National Environment Protection (Assessment of Site Contamination) Measure 1999

as amended

made under section 14(1) of the

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This compilation has been split into 22 volumes

Volume 1: sections 1–6, Schedules A and B
Volume 2: Schedule B1
Volume 3: Schedule B2
Volume 4: Schedule B3
Volume 5: Schedule B4
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Volume 10: Schedule B7 - Appendix 1
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About this compilation

The compiled instrument

This is a compilation of the *National Environment Protection (Assessment of Site Contamination) Measure 1999* as amended and in force on 16 May 2013. It includes any amendment affecting the compiled instrument to that date.

This compilation was prepared on 22 May 2013.

The notes at the end of this compilation (the ***endnotes***) include information about amending Acts and instruments and the amendment history of each amended provision.

Uncommenced provisions and amendments

If a provision of the compiled instrument is affected by an uncommenced amendment, the text of the uncommenced amendment is set out in the endnotes.

Application, saving and transitional provisions for amendments

If the operation of an amendment is affected by an application, saving or transitional provision, the provision is identified in the endnotes.

Modifications

If a provision of the compiled instrument is affected by a textual modification that is in force, the text of the modifying provision is set out in the endnotes.

Provisions ceasing to have effect

If a provision of the compiled instrument has expired or otherwise ceased to have effect in accordance with a provision of the instrument, details of the provision are set out in the endnotes.

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Schedule B7

APPENDIX A1

The Derivation of HILs for Metals and Inorganics

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1 Arsenic

1.1 General

Several comprehensive reviews of arsenic in the environment and its toxicity to humans are available and should be consulted for more detailed information not presented in this summary (ATSDR 2007; NRC 2001; WHO 2001; and EA 2009a). The following provides a summary of the key aspects of arsenic that are relevant to the derivation of a soil health investigation level (HIL).

Arsenic is a metalloid that can exist in four valence states (-3, 0, +3 and +5) and forms a steel grey, brittle solid in elemental form (ATSDR 2007). Under reducing conditions, arsenite (As III) is the dominant form and, in well oxygenated environments, arsenate (As V) predominates (WHO 2000). Arsenic is the 20th most commonly occurring element in the Earth's crust, occurring at an average concentration of 3.4 ppm (ATSDR 2007).

1.2 Previous HIL

The derivation of the HIL (HIL A = 100 mg/kg) for arsenic is presented by Langley (1991). In summary, the previous HIL was derived on the basis of the following:

- Intakes of arsenic from other sources were estimated, with dietary intakes considered most significant for the general population. Intakes based on data from the 1987 and 1990 Australian Market Basket Surveys were estimated to be 6.7 µg/kg/week for a 2-year-old child. This was approximated to contribute up to 50% of the provisional tolerable weekly intake (PTWI) considered.
- A PTWI of 15 µg/kg/week referenced from the World Health Organization (WHO) was adopted as the toxicity reference value.
- Ingestion of both soil and dust was considered assuming 100% is bioavailable and is absorbed.
- Dermal absorption was considered to be low with 1% of arsenic compounds absorbed in 24 hours;
- Inhalation of arsenic in dust, both outdoors and indoors, has been considered.
- The total absorption of arsenic, based on 100 mg/kg in soil, for a young child was calculated to be 11.4 µg/day, approximately 40% of the adopted toxicity reference value.

1.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed, as noted below.

1.3.1 Oral Bioavailability

Most international jurisdictions have adopted a default value of 100% oral bioavailability in the derivation of investigation levels, allowing site-specific bioavailability to then be considered in further assessment. It is also understood that review of arsenic bioavailability in Australia (Ng et al. 2009) has not identified a default value.

As a note, some default bioavailability values have been adopted in the USA (based on reviews of state-specific data) as follows:

- Region 8 (US EPA 2009) recommends a default of 0.5 (50%), noting that where concentrations are near a level of concern, site-specific bioavailability data is recommended.

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- Region 10 (US EPA 2000) recommends a default of 0.8 (80%) for soil at smelter sites, 0.6 (60%) for soil at mine sites and 1 (100%) for all other sites.
- Texas recommends a default of 0.78 (78%).

While it may not be sufficiently conservative to apply a low value as adopted by the Australian Pesticides and Veterinary Medicines Authority (APVMA) (25%), some consideration of a conservative default in Australia is presented. It is noted that bioavailability is complex; however, based on relative bioavailability data available for Australian sites (presented in Ng et al. 2009; Juhasz et al. 2003), upper values were in the range of approximately 50–70% with most significantly lower than these values, and a few studies reporting upper limit values that are higher (up to 97%). Juhasz et al. (2003) suggested a worst-case value of 50% could be considered. When considering long-term exposures from soil it is overly conservative to consider the maximum bioavailability value from one particular study, as exposures will be averaged over accessible soil/dust. Hence it would be reasonable to consider a conservative value of 70% bioavailability as a reasonable upper estimate that adequately addresses arsenic that may be derived from mine sites, smelters, railway corridors and other areas where herbicides/pesticides have been used.

Roberts et al. (2002) showed monkey absorption of arsenic from pesticide-treated soil and cattle dip soil is 10.7–24.7%. In August 2001, the US EPA Health Effects Division's Hazard Identification Assessment Review Committee (HIARC) evaluated the toxicology database for inorganic arsenic and established toxicological end points for incidental residential and commercial/industrial exposure risk assessments (US EPA 2001). As a key component of that assessment, HIARC established the appropriate relative bioavailability of arsenic in soil versus arsenic in water. For purposes of health risk assessment, US EPA evaluated a number of studies of relative bioavailability of arsenic (US EPA 2001). After careful consideration of data reported in the various bioavailability studies, US EPA determined that the monkey was considered an appropriate study model for humans due to its similarity in excretion and gastrointestinal absorption characteristics (US EPA 2001). The US EPA identified the comprehensive monkey study conducted by Roberts et al. (2002) as the study of choice. This study was conducted on behalf of the Florida Department of Environmental Protection (DEP) in order to specifically establish a gastrointestinal absorption efficiency factor for arsenic in soil that could be applied to soil risk assessments. The Roberts et al. (2002) study identified the maximum of the arithmetic mean value of 24.7% (for five animals and for relative bioavailability for each of five soil types) as a 'conservative, upper bound case for any particular soil type'. While the maximum individual value reported in the study was 32.4%, the authors did not recommend this value for use as a reasonable maximum exposure (RME) value for risk assessment on the basis that 'only under highly specific, rare circumstances is the maximum value for a particular parameter used in environmental characterisation, exposure assessment and risk assessment' (Roberts et al. 2002). The US EPA agreed with the Florida DEP and selected 25% as an RME value for relative bioavailability for health risk assessments of arsenic in soil (US EPA 2001) and both agencies currently endorse the value of 25%. While the Roberts et al. (2002) study used five soil types typical of Florida soils, another monkey study (using a difference species) was conducted by Freeman et al. (1995) using soil near a smelter in Anaconda, Montana. The mean absolute percentage bioavailabilities, based on urinary excretion data, were 68, 19, and 14% for the gavage (soluble sodium arsenate in oral solution), house dust, and soil treatments, respectively. The values for house dust and soil are consistent with those reported by Roberts et al. (2002) for soil.

Available data from Bendigo in Victoria suggests that the bioavailability of arsenic in soil derived from mine tailings in this region commonly ranges from 10–20% and is generally less than 30%. The value of 25% that is adopted by the US EPA would be appropriate in these areas.

With consideration of the above, a range of 25–70% bioavailability may be appropriate for the assessment of arsenic in soil. The range of bioavailabilities considered would need to be based on suitable data in relation to source and site-specific bioavailability (where lower bioavailability values were considered appropriate).

1.3.2 Dermal Absorption

Review of dermal absorption by the New Zealand Ministry for the Environment (MfE 2011) has noted that 'despite the fact that skin cancer is a primary toxicological effect of concern as a result of exposure to arsenic, dermal absorption of arsenic is generally considered to be negligible. US EPA (2004) guidance uses a dermal absorption factor of 3% based on Wester et al. (1993), who examined the dermal uptake of arsenic in solution. However, recent studies on the dermal absorption of soil-absorbed arsenic in rhesus monkeys indicate that the mean dermal absorption is 0.5%, i.e. negligible (Lowney et al. 2007)'.

On the basis of the above, a dermal absorption value of 0.5% has been considered in the derivation of an HIL for arsenic in soil.

1.3.3 Inhalation of Dust

Arsenic is not volatile and inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, potential inhalation exposures associated with dust have been considered in the HIL derived.

1.3.4 Plant Uptake

In the review of arsenic presented by Langley (1991), a study by Merry et al. (1986) was cited which involved evaluation of the uptake of arsenic by radishes and silverbeets in soil with concentrations ranging from 26–260 ppm. The study showed 'no concentrations that exceeded currently accepted health limits for human consumption' Langley (1991). Langley (1991) also noted that plant growth was likely to be affected before plant concentrations were substantially elevated.
Further review of plant uptake of arsenic is presented by the UK Environment Agency (EA 2009b). This review considered studies that are based on the uptake of arsenic into green vegetables, root vegetables, tuber vegetables, herbaceous fruit, shrub fruit and tree fruit. The review provides recommendations as to relevant soil-to-plant uptake factors that are relevant for these types of produce. The recommendations from this review have been considered in the derivation of a residential HIL A and are summarised below for the range of crops considered:

Produce Group	Plant Uptake Factors (mg/kg produce fresh weight per mg/kg soil) (EA 2009b)
Green vegetables	0.00043
Root vegetables	0.0004
Tuber vegetables	0.00023
Tree fruit	0.0011

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce (also included in background intakes). To address this in the derivation of HIL A, half the intake estimated to be derived from home-grown produce is assumed to be already accounted for in the total background intake (noted below).

1.3.5 Intakes from Other Sources – Background

The most recent Australian Total Diet Survey (ATDS) that addresses arsenic in food was published by FSANZ in 2011 (FSANZ 2011). Based on data presented in this report, dietary intake of arsenic for children aged 2–5 years ranges from a mean of 1.2 µg/kg/day to a 90th percentile of 2.8 µg/kg/day. These intakes are based on total arsenic in produce, rather than inorganic arsenic.

Review of background intakes from food, water, air, soil and contact with play equipment, based on available Australian data presented by APVMA (2005), suggests background intakes of inorganic

arsenic by young children may average 0.62 µg/kg/day. Further review of inorganic arsenic intakes by the Joint FAO/WHO Expert Committee on Food Additives (WHO 2011a) indicated that for populations not located in areas of arsenic-contaminated groundwater, intakes by young children ranged from 0.14–1.39 µg/kg/day. On the basis of the range of intake estimations available, a reasonable estimation of 50% of the oral toxicity reference value (TRV) from sources other than soil has been assumed. It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce (addressed when assessing intakes from home-grown produce).

Intakes from inhalation exposures are low (around 0.0017 µg/kg/day (APVMA 2005)), comprising <1% of the inhalation TRV adopted.

1.4 Identification of Toxicity Reference Values

With respect to arsenic toxicity and the identification of appropriate toxicity reference values, a number of issues need to be considered. These include:

- the relevance of non-threshold carcinogenic values for the assessment of oral exposures
- identification of an appropriate oral toxicity value
- identification of an appropriate approach and value for inhalation exposures.

These are discussed below.

1.4.1 Classification

The International Agency for Research on Cancer (IARC) has classified arsenic and inorganic arsenic compounds as Group 1 – 'carcinogenic to humans' (IARC 2012).

1.4.2 Review of Oral Information

Arsenic is a known human carcinogen, based on human epidemiological studies that show skin and internal cancers (in particular, bladder, liver and lung) associated with chronic exposures to arsenic in drinking water. The research available on arsenic carcinogenicity is dominated by epidemiological studies (which have limitations) rather than animal studies. This differs from carcinogenic assessments undertaken on many other chemicals. The principal reason for the lack of animal studies is because arsenic has not been shown to cause cancer in rodents (the most common species used in animal tests), due to interspecies differences between rodents and humans.

Review of arsenic by IARC (2012) has concluded the following:

- For inorganic arsenic and its metabolites, the evidence points to weak or non-existent direct mutagenesis (genotoxicity), which is seen only at highly cytotoxic concentrations.
- Long-term, low-dose exposures to inorganic arsenic (more relevant to human exposure) is likely to cause increased mutagenesis as a secondary effect of genomic instability. While the mechanism of action (MOA) is not fully understood, it is suggested by IARC (2012) that it may be mediated by increased levels of reactive oxygen species, as well as co-mutagenesis with other agents. The major underlying mechanisms observed at low concentrations include the rapid induction of oxidative DNA damage and DNA-repair inhibition, and slower changes in DNA-methylation patterns, aneuploidy, and gene amplification.
- Inhibition of DNA repair leads to co-carcinogenicity.

Revision to the WHO guidelines on drinking water (WHO 2011b) adopted a practical value based on the analytical limit of reporting rather than based on a dose–response approach. The oral slope factor derived by the US has not been used to derive a guideline, as the slope factor is noted by WHO as likely to be an overestimate.

US EPA reviews have retained the use of a non-threshold approach, based on sufficient supporting evidence associated with increased rates of bladder and lung cancer (for inhalation exposures (US EPA 2001)). The US EPA approach adopted follows a review by the NRC (2001) which concluded that '… internal cancers are more appropriate as end points for risk assessment than non-melanoma skin cancers'. Slope factors relevant for the assessment of these end points range from 0.4–23 $(mg/kg/day)^{-1}$. The use of a non-threshold approach (slope factor), however, is more by default by following the US EPA Carcinogenic Guidelines (US EPA 2005), as there remains uncertainty on the carcinogenic MOA for arsenic (Sams et al. 2007). Further research is required to define and review the MOA prior to the US revising the dose–response approach currently adopted. Inherent in the current US approach (where a non-threshold slope factor is derived) are some key uncertainties that likely result in an overestimate of risk (Boyce et al. 2008), which include (SAB 2005, Brown 2007, Lamm & Kruse 2005 and Chu & Crawford-Brown 2006):

- the choice of the cancer end point
- the choice of the mathematical model used to estimate risk (shape of the dose–response curve at low doses) as there is no clear biological basis for extrapolation–
- the assumptions used to estimate exposure from studies (primarily epidemiological studies).

