to 0.1% of the population reaching the "critical" concentration of 0.2 mg/g of cadmium in the renal cortex after 50 years. The WHO (1992) derived a PTWI range of 0.4 to 0.5 mg for cadmium. The kidney is believed to be the target organ of cadmium, specifically affecting the renal cortex.

The US EPA (1994) has developed oral RfDs for cadmium in food and water also based on kidney effects. The RfD for food is 1.0×10^{-3} mg/kg-day and for water is 5.0×10^{-4} mg/kg-day (US EPA, 1994). Both RfDs are based on significant proteinuria in humans with an assumed 2.5% absorption of cadmium from food and 5% from water. The NOAELs for chronic cadmium exposure were determined to be 5.0 and 10 µg/kg-day for food and water, respectively. An uncertainty factor of 10 to account for human variability was applied to the NOAELs to develop the reference doses for food and water. The US EPA rates the information database and corresponding RfD with high confidence.

The Health Canada TDI of 8.0×10^{-4} mg/kg-day was selected to assess non-carcinogenic effects from oral cadmium exposure.

5.3.2 Cancer Oral Toxicity Reference Values

The lack of suitable positive carcinogenic data precludes the derivation of an oral slope factor or unit risk for cadmium..

5.3.3 Non-Cancer Inhalation Reference Toxicity Values

A non-cancer inhalation TRV has not been selected for this assessment due to the lack of sufficient data.

5.3.4 Cancer Inhalation Reference Toxicity Values

The US EPA (1994) has developed an inhalation unit risk of 1.8 $(mg/m^3)^{-1}$ to be used only if the air concentration does not exceed 6 $\mu g/m^3$. This unit risk is based on lung and upper respiratory tract cancers in cadmium production workers (Thun *et al.*, 1985) and was selected over another study that yielded a more conservative unit risk because it was based on human data which involved a large cohort and took into consideration the effects of arsenic and smoking.

Health Canada (2003a) has calculated an inhalation unit risk of 9.8 $(mg/m^3)^{-1}$ which is equivalent to an inhalation slope factor of 4.29E+01 $(mg/kg\text{-}day)^{-1}$, which was based on a TC_{05} of 5.1 $\mu g/m^3$ (Health Canada, 1996). The estimated TD_{05} for cadmium chloride based on multistage model of lung tumour incidences observed in rats by Takenaka *et al.* (1983). The TD_{05} of 2.9 µg of cadmium/m^3 was amortized to be constant over the entire life of the rat, adjusted for longer than lifetime duration of the experiment and converted to an equivalent concentration for humans using standard breathing rates and body weights which yielded a TC_{05} of 5.1 $\mu g/m^3$ (Environment Canada and Health Canada, 1994). The Health Canada TC_{05} provides a more conservative unit risk estimate of the potency of inhaled cadmium.

Therefore, an inhalation slope factor of 4.29E+01 $(mg/kg\text{-}day)^{-1}$ was adopted for this assessment.

5.4 Bioavailability

Cadmium compounds have varying degrees of solubility ranging from very soluble to nearly insoluble. The solubility affects their absorption and toxicity. Exposure to cadmium and cadmium compounds may occur in both occupational and environmental settings, the latter primarily via the diet and drinking water (ATSDR, 1999).

5.4.1 Oral Bioavailability

Cadmium bound in a soil matrix is expected to be less bioavailable than cadmium in drinking water, as in the study from which the oral RfD was derived. Other studies have reported the oral absorption of cadmium to range from 0.027 (Newton *et al.*, 1984) to 0.06 (Rahola *et al.*, 1975).

The selected oral RfD for cadmium is based on kidney effects following water consumption. Water consumption was assumed to be 5% absorbed in humans (US EPA, 1994). Falling within the range of the above studies. For this assessment, an oral relative bioavailability of 1.0 in soil was used.

5.4.2 Inhalation Bioavailability

Cadmium in air exists primarily as fine suspended particulate matter. When inhaled, some fraction of the larger particles (i.e., greater than 10 microns in diameter) is deposited in the airways or lungs, and the rest is exhaled. Finer particles tend to penetrate into the alveoli. While some soluble cadmium compounds may be absorbed from the airways or lungs, the major site of absorption is the alveoli (ATSDR, 1999). Comprehensive modelling of the kinetics of cadmium