Review of recent studies presented by Boyce et al. (2008) has indicated that, for carcinogenic effects associated with arsenic exposure, a linear (or non-threshold) dose–response is not supported (also note discussion by Clewell et al. 2007). This is based on the following:

- Epidemiological studies (worldwide) that have repeatedly demonstrated that cancers associated with inorganic arsenic ingestion are observed only in populations exposed to arsenic concentrations in drinking water that are greater than 150 µg/L. In the US, exposures to concentrations in drinking water have only been associated with carcinogenic effects where mean concentrations are greater than 190 µg/L (Schoen et al. 2004).
- Mechanistic information on how arsenic affects the cellular processes associate with carcinogenicity. This includes consideration that arsenic and its metabolites may modify DNA function through more indirect mechanisms such as inhibition of DNA repair, induction of dysfunctional cell division, perturbation of DNA methylation patterns, modulation of signal transduction pathways (leading to changes in transcriptional controls and the over-stimulation of growth factors), and generation of oxidative stress (ATSDR 2007 and IARC 2012) and that evidence for the indirect mechanisms for genotoxicity identified in in vitro studies have nearly all been at concentrations that are cytotoxic (Klein et al. 2007).

Hence the default approach adopted by the US EPA in adopting a non-threshold approach to the assessment of the carcinogenic effects associated with arsenic exposure is not well supported by the available data. This is consistent with the most recent Australian review available (APVMA 2005). The review conducted considered current information on arsenic carcinogenicity and genotoxicity which noted the following:

'Although exposure to high concentrations of inorganic arsenic results in tumour formation and chromosomal damage (clastogenic effect), the mechanism by which these tumours develop does not appear to involve mutagenesis. Arsenic appears to act on the chromosomes and acts as a tumour promoter rather than as an initiator …'. 'Furthermore, the epidemiological evidence from occupational exposure studies indicates that arsenic acts at a later stage in the development of cancer, as noted with the increased risk of lung cancer mortality with increasing age of initial exposure, independent of time after exposure …' 'Hence arsenic appears to behave like a carcinogen which exhibits a threshold effect. This would also be conceptually consistent with the notion that humans have ingested food and water containing arsenic over millennia and so the presence of a threshold seems likely. Nevertheless

the mechanism by which tumour formation develops following arsenic exposure has been and still continues to be a source of intensive scientific investigation.'

On the basis of the above the use of a threshold dose–response approach for the assessment of carcinogenic effects associated with arsenic exposure is considered appropriate and has been adopted in the derivation of soil HILs.

The review of arsenic by the New Zealand Ministry for the Environment (MfE 2011) noted that, while there is general consensus that arsenic is likely to act indirectly on DNA in a sub-linear or threshold manner, it is considered that there is insufficient data available to determine a 'well-defined non-linear dose–response'. For this reason the derivation of the New Zealand soil guideline values has adopted a non-threshold (linear) approach for arsenic (i.e. adopting a default non-threshold approach similar to that adopted by default by the US EPA). This differs from the approach adopted in Australia.

1.4.3 Assessment of End Points – Oral Exposures

1.4.3.1 Existing Oral Dose–Response Approaches – Australia

Arsenic intakes (oral) have been considered in Australia in the derivation of the current HIL (Langley 1991) and the Australian Drinking Water Guidelines (ADWG) (NHMRC 2011). The following can be noted from these guidelines:

- The derivation of the HIL for arsenic is dated (Langley 1991) and considers all intakes of arsenic on the basis of a threshold PTWI established by WHO in 1983, and reconfirmed in 1988 (WHO 1989). The PTWI adopted is 15 µg/kg/week. In setting the PTWI it was noted that there is 'a narrow margin between the PTWI and intakes reported to have toxic effects in epidemiological studies' (WHO 1989). The PTWI was withdrawn by JECFA (WHO 2011a) following further review (refer to discussion below).
- The previous ADWG (NHMRC 2004) derived criteria of 7 µg/L for inorganic arsenic in drinking water, based on the former WHO PTWI (noted above) converted to a daily intake (provisional maximum tolerable daily intake) of 2 µg/kg/day. The current ADWG (NHMRC 2011) has adopted a guideline of 10 µg/L based on a 'practicable achievable' approach supported by contemporary epidemiological studies in which elevated cancer risks and other adverse effects are not demonstrable at arsenic concentrations around 10 µg/L. It is noted that this level is equivalent to an adult (70 kg) intake of 0.28 µg/kg/day.

A review of arsenic toxicity was conducted by APVMA (2005) where a threshold approach was considered appropriate (noted above). A threshold value of 3 µg/kg/day was derived by the Australian and New Zealand Food Authority (ANZFA, now Food Standards Australia New Zealand (FSANZ)) in 1999, and considered in the APVMA (2005) review. The review considered that skin cancers appear to be the most sensitive indicator of carcinogenicity of inorganic arsenic in humans and, based on epidemiological studies, a threshold of 2.9 µg/kg/day (rounded to 3 µg/kg/day) can be obtained. This threshold is the value adopted as a provisional tolerable daily intake (PTDI) by FSANZ (FSANZ 2003), similar to the former PTWI available from WHO (noted above). This approach has been considered by APVMA for all intakes of arsenic (oral, dermal and inhalation). The evaluation has not been further updated.

1.4.3.2 Oral Dose–Response Approaches - International

Evaluation of arsenic by JECFA (WHO 2011a) considered the available epidemiological data in relation to the increased incidence of lung cancer and urinary tract cancer associated with exposure to arsenic in water and food. Using the data associated with these end points, JECFA derived a benchmark dose lower confidence limit for a 0.5% increased incidence ($BMDL_{0.5}$) of lung cancer (most sensitive end point) of 3 µg/kg/day (ranging from 2–7 µg/kg/day). Uncertainties associated with the assumptions associated with total exposure, extrapolation of the $BMDL_{0.5}$ and influences of the existing health status of the population were identified. Given the uncertainties and that the $BMDL_{0.5}$

was essentially equal to the PTWI (WHO 1989), the PTWI was withdrawn. No alternative threshold values were suggested by JECFA, as the application of the BMDL needs to be addressed on a regulatory level, including when establishing guideline levels.

The review conducted by JECFA is generally consistent with that conducted by the European Food Safety Authority (EFSA) Panel on Contaminants in the Food Chain (CONTAM) (EFSA 2010). The review concluded that the PTWI was 'no longer appropriate as data is available that shows inorganic arsenic causes cancer of the lung and bladder in addition to skin, and that the range of adverse effects had been reported at exposures lower than those reviewed by the JECFA' in establishing the PTWI. Modelling conducted by EFSA considered the available epidemiological studies and selected a benchmark response (lower limits) of 1% extra risk ($BMDL_{01}$). $BMDL_{01}$ range from 0.3–8 µg/kg/day for cancers of the lung, bladder and skin. The CONTAM Panel (EFSA 2010) concluded that the overall range of $BMDL_{01}$ values of 0.3–8 µg/kg/day should be used for the risk characterisation of inorganic arsenic rather than a single reference point, primarily due to the number of uncertainties associated with the possible dose–response relationships considered. On this basis it would not be appropriate to consider just one value in the range presented.

The derivation of a soil HIL requires the identification of an appropriate TRV, rather than a wide range of values, that is considered adequately protective of the population potentially exposed. The determination of an appropriate TRV for arsenic in soil in Australia has therefore considered the following:

- The studies considered in the derivation of the different ranges of BMDL values (WHO 2011a and EFSA 2010) are based on drinking water studies. No studies considered are derived from other sources including soil. There are uncertainties inherent in the epidemiological studies considered by WHO (2011a) and EFSA (2010). These uncertainties include limitations or absence of information on levels of individual exposure or arsenic intake (from drinking water), limited quantification of arsenic intakes from other sources including food, size of the studies (variable) and the assumption that arsenic intake is the single cause of all end points identified.
- The drinking water studies are primarily associated with populations that have poorer nutritional status (i.e. Taiwan and Bangladesh). Studies (as summarised by EFSA 2010) have shown that populations with poor nutrition (and health status) are more susceptible to the prevalence and severity of arsenic-related health effects.
- The largest of the studies conducted was within rural Asian populations, which differ from Australian populations with respect to generic lifestyle factors.

In view of the above, consideration of the lower end of the range of BMDL values available from WHO (2011a) and EFSA (2010) is not considered appropriate for the Australian population.

Based on the above considerations, a TRV of 2 µg/kg/day has been adopted in the derivation of a soil HIL. The TRV has been selected on the basis of the following:

- The TRV is the lower end of the range derived from JECFA (WHO 2011a), and also lies within, but is not at the lower end of, the range presented by EFSA (2010).
- The value is within the range of no observable adverse effect levels (NOAELs) identified by RIVM (2001), US EPA (US EPA 1998) and ATSDR (2007) that are associated with non-carcinogenic effects (and derived from drinking water studies in Taiwan and Bangladesh) of 0.8–8 µg/kg/day. Consistent with the approach discussed above in relation to the range of TRVs relevant to a cancer end point, it is not considered appropriate that the most conservative end of this range is adopted for the Australian population.

Due to the level of uncertainty in relation to determining a single TRV for the assessment of arsenic exposures, the oral TRV used for the derivation of the soil HIL has not been considered to be a

definitive value (refer to the calculations presented below). In addition, the approach adopted is based on developing science that should be reviewed in line with further developments in both science and policy.

1.4.4 Inhalation Values

Less data is available with respect to inhalation exposures to arsenic, though trivalent arsenic has been shown to be carcinogenic via inhalation exposures (with lung cancer as the end point). Review of the relevant mechanisms for carcinogenicity by RIVM (2001) suggests that the mechanism for arsenic carcinogenicity is the same regardless of the route of exposure. Hence a threshold is also considered relevant for the assessment of inhalation exposures. This is consistent with the approach adopted in the derivation of the previous arsenic HIL (Langley 1991) and in the review undertaken by APVMA (2005). While NEPC and APVMA adopted the oral PTWI as relevant for all routes of exposure, RIVM (2001) has derived an inhalation-specific threshold value. The RIVM (2001) review identified that the critical effect associated with chronic inhalation exposures in humans is lung cancer. The lowest observable adverse effect concentration (LOAEC) for trivalent arsenic associated with these effects is 10 $\mu g/m^3$ (based on the review by ATSDR 2007). Applying an uncertainty factor of 10 to address variability in human susceptibility, a tolerable concentration (TC) in air of 1 $\mu g/m^3$ was derived.

Given the above, there is some basis for the assessment of inhalation exposures to arsenic to adopt an appropriate threshold value but the available epidemiological studies associated with exposures in copper smelters suggest a linear or non-threshold approach may be relevant. The WHO (2000) review of arsenic also suggested the use of a linear (non-threshold) approach to the assessment of inhalation exposures to arsenic. The assessment presented is limited and essentially adopts the US approach with no discussion or consideration of the relevance of the linear model adopted. The review by WHO (2001) with respect to inhalation exposures and lung cancer provides a more comprehensive review and assessment. The review presented identified that a linear dose–response relationship is supported by the occupational and epidemiological studies. The three key studies associated with copper smelters in Tacoma, Washington (USA), Anaconda, Montana (USA) and Ronnskar (Sweden) (as summarised by WHO 2001) demonstrate a statistically significant excess risk of lung cancer at cumulative exposure levels of approximately ≥ 0.75 mg/m^3 per year.

The relevance of inhalation values derived from studies near smelters to the assessment of contaminated arsenic in soil in areas away from smelters is not well founded. Hence it is recommended that a threshold approach is considered for the assessment of inhalation exposures associated with arsenic in soil. The threshold TC derived by RIVM (2001) of 1 μg/m3 is lower than the cumulative exposure value identified by WHO (2001) of 750 μg/m3.years as statistically associated with an increase in lung cancer. The values are considered reasonably comparable if the exposure occurs over a period of 40 years and appropriate uncertainty factors are applied to convert from a lowest observable adverse effect level (LOAEL) to a NOAEL. In addition the TC is consistent with the TC05 value derived by Health Canada (1993) associated with lung cancer in humans and an incremental lifetime risk of 1 in 100,000. The value adopted is lower than the recommended PTDI adopted for the assessment of oral intakes (when the TC is converted to a daily intake). Hence use of the RIVM TC has been considered appropriate and adequately protective of all health effects associated with inhalation exposures that may be derived from soil, including carcinogenicity.

1.4.5 Recommendation

On the basis of the discussion above the following toxicity reference values (TRVs) have been adopted for arsenic in the derivation of HILs:

Recommendations for Arsenic

Oral TRV (TRV_O) = 0.002 mg/kg/day for oral and dermal intakes (refer to discussion above)

Oral Bioavailability (BA_O) = may vary from around 25–70% (with the value adopted dependent on the available site data to support the use of these values). Values of 100%, 70% and 25% reviewed as discussed below.

Inhalation TRV (TRV_I) = 0.001 mg/m^3 (RIVM 2001)

Dermal absorption factor (DAF) = 0.005 (or 0.5%) (Lowney et al. 2007)

Background Intakes from other sources (as % of TRV):

BI_O = 50% for oral and dermal

BI_i = 0% for inhalation

Uptake into home-grown produce addressed for HIL A.

1.5 Calculated HILs

The following comments relate to the derivation of an HIL A (the most sensitive exposure scenario) for arsenic:

- Using the proposed oral TRV, and the exposure pathways/assumptions presented in this document, with 100% bioavailability, HIL A = 130 mg/kg. Given the uncertainties discussed above in relation to the identification of a relevant TRV, and uncertainties associated with the calculation of the HIL, the calculated value is considered to be essentially no different from the previous HIL of 100 mg/kg.
- Using the proposed oral TRV, and the exposure pathways/assumptions presented in this document, with 70% bioavailability, HIL A = 180 mg/kg. Given the uncertainties discussed above in relation to the identification of a relevant TRV, and uncertainties associated with the calculation of the HIL, the calculated value is considered to be essentially no different from the previous HIL of 100 mg/kg.
- Using the proposed oral TRV, and the exposure pathways/assumptions presented in this document, with 25% bioavailability, HIL A = 380 mg/kg.
- With consideration of the uncertainties noted, it is not considered appropriate to modify the existing HIL A of 100 mg/kg (where arsenic bioaccessibility is within the range of 70–100%).

On the basis of the above the following HILs have been derived for arsenic (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

HIL Scenario	HIL* (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	100	86	9	5	<1
Residential B	500	81	--	19	<1
Recreational C	300	90	--	10	<0.1
Commercial D	3000	72	--	28	<1

-- Pathway not included in derivation of HIL

* Value derived is based on consideration of the range of oral TRVs derived by JECFA (WHO 2011a) and EFSA (2010) and relevance of the key studies and derived ranges to the Australian population. The HILs are based on 70–100% bioavailability—a more site specific bioavailability (such as 25%) may be considered where sufficiently justified.

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2 Beryllium

2.1 General

Several comprehensive reviews of beryllium in the environment and its toxicity to humans are available and should be consulted for more detailed information (ATSDR 2002; WHO 1993; WHO 2001). The following provides a summary of the key aspects of beryllium that are relevant to the derivation of a soil HIL.

Beryllium is a steel grey, brittle metal that is not found as the free metal in nature. There are approximately 45 mineralised forms of beryllium. The most important beryllium minerals in the world are beryl ($3BeOAl_2O_36SiO_2$) and bertrandite ($Be_4Si_2O_7(OH)_2$) (ATSDR 2002). Beryllium is the lightest of all solids and chemically stable substances, with an unusually high melting point, specific heat, heat of fusion, and strength-to-weight ratio. Due to its high affinity for oxygen, a very stable surface film of beryllium oxide (BeO) is formed on the surface of metallic beryllium and beryllium alloys, providing high resistance to corrosion, water and cold oxidising acids (WHO 1993).

Occupational exposure to beryllium has been associated with acute and chronic lung diseases. The acute disease is normally associated with inhalation exposures to high levels of soluble beryllium salts (e.g. sulphate, chloride) and BeO, and may lead to chronic disease. The chronic disease is associated with long-term inhalation exposures to dust particles containing beryllium, has an immunological component and a latent period, which varies depending on the beryllium species. Dermatological effects may also occur on skin contact (Di Marco & Buckett 1996).

2.2 Previous HIL

The derivation of the previous HIL (HIL A = 20 mg/kg) for beryllium is presented by Di Marco & Buckett (1996). In summary, the HIL was derived on the basis of the following:

- Intakes of beryllium from other sources were estimated with dietary intakes considered most significant for the general population. Based on the information available from Canada (considered more relevant than US data), background intakes of beryllium were assumed to be 0.65 µg/kg/day for preschoolers and 0.17 µg/kg/day for adults.
- A provisional tolerable daily intake (PTDI) of 1 µg/kg/week based on the US EPA RfD of 5 µg/kg/day (derived from a NOEL of 0.54 mg/kg/day and an uncertainty factor of 100), however an additional uncertainty factor of 5 was considered more appropriate to address limitations with the critical study used (no other studies were available)
- Ingestion of both soil and dust by an infant (2.5 years) has been considered assuming 1% is bioavailable.
- Dermal absorption has been considered to be low with a conservative assumption of 0.1% considered.
- Inhalation of beryllium in dust has been considered outdoors and indoors, assuming a dust concentration of 100 µg/m^3 and outdoor dust contributes 75% to indoor dust.
- Soil criteria derived on the basis of inhalation cancer risk values available from US EPA were calculated to be higher than the HIL of 20 mg/kg for infants (adopting a risk level of 10^{-5}).

2.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed, as noted below.

2.3.1 Oral Bioavailability

While oral bioavailability has been considered in the previous HIL, insufficient data is available to adequately define the bioavailability of beryllium in the range of contaminated sites that may need to be considered in Australia. On this basis, a default approach of assuming 100% oral bioavailability has been adopted in the derivation of an HIL. It is noted that a site-specific assessment of bioavailability can be undertaken where required.

2.3.2 Dermal absorption

In humans and animals sensitised to beryllium, contact with beryllium and its soluble and insoluble compounds can cause dermatitis and skin granulomas. In general, the more soluble the compound the greater the sensitising potential. Dermal effects usually occur on abraded skin. Dermal absorption of beryllium is assumed to be poor and would not likely cause further systemic effects. While it is noted that absorption through damaged/injured skin is expected to be higher, review of dermal absorption of beryllium (Deubner et al. 2001) noted that absorption through intact skin is considered negligible (<<1%). Hence the assumption of 0.1% dermal absorption considered in the previous HIL is considered appropriate. The value is consistent with the default presented by RAIS (2010).

It is noted that US EPA (2004) has recommended the use of a gastrointestinal absorption factor (GAF) of 0.7%, based on consideration of the rat study (with water) used in the derivation of the oral RfD. The GAF is used to modify the oral toxicity reference value to a dermal value in accordance with the US EPA (2004) guidance provided.

2.3.3 Inhalation of Dust

Beryllium is not volatile and inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, potential inhalation exposures associated with dust have been considered in the HIL derived.

2.3.4 Plant Uptake

Limited data is available on the potential for the uptake of beryllium into plants, in particular, edible fruit and vegetable crops. Review by ATSDR (2002) notes that in plants the uptake of beryllium appears to be restricted to the root system, with no significant translocation of beryllium to above-ground parts of the plant. Soluble forms of beryllium must be present for plant uptake to occur. In solution in the pH range of 6–8, beryllium is most commonly transformed to beryllium hydroxide, which has a very low solubility. Hence the potential for significant plant uptake is considered to be low.

Based on the above, the uptake of beryllium into root crops only has been considered in the derivation of the HIL. Limited plant uptake data is available, hence the value presented by RAIS (2010) of 0.0025 mg/kg fresh produce per mg/kg soil has been considered.

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce (also included in background intakes). To address this in the derivation of HIL A, half the intake estimated to be derived from home-grown produce is assumed to be already accounted for in the total background intake (noted below).

2.3.5 Intakes from Other Sources – Background

Limited data is available from Australia with respect to levels of beryllium in drinking water or food. ATSDR (2002) report concentrations of beryllium in Australian rainwater tanks between 0.05 and 0.08 µg/L. Beryllium is not routinely tested in drinking water supplies in Australia. Beryllium was not

detected in any air sample collected in New South Wales (DEC 2003). Hence intakes that may be derived from ambient air are considered negligible.

The ATSDR (2002) and WHO (2001) reviews have not provided an update of potential background exposures from that considered in derivation of the current HIL (Di Marco & Buckett 1996). There is no data available to suggest that the background intakes considered in the derivation of the current HIL are an underestimate and hence these intakes are recommended to be retained in the derivation of revised HILs. For pre-schoolers a background intake of 0.65 µg/kg/day has been adopted, which constitutes approximately 30% of the recommended TRV.

2.4 Identification of Toxicity Reference Values

2.4.1 Classification

IARC (2012) has classified beryllium and beryllium compounds as a Group 1 agent, which implies that it is considered carcinogenic to humans, though it is noted that the evidence of carcinogenicity applies to the inhalation route only.

2.4.2 Review of Available Values/Information

Available data with respect to carcinogenicity was reviewed by WHO (2001). The review provided is no different from that summarised by Di Marco & Buckett (1996). Beryllium and compounds are considered carcinogenic to humans with the most important end point identified as lung cancer following inhalation exposures. WHO (2001) noted that the genotoxicity data for beryllium is mixed and it appears to be somewhat compound-dependent (NRC 2007). Although the bacterial assays have been largely negative, the mammalian test systems exposed to beryllium compounds have shown evidence of mutations, chromosomal aberrations, and cell transformations. ATSDR (2002) has considered beryllium compounds to be weakly genotoxic.

The mode of action for beryllium carcinogenicity is not well understood and the relevance of a non-threshold approach to the quantification of inhalation exposures is not clear. The following is noted by Di Marco & Buckett (1996) and is considered to remain relevant for the assessment of inhalation exposures:
'Whilst lung cancer is the most important end point, it is unlikely to be a concern for beryllium in soil. Acute beryllium lung disease appears to occur prior to the development of lung cancer and may play a role in its induction. In addition, this disease has only been reported after exposure to high levels of specific beryllium compounds in the workplace; conditions which are unlikely to be achieved on exposures to dust generated from beryllium contaminated soil.'

This is supported by a more recent review by Hollins et al. (2009) where it was concluded that 'the increase in potential risk of lung cancer was observed among those exposed to very high levels of beryllium and that beryllium's carcinogenic potential in humans at exposure levels that exist in modern industrial settings should be considered either inadequate or marginally suggestive'.

Further review of carcinogenic risk associated with inhalation exposures in the current HIL by Di Marco & Buckett (1996) indicated that a soil concentration that is protective of carcinogenic risk via inhalation at a level of 1 in 100,000 (more than 1000 mg/kg) was well in excess of the derived HIL (20 mg/kg). This is consistent with calculations that would be conducted using current exposure assumptions.

On the basis of the above it is recommended that a threshold approach be adopted for the derivation of an HIL for beryllium in soil. The following are available from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011)	TDI = 0.002 mg/kg/day	No quantitative evaluation is available in the previous ADWG (NHMRC 2004) due to lack of suitable oral data. TDI presented in ADWG (NHMRC 2011) and is derived from the WHO (2001) evaluation as noted below.
International		
WHO (2001)	TDI = 0.002 mg/kg/day TC = 0.02 µg/m^3	TDI derived on the same basis as the RfD derived by the US EPA (noted below). TC based on the development of chronic beryllium disease in exposed workers, consistent with the study used by the US EPA (noted below). Note that beryllium is included in the rolling revisions to the DWG. The current guidelines (WHO 2011) adopt the same TDI as noted in the WHO (2001) review.
ATSDR (2002)	Oral MRL = 0.002 mg/kg/day	Chronic oral MRL derived on the same basis as the US EPA (IRIS, 2010) evaluation below.
US EPA (IRIS 2012)	RfD = 0.002 mg/kg/day RfC = 0.02 µg/m^3	RfD based on a BMD of 0.46 mg/kg/day associated with a 10% increase in inflammatory lesions in the small intestines of male and female dogs (1976 study) and a 300-fold uncertainty factor. RfC based on a LOAEL (HEC) of 0.0002 mg/kg/day associated with lung effects in a human study and a 10-fold uncertainty factor.

The available international sources reference the same key studies and have derived the same toxicity reference values.
No dermal-specific studies or data are available. For the presence of beryllium in soil it is considered appropriate to consider use of the available TDI for all oral and dermal pathways of exposure (taking into account the relevant gastrointestinal absorption factor noted above).

2.4.3 Recommendation

On the basis of the discussion above, the following toxicity reference values (TRVs) have been adopted for beryllium in the derivation of HILs:

Recommendation for Beryllium

Oral TRV (TRV_O) = 0.002 mg/kg/day (WHO 2001)

Dermal TRV (TRV_D) = 0.000014 mg/kg/day (adjusted from the oral TRV on the basis of a GAF of 0.007 (US EPA 2004)

Inhalation TRV (TRV_I) = 0.00002 mg/m^3 (WHO 2001)

Dermal absorption factor (DAF) = 0.001 (or 0.1%) (assumed relevant, also available from RAIS (2010))

Background Intakes from other sources (as % of TRV):

BI_O = 30% for oral and dermal

BIi = 0% for inhalation.

Uptake into home-grown produce addressed for HIL A.

2.5 Calculated HILs

On the basis of the above, the following HILs have been derived for beryllium (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	60	30	12	56	2
Residential B	90	11	--	86	3
Recreational C	90	20	--	79	1
Commercial D	500	8	--	88	4

-- Pathway not included in derivation of HIL

2.6 References

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US EPA (IRIS 2012). Data and information available from the *Integrated Risk Information System*, an online database, available from http://www.epa.gov/iris/.

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WHO 2001. *Beryllium and Beryllium Compounds*, Concise International Chemicals Assessment Document 32, World Health Organization, Geneva.

WHO 2011, *Guidelines for drinking-water quality, 4th edition*, World Health Organization, Geneva, available from http://www.who.int/water_sanitation_health/dwq/chemicals/en/index.html.

3 Boron

3.1 General

Several comprehensive reviews of boron in the environment and its toxicity to humans are available and should be consulted for more detailed information not presented in this summary (ATSDR 2010; WHO 1998; US EPA 2004b). The following provides a summary of the key aspects of boron that are relevant to the derivation of a soil HIL.

Boron is never found in its elemental form in nature. The most common boron-containing ores are alkali and alkaline earth borates, including borax ($Na_4B_4O_2.10H_2O$), kernite ($Na_2B_4O_7.4H_2O$), colemanite ($Ca_2B_6O_{11}.5H_2O$), and ulexite ($NaCaB_5O_9.8H_2O$), and borosilicate minerals. Common boron-containing compounds used in commerce also include borax pentahydrate, boric acid and boron oxide (ATSDR 2010).

Boron and boron compounds are used in the production of products such as fibreglass, soaps, detergents, enamels, frits, glazes, fertilisers, herbicides and fire retardants. They are also used in industries such as metallurgy, chemical synthesis and in nuclear applications (ATSDR 2010).

The toxicological database is largest for boric acid and borax and most of the toxicological information for inorganic borates in animals and humans is derived from studies on boric acid and borax (Mangas 1998).

Boron is an essential micronutrient for most plants and there is evidence that it is also essential for animals, including humans (ATSDR 2010).

3.2 Previous HIL

The derivation of the previous HIL (HIL A = 3000 mg/kg) for boron is presented by Mangas (1998). In summary, the HIL was derived on the basis of the following:

- Intakes of boron from other sources were estimated with dietary intakes considered most significant for the general population. Background intakes from dietary exposure (based on US data) and soil (background) were estimated to be 3.23 mg/day for an adult and 1.62 mg/day for infants (half the adult intake).
- A provisional tolerable daily intake (PTDI) of 14 µg/day was derived for boron based on a NOAEL of 9.6 mg/kg, body weight of 70kg and an uncertainty factor of 48.
- Ingestion of both soil and dust has been considered, assuming 100% is bioavailable and is absorbed.
- Dermal absorption has been considered to be low, with a conservative assumption of 1% adopted.
- Inhalation of boron in dust has been considered both outdoors and indoors, with 10% bioavailability of inhaled boron assumed and the amount of boron in indoor dust assumed to be 75% of that outdoors.

3.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed as noted below.

3.3.1 Oral Bioavailability

While bioavailability (inhalation only) has been considered in the previous HIL, insufficient data is available to adequately define the bioavailability of boron. On this basis a default approach of assuming 100% oral (and inhalation) bioavailability has been adopted in the derivation of an HIL. It is noted that a site-specific assessment of bioavailability can be undertaken where required.

3.3.2 Dermal absorption

Dermal absorption of boron is considered to be low. While limited data is available, reviews by WHO (1998), ATSDR (2010) and US EPA (2004b) suggest the boron is not absorbed across intact skin. Review by MfE (2011) has also noted that dermal absorption is considered negligible and has not considered this pathway in the derivation of a soil guideline. It is noted that review of the derived HIL (based on 1% dermal absorption) contributes less than 5% of the HIL, and hence it is considered appropriate that, based on the available data, dermal absorption is not considered a significant pathway in the derivation of a soil HIL. This pathway has not been considered further.

3.3.3 Inhalation of Dust

Boron is not volatile and hence inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, inhalation exposures have been considered in the HIL derived.

3.3.4 Plant Uptake

Review of plant uptake of boron by MfE (2011) has indicated that 'it has not been possible to develop bioconcentration factors for boron. Reviewing the literature shows that boron uptake into plants is highly variable between species with no relationship with soil concentration or other soil parameters. Boron is an essential element for plant growth, but what may be optimal boron for one species may be toxic or insufficient for other species'. 'Determining the significance of plant uptake of boron to human exposure is difficult, given the wide-ranging and overlapping concentrations that determine boron essentiality and toxicity in various species. Nonetheless, it appears that 300 mg/kg is a reasonable upper limit of non-toxic plant boron concentrations and thus can be used as the reasonable maximum amount of boron likely to be taken up in home-grown vegetables. Beyond that point vegetables are unlikely to be harvestable.'

The approach adopted by MfE (2011) in the derivation of a soil guideline for boron was to consider potential intakes associated with consumption of home-grown produce in soil concentrations that are not phytotoxic (300 mg/kg), as part of the overall intake from other sources. To obtain the additional background intake, a child's produce consumption (0.048 kg DW[1]/day) was multiplied by 300 mg/kg and divided by the child body weight of 15.5 kg to obtain the maximum additional background daily intake for 100 % of produce being home-grown. For the consumption of 10% home-grown produce, this results in an additional intake of 0.09 mg/kg/day being considered.

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce (also included in background intakes). To address this in the derivation of HIL A, half the intake estimated to be derived from home-grown produce is assumed to be already accounted for in the total background intake (noted below). Hence background intakes that may be derived from all sources, including home-grown produce, are estimated to be 0.17 mg/kg/day.

[1] It has been assumed that fruit and vegetable crops contain at least 80% moisture. This value has been used to convert wet weight consumption rates into dry weight consumption rates.

3.3.5 Intakes from Other Sources – Background

No data is available on intakes of boron from sources other than soil in Australia. Hence the assessment of potential intakes from these sources has considered available international data.

Reviews of boron (WHO 1998 and ATSDR 2010) suggest that mean intakes of boron from the diet are approximately 1.2 mg/day for adults (and 0.85 mg/day for children), with intakes from consumer products approximately 0.1 mg/day (WHO 1998) and the contribution from air negligible. The total background intake presented by WHO (1998) is 1.9 mg/day. If this intake were assumed relevant for young children, it would comprise 0.13 mg/kg/day for young children. This is slightly higher than that estimated by MfE (2011), where intakes were estimated to be 0.08 mg/kg/day for young children (based on the same databut intakes from water were considered to be lower, based on the available water quality data from New Zealand). The higher value of 0.13 mg/kg/day has been adopted in the derivation of a soil HIL.

3.4 Identification of Toxicity Reference Values

3.4.1 Classification

The International Agency for Research on Cancer (IARC) has not evaluated boron due to inadequate data.

3.4.2 Review of Available Values/Information

Available studies on genotoxicity (US EPA 2004b and WHO 2009) were negative. This is consistent with the review presented by Mangas (1998). On the basis of the available information, it is recommended that a threshold approach be adopted for the derivation of an HIL for boron in soil. The following are available from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011)	TDI = 0.16 mg/kg/day	The ADWG (NHMRC 2011) derived a guideline for boron in drinking water on the basis of a TDI of 0.16 mg/kg/day, based on a NOAEL from a developmental rat study (Price et al. 1996) and an uncertainty factor of 60.
International		
WHO (1998)	TDI = 0.4 mg/kg/day	The WHO (1998) review derived a TDI of 0.4 mg/kg/day based on the same study considered in the ADWG (NHMRC 2011) and a different uncertainty factor of 25.
WHO DWG (2009)	TDI = 0.17 mg/kg/day	TDI adopted is consistent with that adopted in the ADWG (NHMRC 2011) and is based on a benchmark dose (BMD) derived from relevant developmental studies of 10.3 mg/kg/day and uncertainty factor of 60. The principal study (noted to be similar to Price et al. 1996) and evaluation is consistent with that presented in the US EPA review (note the US EPA rounded the TDI in its evaluation).
ATSDR (2010)	No evaluation available	
US EPA (IRIS 2012)	RfD = 0.2 mg/kg/day	RfD (last reviewed in 2004) based on a BMD of 10.3 mg/kg/day associated with developmental effects in rats and an uncertainty factor of 66.

The ADI currently considered in the ADWG (NHMRC 2011) and by US EPA (2004b) and WHO (2011) are essentially the same value (from studies that have resulted in consistent evaluations), namely 0.2 mg/kg/day. This threshold value is therefore recommended for derivation of the HIL.

No inhalation specific studies or data are available. For the presence of boron in soil it is considered appropriate to consider use of the available TDI for all pathways of exposure.

3.4.3 Recommendation

On the basis of the discussion above, the following toxicity reference values (TRVs) have been adopted for boron in the derivation of HILs:

Recommendation for Boron

Oral TRV (TRV_O) = 0.2 mg/kg/day (NHMRC 2011 and US EPA 2004b) for all routes of exposure

Inhalation TRV (TRV_I) = 0.7 mg/m^3 (based on the TRV_O assuming body weight of 70 kg and inhalation of 20m^3/day)

Dermal absorption factor (DAF) = negligible (0%)

Background intakes for the general population = 0.13 mg/kg/day = 65% of the oral TRV (adopted for HIL B, C and D)

Background intakes, including plant uptake = 0.17 mg/kg/day = 85% of oral TRV (adopted for HIL A)

Background intake assumed relevant for all pathways of exposure (BI_O and BIi)

3.5 Calculated HILs

On the basis of the above, the following HILs have been derived for boron (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	4500	100	Included in background	--	<1
Residential B	40 000	100	--	--	<1
Recreational C	20 000	100	--	--	<1
Commercial D	300 000	100	--	--	<1

-- Pathway not included in derivation of HIL

3.6 References

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WHO 1998, *Environmental Health Criteria 204 – Boron*, World Health Organization, Geneva.

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WHO 2011, *Guidelines for drinking-water quality, 4th edition*, World Health Organization, Geneva. Available from http://www.who.int/water_sanitation_health/dwq/chemicals/en/index.html.

4 Cadmium

4.1 General

Several comprehensive reviews of cadmium in the environment and its toxicity to humans are available and should be consulted for more detailed information (ATSDR 2008; EA 2009a; WHO 2004). The following provides a summary of the key aspects of cadmium that are relevant to the derivation of a soil HIL.

Pure cadmium is a silver-white lustrous and malleable metal, is a solid at room temperature, is insoluble in water, and has a relatively low melting point and vapour pressure. The most common oxidation state of cadmium is 2+. Naturally occurring cadmium is commonly found in the Earth's crust associated with zinc, lead and copper ores. Whereas pure cadmium and cadmium oxides are insoluble in water, some cadmium salts including cadmium chloride, cadmium nitrate, cadmium sulfate and cadmium sulfide are soluble in water (ATSDR 2008).

Cadmium is found naturally in mineral forms (primarily sulfide minerals) in association with zinc ores, zinc-bearing lead ores, and complex copper-lead-zinc ores. Due to its corrosion-resistant properties, a wide range of commercial and industrial applications have been developed involving cadmium-containing compounds and alloys that are used in a wide range of materials and products including batteries, pigments, metal coatings and platings, stabilisers for plastics, nonferrous alloys and solar cell devices (ATSDR 2008).

Cadmium is toxic to a wide range of organs and tissues, and a variety of toxicological end points (reproductive toxicity, neurotoxicity, carcinogenicity) have been observed in experimental animals and subsequently investigated in human populations (MfE 2011).

4.2 Previous HIL

The derivation of the previous HIL (HIL A = 20 mg/kg) for cadmium is presented by Langley (1991). In summary, the HIL was derived on the basis of the following:

- Intakes of cadmium from other sources were estimated with dietary intakes considered most significant for the general population. Background intakes were considered in the derivation of the current HIL (Langley 1991), where intakes from other sources were estimated to be up to 80% of the adopted PTWI.
- A provisional tolerable weekly intake (PTWI) of 7 µg/kg/week, referenced from WHO, was adopted as the toxicity reference value.
- Ingestion of both soil and dust has been considered assuming 100% is bioavailable and is absorbed.
- Dermal absorption has been considered to be low with a conservative assumption of 0.1% assumed.
- Inhalation of cadmium in dust has been considered both outdoors and indoors.
- The total absorption of cadmium, based on 20 mg/kg in soil, for a young child was calculated to be 0.32 µg/day, approximately 28% of the adopted toxicity reference value. This intake was considered to provide a significant buffer below the tolerable daily absorption.

4.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed, as noted below.

4.3.1 Oral Bioavailability

While bioavailability (inhalation only) has been considered in the previous HIL, insufficient data is available to adequately define the bioavailability of cadmium. On this basis, a default approach of assuming 100% oral (and inhalation) bioavailability has been adopted in the derivation of an HIL. It is noted that a site-specific assessment of bioavailability can be undertaken where required.

4.3.2 Dermal absorption

Review of dermal absorption by MfE (2011) has noted the following: 'The US EPA (2004) recommends a dermal absorption factor of 0.001 (0.1%) for cadmium, based on Wester et al. (1992). These authors determined the in vitro percutaneous absorption of cadmium as the chloride salt from soil and water, using human skin. Cadmium from soil penetrated the skin at 0.06% and 0.13% of the applied dose, with 0.01% and 0.07% respectively absorbed into the receptor fluid after 16 hours of exposure. Taking the geometric mean of the summed amounts bound to skin and that in the receptor fluid yields an average absorption factor of 0.0012 or 0.12%, similar to that recommended by the US EPA (2004). This low rate of absorption indicates that dermal exposure is a negligible route of exposure, and could be ignored in the derivation of soil guideline values for contaminated land in New Zealand, as has been done by other jurisdictions.'

On the basis of the above, dermal absorption has not been considered in the derivation of soil HILs.

4.3.3 Inhalation of Dust

Cadmium is not volatile and inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, potential inhalation exposures associated with dust have been considered in the HIL derived.

4.3.4 Plant Uptake

In the review of cadmium presented by Langley (1991), a study by Tiller et al. (1976) was cited that involved evaluation of the uptake of cadmium into home-grown fruit and vegetables from soil in Port Pirie. The study showed concentrations of cadmium that were higher than those reported in produce samples from Adelaide shops. Hence cadmium uptake by edible fruit and vegetable crops is expected to be sufficiently significant to warrant inclusion in the derivation of soil HILs.

Further review of plant uptake of cadmium is presented by the EA (EA 2009b). This review considered studies that are based on the uptake of cadmium into green vegetables, root vegetables, tuber vegetables, herbaceous fruit, shrub fruit and tree fruit. The review provides recommendations on soil-to-plant uptake factors that are relevant for these types of produce. The recommendations from this review have been considered in the derivation of a residential A HIL and are summarised below for the range of crops considered:

Produce Group	Plant Uptake Factors (mg/kg produce fresh weight per mg/kg soil) (EA, 2009b)
Green vegetables	0.052
Root vegetables	0.029
Tuber vegetables	0.031
Tree fruit	0.0014

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce (also included in background intakes). To address this in the derivation of HIL A, half the intake estimated to be derived from home-grown produce is assumed to be already accounted for in the total background intake (noted below).

4.3.5 Intakes from Other Sources – Background

Reviews of cadmium (WHO 2004) included food intakes provided by FSANZ (consistent with current data from FSANZ (2003)) of 0.1 µg/kg/day. Intakes for a young child aged 2–5 years from the 23rd Australian Food Survey (FSANZ 2011) ranged from a mean of 0.32 µg/kg/day to a 90th percentile of 0.44 µg/kg/day. While the WHO (2004) review notes that intakes of cadmium from food can exceed the adopted toxicity reference value, data from FSANZ (2011) does not suggest this is the case.

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce. The amount of double counting cannot be easily determined and hence intakes from food sources have not been further reduced to address this issue, though the use of the data from FSANZ is considered conservative for HIL A. Based on the available data from FSANZ (2011), intakes from food comprise up to 60% of the recommended oral TRV.

Cadmium was detected in air samples collected from urban and rural areas in NSW (DEC 2003). The average concentration reported was 0.17 ng/m^3, ranging from 0.3 to 1 ng/m^3. These concentrations constitute <5–20% of the recommended inhalation TRV in air (also considered as an international target in the DEC document). Background levels for cadmium in air can be conservatively assumed to comprise 20% of the recommended inhalation TRV.

4.4 Identification of Toxicity Reference Values

4.4.1 Classification

IARC (2012) has classified cadmium and cadmium compounds as a Group 1 agent (i.e. carcinogenic to humans) based on additional evidence of carcinogenicity in humans and animals. It is noted that there is limited evidence of carcinogenicity in experimental animals following exposure to cadmium metal.

4.4.2 Review of Available Values/Information

The following has been summarised from the review of cadmium presented by MfE (2011):

- Cadmium is primarily toxic to the kidney, especially to the proximal tubular cells where it accumulates over time and may cause renal dysfunction. Loss of calcium from the bone and increased urinary excretion of calcium are also associated with chronic cadmium exposure. Recent studies have reported the potential for endocrine disruption in humans as a result of exposure to cadmium. Notably, depending on the dosage, cadmium exposure may either enhance or inhibit the biosynthesis of progesterone, a hormone linked to both normal ovarian cyclicity and maintenance of pregnancy. Exposure to cadmium during human pregnancy has also been linked to decreased birth weight and premature birth.
- While cadmium has been classified as a known human carcinogen (based on inhalation data from occupational inhalation data), there is no evidence of carcinogenicity via the oral route of exposure.
- There is conflicting data on the genotoxicity of cadmium. Some studies indicate that chromosomal aberrations occur as a result of oral or inhalation exposures in humans,

while others do not (ATSDR 2008). Studies in prokaryotic organisms largely indicate that cadmium is weakly mutagenic. In animal studies, genetic damage has been reported, including DNA strand breaks, chromosomal damage, mutations and cell transformations (ATSDR 2008). IARC (2012) concluded that several mechanisms have been identified that potentially contribute to cadmium-induced carcinogenicity. Direct binding to DNA appears to be of minor importance and mutagenic responses are weak. Based on the weight of evidence, MfE considered there to be weak evidence for the genotoxicity of cadmium.

On the basis of the available information TRVs relevant for oral (and dermal) intakes and inhalation intakes have been considered separately.

4.4.3 Oral (and Dermal) Intakes

Insufficient data is available to assess carcinogenicity via oral intakes and therefore the oral TRV has been based on a threshold approach with renal tubular dysfunction considered to be the most sensitive end point. The following are available for oral intakes from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG(NHMRC 2011)	TDI = 0.0007 mg/kg/day	The threshold oral value available from the ADWG (NHMRC 2011) of 0.0007 mg/kg/day is derived from a WHO/JECFA evaluation in 2000. The JECFA summary provided in 2004 noted that a PTWI of 0.007 mg/kg was established in 1988. This differs from that referenced (not cited) and considered in the ADWG. It is noted however that WHO may have rounded the TDI adapted as both values are similar.
International		
JECFA (WHO 2010)	PTMI = 0.025 mg/kg (equivalent to PTDI = 0.0008 mg/kg/day)	Review of cadmium by JECFA in 2010 withdrew the previous PTWI (noted below). The review considered more recent epidemiological studies where cadmium-related biomarkers were reported in urine following environmental exposures. They identified that in view of the long half-life of cadmium in the body, dietary intakes should be assessed over months and tolerable intakes assessed over a period of at least a month. Hence the committee established a PTMI of 0.025 mg/kg. While established over a month, use of the value in the methodology adopted for establishing HILs requires a daily value. Exposures assessed in the HILs are chronic and hence, while used as a daily value, it relates to long-term exposures to cadmium. The former JECFA (WHO 2005) review provided a PTWI of 0.007 mg/kg for cadmium in reviews available from 1972 to 2005. This is equivalent to an oral PTDI of 0.001 mg/kg/day. This is based on a review by JECFA where renal tubular dysfunction was identified as the critical health outcome with regard to the toxicity of cadmium. The PTWI is derived on the basis of not allowing

Source	Value	Basis/Comments
		cadmium levels in the kidney to exceed 50 mg/kg following exposure over 40–50 years. This PTDI is adopted by FSANZ (2003), the current WHO DWG (2011) and was used in the derivation of the current HIL (Langley 1991).
WHO (2011)	PTMI = 0.025 mg/kg (equivalent to PTDI = 0.0008 mg/kg/day)	Based on JECFA review noted above
RIVM (2001)	TDI = 0.0005 mg/kg/day	Value derived on the same basis as JECFA (WHO 2005), however RIVM has included an additional uncertainty factor of 2 to address potentially sensitive populations.
ATSDR (2008)	Oral MRL = 0.0001 mg/kg/day	The MRL is based on the $BMDL_{10}$ for low molecular weight proteinuria estimated from a meta-analysis of environmental exposure data (from ATSDR).
US EPA (IRIS 2012)	RfD = 0.0005 mg/kg/day for intakes from water and RfD = 0.001 mg/kg/day for intakes from food	Cadmium was last reviewed by the US EPA in 1994. The RfD for intakes from water were derived on the same basis as considered by ATSDR. RfD were derived for intakes from food on the basis of a NOAEL of 0.01 mg/kg/day from chronic human studies and an uncertainty factor of 10.

The available toxicity reference values or oral intakes are similar from the above sources with the PTMI established by JECFA (WHO 2010) providing the most current review of the available studies. This value has therefore been recommended for use as the oral TRV in the derivation of a soil HIL. This is consistent with that adopted in the ADWG (NHMRC 2011).

4.4.4 Inhalation Exposures

Inhalation of cadmium has been associated with carcinogenic effects (as well as others). Sufficient evidence is available (IARC 2012) to conclude that cadmium can produce lung cancers via inhalation. While cadmium is thought to be potentially genotoxic, the weight of evidence is not clear. In addition, epidemiology studies associated with lung cancer have confounding issues that limit useful interpretation (WHO 2000). It is noted that US EPA derived its inhalation unit risk on the basis of the same study that WHO dismissed due to confounding factors. In particular, a significant amount of the epidemiological data available also includes co-exposures with zinc and, in some cases, both zinc and lead.

With respect to the derivation of a soil HIL, cadmium is not volatile and hence inhalation exposures are only relevant to dust intakes. These are not likely to be significant for soil contamination and hence the consideration of carcinogenic effects (where the mode of action is not clear) using a non-threshold approach is not considered appropriate. It is appropriate to consider intakes on the basis of a threshold approach associated with the most significant end point. This is consistent with the approach noted by RIVM (2001) and considered by WHO (2000) and EA (2009a), where a threshold value for inhalation based on the protection of kidney toxicity (the most significant end point) has been considered. The value derived was then reviewed (based on the US cancer value) and considered to be adequately protective of lung cancer effects. On this basis WHO (2000) derived a guideline value of 0.005 µg/m^3 and EA (2009a) derived an inhalation TDI of 0.0014 µg/kg/day (which can be converted to a guideline value of 0.005 µg/m^3—the same as the WHO value).

4.4.5 Recommendation

On the basis of the discussion above, the following toxicity reference values (TRVs) have been adopted for cadmium in the derivation of HILs:

Recommendation for Cadmium

Oral TRV (TRV_O) = 0.0008 mg/kg/day (WHO 2010)

Dermal absorption factor (DAF) = negligible (0%)

Inhalation TRV (TRV_I) = 0.000005 mg/m^3 (WHO 2000)

Background intakes from other sources:

BI_O = 60% for oral intakes

BI_i = 20% for inhalation

4.5 Calculated HILs

On the basis of the above (and using the assumptions presented in this document), an HIL A has been derived at 15 mg/kg, essentially the same (with consideration of uncertainties and accuracy of HIL calculations) as the existing HIL of 20 mg/kg. There is no new data available that suggests that the existing HIL is not adequately protective and therefore, given the level of uncertainty in the calculation of any HIL, the existing HIL A has been retained. HILs B, C and D have been calculated on the basis of the parameters presented above.

On the basis of the above, the following HILs have been derived for cadmium (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	20	31	67%	--	2
Residential B	150	78	--	--	22
Recreational C	90	97	--	--	3
Commercial D	900	65	--	--	35

-- Pathway not included in derivation of HIL

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5 Chromium VI

5.1 General

Several comprehensive reviews of chromium VI (Cr VI) in the environment and its toxicity to humans are available and should be consulted for more detailed information not presented in this summary (ATSDR 1997 and 2008; DEFRA and EA 2002; APVMA 2005). The following provides a summary of the key aspects of Cr VI that are relevant to the derivation of a soil HIL.

Cr VI is less stable than the commonly occurring trivalent chromium but can be found naturally in the rare mineral crocoite. Cr VI typically exists as strongly oxidising species such as CrO_3 and CrO_4^{2-}. Some Cr VI compounds, such as chromic acid and the ammonium and alkali metal salts (e.g. sodium and potassium) of chromic acid are readily soluble in water. The Cr VI compounds are reduced to the trivalent form in the presence of oxidisable organic matter. However, in natural waters where there is a low concentration of reducing materials, Cr VI compounds are more stable (ATSDR 2008).

Chromium is of fundamental use in a wide range of industries, including the metallurgical (to produce stainless steels, alloy cast irons and nonferrous alloys), refractory (to produce linings used for high-temperature industrial furnaces) and chemical industries. In the chemical industry, Cr VI is used in pigments, metal finishing and in wood preservatives (ATSDR 2008).

The soil chemistry and toxicity of chromium is complex and hence the form of chromium in soil is of importance. In general, soil chromium is present as Cr III but the distribution of Cr III and Cr VI depends of factors such as Redox potential, pH, presence of oxidising or reducing compounds and formation of Cr complexes and salts.

Cr VI can readily pass through cell membranes and be absorbed by the body. Inside the body, Cr VI is rapidly reduced to Cr III. This reduction reaction can act as a detoxification process when it occurs at a distance from the target site for toxic or genotoxic effect. Similarly, if Cr VI is reduced to Cr III extracellularly, this form of the metal is not readily transported into cells and so toxicity is not observed (ATSDR 2008). However, if Cr VI is transported into cells, and close to the target site for toxic effect, under physiological conditions it can be reduced. This reduction reaction produces reactive intermediates, which can attack DNA, proteins, and membrane lipids, thereby disrupting cellular integrity and functions (ATSDR 2008).

5.2 Previous HIL

The derivation of the previous HIL (HIL A = 100 mg/kg) for Cr VI is presented by Soong & Emmett (1993). In summary, the HIL was derived on the basis of the following:

- Intakes of Cr VI from other sources were estimated with dietary intakes considered most significant for the general population. Intakes from air, water and food were estimated to be approximately 600 µg/day for a young child.
- A provisional tolerable daily intake (PTDI) of 5 µg/kg/week referenced from the US EPA was adopted as the toxicity reference value.
- Ingestion of both soil and dust has been considered assuming 100% is bioavailable and is absorbed.
- Dermal absorption and inhalation of dust were not specifically included in the derivation; however, consideration of a cancer potency factor for inhalation exposures was reviewed and noted to result in higher HIL.
- Skin hypersensitivity was also assessed, noting that the derived criteria ranging from 100–200 mg/kg was considered not to pose a risk to health.

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5.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed, as noted below.

5.3.1 Oral Bioavailability

Bioavailability has not been considered in the previous HIL, as insufficient data is available. On this basis, a default approach of assuming 100% oral (and inhalation) bioavailability has been adopted in the derivation of an HIL. It is noted that a site-specific assessment of bioavailability can be undertaken where required.

5.3.2 Dermal absorption

Review of dermal exposure to chromium by MfE (2011) has indicated the following:

- Dermal exposure to chromium has been demonstrated to produce irritant and allergic contact dermatitis (Guy et al. 1999; ATSDR 2008; Baars et al. 2001). Primary irritant dermatitis is related to the direct cytotoxic properties of chromium, while allergic contact dermatitis is an inflammatory response mediated by the immune system (ATSDR 2008).
- A number of studies have investigated the exposure level necessary to elicit a 10% response in sensitised individuals. These authors also suggest that a soil concentration of 500 mg Cr VI/kg would be protective of 90% of those individuals that are sensitised to chromium, and 99.84% of the general population, assuming that 10% of the Cr VI is bioavailable. Another study estimated that 0.1% or less of the Cr VI in chromite ore processing residue would leach out in the presence of human sweat (Horowitz & Finley 1993, cited in ATSDR 2008), suggesting that soil concentrations up to 50 000 mg/kg may not elicit an allergic response.
- As allergic contact dermatitis is an inflammatory response mediated by the immune system, this suggests that at least some chromium is absorbed through the skin. Studies that have investigated this response typically express dermal absorption as a function of skin surface area or flux, and thus are difficult to express as a percentage absorbed over time.
- It is recommended that the adverse effects arising from dermal exposure are considered separately from those arising from oral exposure and that allergic contact dermatitis is the main effect of interest, for which a soil guideline value could be established. However, it is likely that a soil guideline value protective of effects arising from oral exposure will also be protective against allergic contact dermatitis.

It is noted that based on the review presented by Soong & Emmett (1993), the HIL derived on the basis of oral intakes was shown to be adequately protective of allergic contact dermatitis. On the basis of this approach, dermal absorption has been considered negligible for Cr VI, consistent with the approach adopted by MfE (2011).

5.3.3 Inhalation of Dust

Cr VI is not volatile and inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, potential inhalation exposures associated with dust have been considered in the HIL derived.

5.3.4 Plant Uptake

Review of plant uptake by MfE (2011) has noted that concentrations of chromium in a form that can be taken up by plants is extremely low in most soils, consistent with the available data., The approach

adopted by MfE (2011) has been to adopt an arithmetic average of plant uptake values available from available reviews that relate to Cr VI and Cr in general (0.0324 mg/kg fresh produce per mg/kg soil). There is limited data available on concentrations of Cr VI in edible fruit and vegetable crops and uptake is expected to be limited. In addition ATSDR (2008) has noted that translocation of chromium within plants is poor. Hence the plant uptake value recommended by MfE (2011) has been considered for root and tuber crops only.

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce (also included in background intakes). To address this in the derivation of HIL A, half the intake estimated to be derived from home-grown produce is assumed to be already accounted for in the total background intake (noted below).

5.3.5 Intakes from Other Sources – Background

Intakes of total chromium were addressed in the FSANZ *22nd Australian Total Diet Survey* (2008). Estimated dietary intakes of chromium (total) for infants and 2–3-year-olds ranged from 14–26 µg/day, and for adults ranged from 14–53 µg/day for males 19–30 years. The average values reported are consistent with intakes reported from Germany and USA by APVMA (2005). Dietary intakes of total chromium may comprise a significant portion of the TDI for Cr VI. However it is noted that the most common form of chromium in fresh produce is Cr III. If Cr VI comprised 10% of the total Cr intake from the diet (based on data from bread analyses, Soares et al. 2010) then background intakes may comprise 0.09–0.17 µg/kg/day for young children aged 2–3 years. It is considered reasonable that an average intake be adopted given additional intakes from plant uptake are included in addition to these intakes, resulting in some doubling up of intakes from food sources. The average intake of Cr VI is estimated to be 0.13 µg/kg/day for 2–3 year olds, approximately 10% of the recommended oral TRV.

No data on Cr VI in air is available for Australia. Intakes of Cr VI from air may comprise up to 30% of total chromium (RIVM 2001), which has been reported up to 1.5 ng/m^3 (RIVM 2001) to 3 ng/m^3 (DEFRA & EA 2002). It is noted that concentrations of Cr VI in Europe and the UK are expected to be higher than in Australia due to the potential for long-range atmospheric transport from a greater proportion of industry in these general regions. Based on the recommended TRV for particulate-phase Cr VI, these conservative air concentrations comprise less than 1% of the TC and are assumed negligible.

5.4 Identification of Toxicity Reference Values

5.4.1 Classification

IARC (2012) has classified Cr VI compounds as Group 1 carcinogens—carcinogenic to humans based on: sufficient evidence in humans for the carcinogenicity of Cr VI compounds as encountered in the chromate production, chromate pigment production and chromium plating industries.

Chromium is classified by the US EPA as a Group A (known human carcinogen by the inhalation route), with carcinogenicity by the oral route of exposure noted to be Group D (not classified).

5.4.2 Review of Available Values/Information

Oral and inhalation exposures have been reviewed separately as follows.

5.4.2.1 Oral Intakes

There is limited data available regarding the carcinogenic potential of ingested Cr VI. Cr VI compounds appear to be genotoxic and some reviews (RIVM 2001) suggest that a non-threshold approach is relevant to all routes of exposure. Some drinking water studies (NTP 2008) are available

that show a statistically significant increase in tumours in rats and mice. However, there is currently no peer-reviewed data available to determine a quantitative non-threshold value for ingestion of Cr VI compounds (note a draft value has been recently published by OEHHA 2009). There is also some suggestion (De Flora et al. 1997; Jones 1990) that there may be a threshold for the carcinogenicity of Cr VI based on the hypothesis that it is a high-dose phenomenon, where the dose must exceed the extracellular capacity to reduce Cr VI to Cr III.

The following are available for oral intakes from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011)	No evaluation available	The ADWG (NHMRC 2011) does not specifically derive a guideline; however it references the WHO DWG assessment, where the basis for derivation is not clear. No quantitative toxicity values can be obtained from these sources.
International		
WHO (2011)	No evaluation available	Current guideline based on limit of detection as no adequate toxicity studies were available to provide the basis for a NOAEL. It is noted that chromium is included in the plan of work of rolling revisions to the DWG WHO (2011).
DEFRA & EA (2002)	TDI = 0.003 mg/kg/day	Adopted oral RfD from the US EPA.
RIVM (2001)	TDI = 0.005 mg/kg/day	RIVM has adopted a provisional threshold TDI of 0.005 mg/kg/day based on a 1-year drinking water study in rats as used in the derivation of the former and current US EPA RfD (with a small difference in the application of uncertainty factors).
ATSDR (2008)	MRL = 0.001 mg/kg/day	The chronic oral MRL is based on a $BMDL_{10}$ of 0.09 mg/kg/day for non-neoplastic lesions of the duodenum in a 2-year drinking water study in rats and mice (NTP 2008) and an uncertainty factor of 90. The study considered by ATSDR was not available when the other organisations (US EPA, etc.) reviewed Cr VI.
US EPA (IRIS 2012)	RfD = 0.003 mg/kg/day	The US EPA (available on IRIS, but last reviewed in 1998) derived an oral RfD of 0.003 mg/kg/day based on a NOAEL of 2.5 mg/kg/day from a 1-year drinking water study in rats and an uncertainty factor of 300 and modifying factor of 3 to address uncertainties in the study. The confidence level in the study, database and RfD is noted to be low.

It is recommended that the lower value derived by ATSDR (2008) be adopted for the assessment of oral exposures to Cr VI, as the assessment provides the most current comprehensive assessment of the available studies, including a more recent key study (NTP 2008) not available at the time of review by other organisations. The values adopted by RIVM and the UK are essentially the same, using the study considered by the US EPA (McKenzie et al. 1958) in the derivation of the RfD. It is noted that review by Health Canada (2004) considered the study used by US EPA was of poor quality, though it was used due to the lack of additional, better quality data.

5.4.2.2 Inhalation Exposures

Epidemiological studies have shown an association between exposure to Cr VI and lung cancer. These studies have involved chromate production, chromate pigment production and use, chromium plating, stainless steel welding, ferrochromium alloy production and leather tanning. Various Cr VI compounds have also been shown to be carcinogenic via inhalation in experimental animals. Cr VI has also been shown to be genotoxic. As noted by DEFRA & EA (2002), there is some suggestion that

chromium-induced cancer of the respiratory tract may be exclusively a high-dose phenomenon with a threshold relevant to low-dose exposures but quantitative data is lacking.

With respect to the derivation of a soil HIL, chromium is not volatile and hence inhalation exposures are only relevant to dust intakes. These are not likely to be significant for soil contamination and hence the consideration of carcinogenic effects using a non-threshold approach may not be appropriate. It is appropriate to consider intakes on the basis of a threshold approach associated with the most significant end-point. In addition inhalation exposures relating to soil contamination (dust) are expected to differ from the occupation studies from which the non-threshold criteria are derived (where inhalation of fine dust and chromic acid mists occurs). These issues were considered by ITER (1998) in the derivation of an RfC that is relevant for environmental exposures only, not to occupational exposures associated with mists and aerosols, and US EPA (IRIS 2012 and as outlined in US EPA 1998) in the derivation of an RfC.

The following are available for inhalation exposures for Cr VI particulates or dust from Level 1 Australian and International sources:

- No Australian guideline values are available for Cr VI.
- US EPA (available on IRIS) derived an inhalation RfC of 0.0001 mg/m^3 for Cr VI particulates based on lower respiratory effects in a subchronic rat study. The US EPA review of particulate exposures indicated chromium inhalation induced pneumocyte toxicity and suggested that inflammation is essential for the induction of most chromium inhalation effects and may influence the carcinogenicity of Cr(VI) compounds. The US EPA has also derived a separate RfC (lower) for exposure to chromic acid mists and dissolved Cr VI aerosols, which would be relevant for the assessment of an occupational environment.
- ITER (1998) derived an inhalation RfC of 0.0003 mg/m^3 for Cr VI particulates based on the same study as US EPA considered but the value derived was on the basis of an arithmetic average of benchmark concentrations for the pulmonary inflammation end point.

In addition the following are also available:

- WHO (2000) has derived a range of air guideline values based on an inhalation unit risk of 0.04 (μg/m^3)$^{-1}$ derived from the mean of a number of occupational studies. US EPA (IRIS 2012) also derived a unit risk of 0.012 (μg/m^3)$^{-1}$ derived from one occupational study (also considered by WHO).
- DEFRA & EA (2002) has derived an index dose of 0.001 μg/kg/day for Cr VI based on occupational inhalation studies based on a lung cancer end point, consideration of the WHO non-threshold approach and a target risk level of 10^{-4}.
- RIVM (2001) has adopted a cancer risk value of 0.0025 μg/m^3 based on occupational inhalation studies based on a lung cancer end point, consideration of the WHO non-threshold approach and a target risk level of 10^{-4}. It is noted that a 10^{-4} target risk level is used for inhalation guidelines by DEFRA & EA (2002) and RIVM (2001). The value results in guidelines that address background levels of Cr VI reported in ambient air, which range up to 30% of total chromium reported (up to 0.0015–0.0025 μg/m^3).
- ATSDR (2008) has derived a chronic inhalation MRL for Cr VI aerosols and mists, not considered relevant to the derivation of a soil HIL.

5.4.3 Recommendation

On the basis of the discussion above, the following toxicity reference values (TRVs) have been adopted for Cr VI in the derivation of HILs:

Recommendation for Chromium VI

Oral TRV (TRV_O) = 0.001 mg/kg/day (ATDSR 2008)

Dermal absorption factor (DAF) = negligible (0%). Note, however, that the approach adopted for derivation of HILs is considered adequately protective of allergic contact dermatitis effects.

Inhalation TRV (TRV_I) = 0.0001 mg/m^3 (US EPA, current)

Background intakes from other sources (as % of TRV):

BI_O = 10% for oral intakes

BIi = 0% for inhalation

Uptake in home-grown produce considered in derivation of HIL A.

5.5 Calculated HILs

On the basis of the above (and using the assumptions presented in this document) an HIL A has been derived at 80 mg/kg, essentially the same (with consideration of uncertainties and accuracy of HIL calculations) as the existing HIL of 100 mg/kg. There is no new data available that suggests that the existing HIL is not adequately protective and therefore, given the level of uncertainty in the calculation of any HIL (including consideration of other oral TRVs available that are less conservative than the TRV adopted), the existing HIL A has been retained. HILs B, C and D have been calculated on the basis of the parameters referenced above.

On the basis of the above, the following HILs have been derived for Cr VI (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	100	58	41	--	1
Residential B	500	97	--	--	3
Recreational C	300	99	--	--	1
Commercial D	3600	94	--	--	6

-- Pathway not included in derivation of HIL

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6 Cobalt

6.1 General

Several comprehensive reviews of cobalt in the environment and its toxicity to humans are available and should be consulted for more detailed information (ATSDR 2004; WHO 2006). The following provides a summary of the key aspects of cobalt that are relevant to the derivation of a soil HIL.

Cobalt (Co) is a silvery grey solid at room temperature. Naturally occurring cobalt is most commonly found in association with nickel, silver, lead, copper, and iron ores. Common cobalt minerals include linnaeite (Co_3S_4), carrolite ($CuCo_2S_4$), safflorite ($CoAs_2$), skutterudite ($CoAs_3$) and glaucodot (CoAsS). In the natural environment, cobalt may be found in two oxidation states, Co^{2+} and Co^{3+}, dependent upon Redox potential and pH of the environment (WHO 2006).

Cobalt comprises approximately 0.0025% of the weight of the Earth's crust, making it the 33rd most abundant element. Cobalt is a key constituent in several alloys including alnico, an alloy with powerful permanent magnetic properties that is used for high-speed, heavy-duty, high-temperature cutting tools. Cobalt has also been used as a colourant in glass, ceramics, and paints, is of catalytic use to the petrochemical and plastic industries, and is applied to soils as a fertiliser to increase plant yields or to increase the cobalt concentration in forage crops and prevent the symptoms of cobalt deficiency in livestock (ATSDR 2004; WHO 2006).

Cobalt is a dietary essential element as it is a key component of Vitamin B12 (ATSDR 2004). As such, adverse effects can occur as a result of deficiency as well as contamination. Without sufficient levels of dietary cobalt, red blood cell production may be severely inhibited, leading to anaemia, heart disease, reduced growth and the breakdown of both the nervous and the immune systems in humans (IARC 1991). Excess amounts of cobalt may also have harmful effects in humans. Inhaled cobalt primarily targets the respiratory tract. From the respiratory tract, cobalt particles may be absorbed into the blood via dissolution or transported to the gastrointestinal tract with mucous when swallowing. Gastrointestinal cobalt absorption rates are reported to vary greatly in humans, with some studies associating iron deficiencies with increased cobalt absorption rates (ATSDR 2004). Cobalt in the body partakes in reactions that generate oxidants and free radicals capable of deoxyribonucleic acid (DNA) damage and other deleterious effects (ATSDR 2004).

6.2 Previous HIL

The derivation of the previous HIL (HIL A = 100 mg/kg) for cobalt is presented by Buckett & Di Marco (1998). In summary, the HIL was derived on the basis of the following:

- Intakes of cobalt from other sources were estimated with dietary intakes considered most significant for the general population. Intakes calculated were based on limited data where total background intakes were estimated to be 1 µg/kg/day, up to 20% of the adopted upper PTDI of 5 µg/kg/day.
- A provisional tolerable daily intake (PTDI) range of 1–5 µg/kg/day was derived, based on a LOAEL of 0.5 mg/kg/day from human therapeutic studies and a combined safety factor of 100–500.
- Ingestion of both soil and dust has been considered assuming 50% is bioavailable.
- Dermal absorption has been considered to be negligible.
- Inhalation of cobalt in dust has been considered both outdoors and indoors.

6.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed, as noted below.

6.3.1 Oral Bioavailability

According to ATSDR (2004), the oral bioavailability of cobalt varies from 18–97% depending on dose, form of cobalt compound and nutritional status of the subjects.

While bioavailability has been considered in the previous HIL, insufficient data is available to adequately define the bioavailability of cobalt from soil. On this basis, a default approach of assuming 100% oral (and inhalation) bioavailability has been adopted in the derivation of an HIL. It is noted that a site-specific assessment of bioavailability can be undertaken where required.

6.3.2 Dermal absorption

In humans, inhalation and dermal exposure have been observed to result in sensitisation to cobalt (WHO 2006), hence it is reasonable to consider that dermal absorption may be more than negligible. Limited data is available regarding the dermal absorption of cobalt from soil and hence a default value of 0.1% has been considered. The default value of 0.1% is the lower end of the range considered relevant for metals as presented by US EPA (1995), which is higher than the dermally absorbed fraction of 0.0004 cited by Paustenbach (2000) for cobalt chloride (0.04%) in aqueous solution.

6.3.3 Inhalation of Dust

Cobalt is not volatile and hence inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, inhalation exposures have been considered in the HIL derived.

6.3.4 Plant Uptake

In the review of cobalt presented by Buckett & Di Marco (1998), it was noted that, based on data presented by IARC (1991), cobalt can be detected in plants. Whether cobalt is essential to plant growth has not been well established, however it appears that plant uptake may be somewhat significant and, as such, has been included in the derivation of HIL A. Review by WHO (2006) notes that, although plants may take up cobalt from the soil, the translocation of cobalt from the roots to other parts of the plant is not significant.

Based on the above, the uptake of cobalt into all crops has been considered in the derivation of the HIL A. Limited plant uptake data is available, and translocation into above ground crops is assumed to be negligible, hence the value presented by RAIS (2010) of 0.023 mg/kg fresh produce per mg/kg soil has been considered for root and tuber crops only.

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce (also included in background intakes). To address this in the derivation of HIL A, half the intake estimated to be derived from home-grown produce is assumed to be already accounted for in the total background intake (noted below).

6.3.5 Intakes from Other Sources – Background

The most significant source of intake of cobalt from sources other than contamination is dietary intake (WHO 2006). Cobalt intakes were considered in the *23rd Australian Total Diet Study* (FSANZ 2011), where intakes for a child aged 2–3 years ranged from a mean of 1 µg/kg/day to a 90th percentile of 1.3

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µg/kg/day. RIVM (2001) reviewed background intakes of cobalt, which were considered to be 0.3 µg/kg/day, consistent with intakes from food noted by WHO (2006, where a body weight of 70 kg was assumed). These intakes are between 20% and 70% of the recommended oral TRV. Given the lack of data in support of oral TRVs for cobalt, the only available value from RIVM has been adopted, the lower value of 20% in the derivation of soil HILs.

Cobalt was reported in ambient air data collected in NSW (DEC 2003) where concentrations in urban, regional and industrial areas assessed ranged from 0.1–0.39 ng/m^3. Intakes associated with these concentrations are negligible compared with intakes from food and the recommended inhalation TRV.

6.4 Identification of Toxicity Reference Values

6.4.1 Classification

The International Agency for Research on Cancer (IARC 1991) has classified cobalt metal, cobalt sulphate and other soluble cobalt (II) salts as Group 2B—possible human carcinogen. IARC provided further review in 2006 classifying cobalt sulphate and other soluble cobalt (II) salts as Group 2B, cobalt metal without tungsten carbide as Group 2B and cobalt metal with tungsten carbide as Group 2A (probable human carcinogen).

It is noted that US EPA has not evaluated cobalt with respect to classification of carcinogenicity.

6.4.2 Review of Available Values/Information

While data is limited, based on the weight of evidence cobalt is not (or is weakly) genotoxic (RIVM 2001: ATSDR 2004). However it is noted that some information suggests that some metallic cobalt species may be genotoxic, and this may need to be considered in occupational environments. On this basis, it is recommended that a threshold approach be adopted for the derivation of an HIL for cobalt in soil.

Few quantitative evaluations are available for cobalt, however the following are available from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011)	No evaluation available	
International		
WHO (2011)	No evaluation available	
WHO (2006)	TC = 0.0001 mg/m^3	WHO (2006) derived a TC in air of 0.0001 mg/m^3 based on a NOAEC from an occupational inhalation study with conversions to address exposures by the general population. WHO did not derive an oral threshold value, due to the lack of suitable data.
RIVM (2001)	TDI = 0.0014 mg/kg/day TC = 0.0005 mg/m^3	RIVM (2001) derived a TDI of 0.0014 mg/kg/day based on a LOAEL of 0.04 mg/kg/day associated with cardiomyopathy from oral exposures in workers and an uncertainty factor of 30. The TC is based on a LOAEC of 0.005 mg/m^3 for interstitial lung disease in workers and an uncertainty factor of 100.
ATSDR (2004)	Inhalation MRL = 0.0001 mg/m^3	Chronic inhalation MRL of 0.0001 mg/m^3 based on a NOAEL of 0.0013 mg/m^3 (adjusted) for decreased respiratory function in workers and an uncertainty factor of

Source	Value	Basis/Comments
		10. No chronic oral MRL is available from ATSDR (2004).
US EPA (IRIS 2012)	No evaluation available	

Note that the current HIL for cobalt was established on the basis of a derived PTDI that ranged from 1–5 µg/kg/day.

Only one oral value is available from RIVM (2001), which is recommended to be adopted for the derivation of a soil HIL. The available inhalation values are fairly consistent with the most recent detailed evaluations provided by WHO and ATSDR, which are recommended.

6.4.3 Recommendation

On the basis of the discussion above, the following toxicity reference values (TRVs) have been adopted for cobalt in the derivation of HILs:

Recommendation for Cobalt

Oral TRV (TRV_O) = 0.0014 mg/kg/day (RIVM 2001) for oral and dermal routes of exposure

Dermal absorption factor (DAF) = 0.001 (or 0.1%) (US EPA 1995)

Inhalation TRV (TRV_I) = 0.0001 mg/m^3 (WHO 2006; ATSDR 2004)

Background intakes from other sources (as % of TRV):

BI_O = 20% for oral intakes

BIi = 0% for inhalation

Uptake in home-grown produce considered in derivation of HIL A.

6.5 Calculated HILs

On the basis of the above, the following HILs have been derived for cobalt (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	100	65	33	1	1
Residential B	600	91	--	5	4
Recreational C	300	97	--	3	<1
Commercial D	4000	87	--	7	6

-- Pathway not included in derivation of HIL

6.6 References

ATSDR 2004, *Toxicological Profile for Cobalt*, Agency for Toxic Substances and Disease Registry, available from: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=373&tid=64.

Buckett, KJ & Di Marco, PN 1998, 'Derivation of Health Investigation Levels for Cobalt and Cobalt Compounds', presented in the proceedings of the *Fourth National Workshop on the Health Risk Assessment and Management of Contaminated Sites, Contaminated Sites Monograph Series, No. 7.*

DEC 2003, Ambient Air Quality Research Project (1996-2001), Internal working paper no. 4, Ambient concentrations of heavy metals in NSW, Department of Environment and conservation (NSW).

FSANZ 2011, *The 23rd Australian Total Diet Study*, Food Standards Australia and New Zealand.

IARC1991, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Metallic Cobalt Compounds (With or Without Tungsten Carbide), International Agency for Research on Cancer , World Health Organization, Lyons, France.

NHMRC 2011, National water quality management strategy. Australian drinking water guidelines, National Health and Medical Research Council, Australia.

Paustenbach, DJ 2000, 'The practice of exposure assessment: A state-of-the-art review', *J.Toxicol.Environ. Health. Part B, vol.* 3,pp. 179–291.

RAIS 2010, *Risk Assessment Information System*, website and database maintained by the Oak Ridge Operations Office, available from: http://rais.ornl.gov/.

RIVM 2001, *Re-evaluation of human-toxicological Maximum Permissible Risk levels*, National Institute of Public Health and the Environment, Bilthoven, Netherlands,. available from: http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

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US EPA (IRIS 2012), Data and information available from the *Integrated Risk Information System*, an online database, available from http://www.epa.gov/iris/

WHO 2006, *Cobalt and Inorganic Cobalt Compounds. Concise International Chemical Assessment Document 69*, available from: http://www.inchem.org/documents/cicads/cicads/cicad69.htm.

7 Copper

7.1 General

Several comprehensive reviews of copper in the environment and its toxicity to humans are available and should be consulted for more detailed information (ATSDR 2004; WHO 1998; NEHF 1997). The following provides a summary of the key aspects of copper that are relevant to the derivation of a soil HIL.

Copper (Cu) can occur naturally in its elemental form. Copper may also occur in the environment in various mineral forms including cuprite (Cu_2O), malachite ($CuCO_3 \cdot Cu(OH)_2$), azurite ($2CuCO_3 \cdot Cu(OH)_2$), chalcopyrite ($CuFeS_2$), chalcocite (Cu_2S), and bornite (Cu_5FeS_4). Metallic copper is a malleable and ductile solid that has strong electrical and thermal conducting properties and low corrosiveness. Copper is a transition metal and may occur as either the monovalent or divalent cation. Copper may exist in four oxidation states Cu(0), Cu(I), Cu(II) and Cu(III) (ATSDR 2004; WHO 1998).

Copper is a naturally occurring trace element of significant societal importance. It is not only an essential nutrient in virtually all forms of life, it is also an important constituent in numerous consumer and industrial materials, both as the free metal and as a component in metal alloys. Common copper metal alloys include brass, bronze and gun metal. Copper and copper alloys are used in plumbing, telecommunications, power utilities, air conditioning, automotives, business electronics and industrial valves. Copper sulfate and other copper compounds are important constituents in products having agricultural (namely fungicides) and other applications, including metal finishing, wood preservatives and water treatment (ATSDR 2004).

Copper is an essential element and, as such, adverse effects may occur as a result of deficiency as well as excess intakes resulting from contamination.

7.2 Previous HIL

The derivation of the previous HIL (HIL A = 1000 mg/kg) for copper is presented by Soong & Emmett (1993) and as summarised in NEPC (1999). In summary, the HIL was derived on the basis of the following:

- Intakes of copper from other sources were estimated with dietary intakes considered most significant for the general population. Background intakes for a 2-year-old child were estimated to be 1.1 mg/day (based on 95% intake from 1992 National Food Authority data) and 0.05 mg/day derived from drinking water.
- A provisional tolerable daily intake (PTDI) of 170 µg/kg/week referenced from a study by Sloof et al. (1989) was adopted as the toxicity reference value.
- Ingestion of both soil and dust has been considered assuming 100% is bioavailable and is absorbed.
- The HIL was derived considering the above, as well as an additional safety factor of 10 to provide a margin of safety, as there is the likelihood of greater intakes of copper from drinking water in many households. The HIL derived was considered preliminary.

7.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed as noted below:

7.3.1 Oral Bioavailability

Bioavailability has not been considered in the previous HIL, as insufficient data is available to adequately define the bioavailability of copper from soil. On this basis, a default approach of assuming 100% oral (and inhalation) bioavailability has been adopted in the derivation of an HIL. It is noted that a site-specific assessment of bioavailability can be undertaken where required.

7.3.2 Dermal absorption

Review of dermal absorption by MfE (2011) indicated the following with respect to copper: 'Organometallic copper salts are indicated to penetrate the skin, producing anti-inflammatory and anti-arthritic activity (Guy et al. 1999), but limited quantitative dermal absorption data is available. The available data indicates permeability coefficients for copper as copper chloride and copper sulphate are in the order of 0.013×10^{-4} to 0.16×10^{-4} cm/h after 72 h. Although higher permeability coefficients are observed during initial exposures they decrease over the time of exposure (Guy et al. 1999). While this data provides an indication of dermal absorption of copper, they are not readily amenable to expression as a skin absorption factor. Further, in these studies the copper salts were applied in petroleum, aqueous gels or emulsions; it is likely that lower absorption/permeability coefficients would be observed for copper present in contaminated soil. Finally, all the agencies considered in this report that have developed soil guideline values for copper (Canada, The Netherlands, US) have considered dermal exposure to copper to be negligible (NCSRP 1995; Baars et al. 2001; US EPA 2003).' Consistent with the above, dermal absorption of copper has been considered to be negligible.

7.3.3 Inhalation of Dust

Copper is not volatile and inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, potential inhalation exposures associated with dust have been considered in the HIL derived.

7.3.4 Plant Uptake

Copper is a micronutrient required by plants for metabolism. Plant growth is affected by copper deficiency as well as toxicity associated with excess levels of copper. The potential for plant uptake and toxicity will be dependent on the form present. Review by MfE (2011) notes that copper is phytotoxic at relatively low tissue concentrations and plant uptake will be limited by its toxic effect on plants. A tissue copper concentration of 15–20 mg/kg (dry weight) is considered to be representative of excessive tissue concentration in agronomic species, while a 10% growth yield decrease is most likely at 10–30 mg/kg (dry weight) tissue copper concentrations.

Given the variable uptake of copper by plants from soil, and the known phytotoxic effects of copper, it is recommended that a maximal concentration of copper in produce is used in preference to a plant uptake factor (which is not limiting). A produce concentration of 30 mg/kg (dry weight) has been considered by MfE (2011) as the maximum amount of copper likely to be taken up in home-grown vegetables. Vegetables containing greater than this concentration would be so stunted and deformed that harvesting would be unlikely.

To obtain the additional background intake, a child's produce consumption (0.048 kg DW[2]/day) was multiplied by 30 mg/kg and divided by the child body weight of 15.5 kg to obtain the maximum additional background daily intake for 100 % of produce being home-grown. For the consumption of 10% home-grown produce, this results in an additional intake of 0.009 mg/kg/day being considered.

[2] It has been assumed that fruit and vegetable crops contain at least 80% moisture. This value has been used to convert wet weight consumption rates into dry weight consumption rates.

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce (also included in background intakes). Given the low tissue concentration required for phytotoxicity it is expected that existing background intakes already address maximum amounts of copper uptake, however, to be conservative the additional uptake calculated here has been assumed to be in addition to the background intakes (noted below).

7.3.5 Intakes from Other Sources – Background

Review of current information from Australia with respect to copper indicates the following:

- Intakes of copper were reported in the *20th Total Diet Survey* (FSANZ 2003) where intakes by infants were identified as highest, at 0.065 mg/kg/day. Intakes by toddlers (2 years) were up to 0.04 mg/kg/day. Intakes of copper in the *23rd Australian Total Diet Study* (FSANZ 2011) indicated intakes by young children aged 2–3 years ranged from a mean of 0.068 mg/kg/day to a 90th percentile of 0.094 mg/kg/day.
- Typical concentrations of copper reported in the ADWG (NHMRC 2011) are 0.05 mg/L, resulting in an intake (1 L/day and body weight of 15.5 kg) by toddlers of 0.004 mg/kg/day. It is noted that intakes of copper in drinking water supplies in New Zealand (MfE 2011) were higher, with intakes by a young child estimated to be 0.013 mg/kg/day.
- Copper was reported in ambient air data collected in NSW (DEC 2003) where concentrations in urban, regional and industrial areas assessed ranged from 2.4–28 ng/m^3. Intakes associated with these concentrations are negligible compared with intakes from food.

RIVM (2001) reviewed background intakes, which were considered to be 30 µg/kg/day for adults. Based on data from Australia and New Zealand for infants and young children, background intakes may comprise approximately 0.08 mg/kg/day, which is 60% of the recommended oral TRV.

7.4 Identification of Toxicity Reference Values

7.4.1 Classification

The International Agency for Research on Cancer (IARC) has not classified copper and copper compounds, however copper 8-hydroxyquinoline has been classified (IARC 1977) as Group 3—not classifiable. It is noted that US EPA has assessed copper as Group D: not classified.

7.4.2 Review of Available Values/Information

Copper is not considered to be carcinogenic and therefore the consideration of a threshold dose-response approach is considered appropriate.

The following threshold values are available from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011)	TDI = 0.5 mg/kg/day	The ADWG (NHMRC 2011) derived a health-based guideline of 2 mg/L based on the provisional TDI of 0.5 mg/kg/day derived from WHO (1982). The evaluation from 1982, which has not been updated, identified a range of provisional maximum tolerable daily intakes (PMTDI) of 0.05-0.5 mg/kg/day. The ADWG have adopted the upper end of the range provided.
OCS (2012)	ADI = 0.2 mg/kg/day	The ADI of 0.2 mg/kg/day is also listed on the current ADI list (OCS 2012), where it is noted to have been set in June 2005, based on the upper safe limit for adults set by FSANZ.
FSANZ (2003)	TL = 0.2 mg/kg/day	FSANZ (2003) has adopted a tolerable limit of 0.2 mg/kg/day for coppe,r referenced from WHO ('Trace Elements in Human Nutrition', 1996).
International		
WHO (2011)	TDI = 0.14 mg/kg/day	The current WHO DWG (2011) have also derived a guideline of 2 mg/L, however they also note that intakes derived from consuming 2–3 L water per day are not expected to exceed a tolerable upper intake level of 10 mg/day (IOM 2001). This upper intake would be equal to a TDI of 0.14 mg/kg/day for a 70 kg adult. Copper is noted to be in the current WHO list for rolling revisions to the drinking water guidelines.
RIVM (2001)	TDI = 0.14 mg/kg/day TC = 0.001 mg/m^3	RIVM (2001) identified an oral TDI of 0.14 mg/kg/day, based on a LOAEL from a chronic oral study in mice. This study was not available at the time when WHO conducted its evaluation. The TDI derived is noted to be above the minimum dietary requirements for copper. Despite a poor database, RIVM also derived an inhalation TC of 0.001 mg/m^3 based on a NOAEC of 0.1 mg/kg/day (adjusted) associated with lung and immune system effects from a subacute study with rabbits and an uncertainty factor of 100. It is not recommended that the inhalation TC be considered in the derivation of a soil HIL, due to the limited data available with respect to chronic inhalation exposures to copper.
ATSDR (2004)	No chronic MRLs available	
US EPA (IRIS 2012)	No evaluation available	

Based on the available data, an oral TRV of 0.14 mg/kg/day is recommended to be adopted for the derivation of soil HILs. The value is based on a tolerable upper limit (IOM 2001) and is similar to the TDI currently adopted by RIVM (2001), OCS (2012) and FSANZ (2003) (where the value may be rounded). The recommended TRV is considered relevant for the assessment of copper intakes from oral, dermal and inhalation routes of exposure.

7.4.3 Recommendation

On the basis of the discussion above, the following toxicity reference values (TRVs) have been adopted for copper in the derivation of HILs:

Recommendation for Copper

Oral TRV (TRV_O) = 0.14 mg/kg/day (WHO 2011; RIVM 2001) for all routes of exposure

Dermal absorption factor (DAF) = negligible (0%)

Background intakes for the general population = 0.08 mg/kg/day = 60% of the oral TRV (adopted for HIL B, C and D)

Background intakes including plant uptake = 0.1 mg/kg/day = 70% of oral TRV (adopted for HIL A)

Background intake assumed relevant for all pathways of exposure (BI_O and BIi)

7.5 Calculated HILs

On the basis of the above, the following HILs have been derived for copper (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	6000	100	Included in background	--	<1
Residential B	30 000	100	--	--	<1
Recreational C	17 000	100	--	--	<1
Commercial D	240 000	100	--	--	<1

-- Pathway not included in derivation of HIL

7.6 References

ATSDR 2004, Toxicological Profile for Copper. Agency for Toxic Substances and Disease Registry, United States Department of Health and Human Services, Atlanta, Georgia, USA.

DEC 2003, Ambient Air Quality Research Project (1996-2001), Internal working paper no. 4, Ambient concentrations of heavy metals in NSW, Department of Environment and conservation (NSW).

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MfE 2011, Toxicological intake values for priority contaminants in soil, New Zealand Ministry for the Environment, Wellington, New Zealand.

NEHF 1997, Copper. National Environmental Health Monographs, Metal Series No. 3, National Environmental Health Forum.

NEPC 1999, Schedule B (7a), Guideline on Health-Based Investigation Levels, National Environment Protection (Assessment of Site Contamination) Measure, National Environment Protection Council, Adelaide, Australia.

NHMRC 2011, National water quality management strategy. Australian drinking water guidelines, National Health and Medical Research Council, Australia.

OCS 2012, ADI List, Acceptable Daily Intakes for Agricultural and Veterinary Chemicals, Current to 31 March 2012, Australian Government, Department of Health and Ageing, Office of Chemical Safety (OCS), available from: http://www.health.gov.au/internet/main/publishing.nsf/content/E8F4D2F95D616584CA2573D700770C2A/$File/ADI-apr12.pdf.

RIVM 2001, Re-evaluation of human-toxicological Maximum Permissible Risk levels, National Institute of Public Health and the Environment, Bilthoven, Netherlands . available from: http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

Sloof, W et al. (eds) 1989, Integrated Criteria Document Copper, Report No. 758474009, National Institute of Public Health and Environmental Protection, Bilthoven, Netherlands.

Soong, FS & Emmett, AJ 1993, 'Assessment and Management of CCA Timber Preservation Plants', presented in the proceedings of the Second National Workshop on the Health Risk Assessment and Management of Contaminated Sites, Contaminated Sites Monograph Series, No. 2.

US EPA (IRIS 2012), Data and information available from the Integrated Risk Information System, an online database, available from http://www.epa.gov/iris/.

WHO, 1998. Environmental Health Criteria 200 Copper, International Programme on Chemical Safety, World Health Organization, Geneva.

WHO 2011, Guidelines for drinking-water quality, 4th edn, World Health Organization, Geneva, available from http://www.who.int/water_sanitation_health/dwq/chemicals/en/index.html.

8 Lead

8.1 General

Several comprehensive reviews of lead in the environment and its toxicity to humans are available and should be consulted for more detailed information (ATSDR 2007; IARC 2006; WHO 1989; WHO 2000). The following provides a summary of the key aspects of lead that are relevant to the derivation of a soil HIL.

Lead (Pb) is a naturally occurring element found in the Earth's crust at an average concentration of approximately 15 to 20 mg/kg. It is most commonly found in ores such as galena (PbS), anglesite ($PbSO_4$) and cerussite ($PbCO_3$). Lead is a bluish-grey, soft, dense, malleable, corrosion-resistant metal that is solid at room temperature and has a low melting point. It exists in three oxidation states—Pb(0) (metallic lead), Pb(II) and Pb(IV). The most common oxidation state of lead is Pb(II) (ATSDR 2007).

Lead is of primary use in a wide range of materials including batteries, metal alloys, X-ray shielding materials, ammunition, chemical-resistant linings and pigments. Lead has been widely used historically as an additive in petrol and also in many paints (ATSDR 2007).

Health effects associated with exposure to inorganic lead and compounds include, but are not limited to, neurotoxicity, developmental delays, hypertension, impaired haemoglobin synthesis, and male reproductive impairment. The most sensitive targets for lead toxicity are the developing nervous system, the haematological and cardiovascular systems and the kidney. However, due to the multi-modes of action of lead in biological systems, lead could potentially affect any system or organ in the body. The effects of lead exposure have often been related to the blood lead content, which is generally considered to be the most accurate means of assessing exposure (MfE 2011).

8.2 Previous HIL

The derivation of the previous HIL (HIL A = 300 mg/kg) for lead is presented by Maynard (1991). In summary, the HIL was derived on the basis of the following:

- Intakes of lead from other sources were estimated from air, water, food, dust and soil (background). Based on available data from Australia these were estimated to be 20.3 µg/day (absorbed). In the calculations undertaken using a PTWI, this comprised 48% of the PTWI, leaving the intake from soil to be 52% of the PTWI.
- Three approaches were presented in relation to the derivation of a soil HIL:
    - Use of a PTWI
        - A provisional tolerable weekly intake (PTWI) of 25 µg/kg/week referenced from the Joint FAO/WHO was adopted as the toxicity reference value
        - Soil intake of 80 mg/day was assumed with 100% bioavailability
        - Dermal absorption was considered negligible
        - Guideline value calculated was 300 mg/kg.
    - Consideration of 'safe' blood lead
        - A blood lead goal of 7.5 µg/dL was considered (based on a NOAEL of 15 µg/dL with a 2-fold safety factor)
        - Based on a US EPA coefficient relating blood lead to exposure, a soil guideline of 1800 mg/kg was derived.

- Use of US EPA Uptake/Biokinetic Model
    - Using the US EPA model, with an air concentration of 1.5 µg/m^3, soil lead levels of 800–1300 mg/kg can be expected.

Based on review of the available approaches a soil guideline of 300 mg/kg for HIL A was determined.

8.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed, as noted below.

8.3.1 Oral Bioavailability

A significant amount of data is available in relation to the bioavailability of lead. In addition, a number of international agencies have considered bioavailability in the derivation of soil guideline values. The available approaches include (MfE 2011):

- RIVM (2001) use a relative bioavailability (the bioavailability from a soil matrix with respect to the bioavailability from the matrix in toxicity studies used to assess tolerable intakes) for lead of 0.6 (60%) in the derivation of serious (human health) risk concentrations.
- UK and US agencies have developed models based on the relationship between exposure and blood lead concentrations to derive soil guideline values.
- The IEUBK model was developed to describe the exposure of children to lead from multiple sources, and incorporates data on the toxicokinetics of lead – five exposure pathways are considered (air, water, diet, soil and dust). Using the various generic default parameters, including absorption factors of 0.3 for soil and dust, and 0.5 for food and water, a soil guideline value of 400 mg/kg is derived, and is considered appropriate for use in a residential scenario.
- In contrast, the UK model considers the background exposure to lead from sources other than soil and dust, and the slope or response of the blood lead concentration versus soil and dust lead relationship.
- WHO (2000) indicates that absorption of lead can range from 3 to 80% with typical absorption rates in adults and infants considered to be 10 and 50% respectively.

It is noted that review by MfE (2011) considered there to be issues in the range of lead bioavailability/ bioaccessibility values, no agreed laboratory methods available and uncertainties with the dose–response used for blood lead. Hence the MfE has considered 100% bioavailability in the derivation of a soil guideline value.

Bioavailability has been considered in the derivation of the previous HIL, with 50% adsorption considered for dietary and water intakes, 40% absorption from inhaled particulates and 30% from ingested soil/dust considered in the assessment of intakes from other sources (background) (Maynard 1991).

Review of bioavailability by IARC (2006) identified a range of values and factors that have the potential to affect absorption. Based on the range of bioavailability values presented by IARC, an oral bioavailability of 50% (from soil/dust, food and water) is considered to be sufficiently conservative. These values have been considered in the derivation of HILs.

8.3.2 Dermal absorption

Studies relating to dermal absorption of lead are reviewed by ATSDR (2007) where low levels of inorganic lead (<1% and much lower (well below 0.1%)) were reported. IARC (2006) notes that in the limited number of studies available, dermal absorption of inorganic lead is negligible, although slightly enhanced by high perspiration rates. Based on the available data, dermal absorption of lead has been considered to be negligible, consistent with the approach adopted in New Zealand (MfE 2011) and the UK (DEFRA & EA 2002)

8.3.3 Inhalation of Dust

Lead is not volatile and inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, potential inhalation exposures associated with dust have been considered in the HIL derived.

8.3.4 Plant Uptake

IARC (2006) has noted that plant uptake of lead from soil is low due to the low bioavailability of lead in soil and its poor translocation from the root to the shoot. Of all the toxic heavy metals, lead is considered the least phytoavailable. While soil properties affect the potential for uptake and translocation, water soluble and exchangeable lead that is readily available for uptake by plants constitutes only 0.1% of the total lead in most soils. Hence a chelate (such as EDTA) is used to increase lead uptake and translocation where phytoremediation is required.

For the derivation of soil HILs it has been assumed that the small amount of lead that may be taken up into home-grown produce is essentially accounted for in the consideration of intakes from the diet. In areas where the form of lead in soil is more soluble and available for plant uptake a site-specific assessment (including the sampling of home-grown produce) should be considered.

8.3.5 Intakes from Other Sources – Background

Information available from Australia in relation to background intakes of lead include the following:

- Dietary intakes of lead have been reported from FSANZ (2003 and 2011). Intakes reported in this study range from 0.02–0.4 µg/kg/day for adults to 0.01–1.2 µg/kg/day for infants. This data is the most current from FSANZ and is noted to comprise up to 33.3% of the adopted TDI (the same as is recommended for oral TRV). The average of the range presented has been considered in calculations presented using the IEUBK model.
- The ADWG (NHMRC 2011) notes that lead concentrations in drinking water range up to 0.01 mg/L with typical concentrations less than 0.005 mg/L. Data available from South Australia (based on 5 years of data) suggest concentrations of lead in drinking water are on average 0.0007 mg/L, with a maximum of 0.014 mg/L. Intakes derived for a young child (consuming 1 L/day and a body weight of 15.5 kg) is approximately 0.04 µg/kg/day.
- Concentrations of lead in air have been derived from Australian data on lead levels in urban, suburban and rural areas. NSW (DEC 2003) report concentrations of lead in air that range from 2.4–99 ng/m^3 with an average of 30 ng/m^3. Intakes derived from urban air are considered negligible in comparison with those derived from dietary and water sources.
- Total intakes from sources other than soil are estimated to be up to 1.2 µg/kg/day. This is comparable with background intakes estimated by MfE (2011) of 0.97 µg/kg/day.

8.4 Identification of Toxicity Reference Values

8.4.1 Classification

The International Agency for Research on Cancer (IARC 2006) has classified inorganic lead as Group 2A—probably carcinogenic to humans. Organolead was classified as Group 3—not classifiable.

It is noted that US EPA (available from IRIS 2012) has classified lead and compounds (last reviewed in 1993) as Class B2—probable human carcinogen.

8.4.2 Review of Available Values/Information

Some evidence of carcinogenic effects has been associated with exposure to lead (in experimental animals, with inadequate evidence in humans). It is noted ,however, that there is evidence from human studies that adverse effects other than cancer may occur at lower lead levels (WHO 2011), hence the adoption of a guideline that addresses the most sensitive non-carcinogenic effects is considered to also be adequately protective of carcinogenic effects.

Blood lead levels have been found to be a good indicator of exposure to lead. A blood lead level reflects lead's dynamic equilibrium between adsorption, excretion and deposition in soft and hard tissues. Epidemiological studies (and expert groups) do not provide definitive evidence of a threshold in relation to blood lead levels and neurotoxic effects (US EPA (IRIS 2012), ATSDR 2007, DEFRA & EA 2002 and RIVM 2001) but blood lead goals and associated intakes have been identified by various agencies for the assessment of lead exposures by the general public. The NHMRC has noted that there are no benefits of human exposure to lead and that all demonstrated effects of exposure are adverse.

The following threshold values are available from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011)	PTDI = 0.0035 mg/kg/day	The PTDI considered in the ADWG (NHMRC 2011) is based on the evaluation provided by JECFA (WHO 1993 and WHO 2011) associated with a PTWI of 0.025 mg/kg/week (see comments below).
NHMRC (2009)	PbB goal <10 µg/dL	Blood lead goal set in 1987 and re-iterated in 1993. The document provides a series of graduated response levels associated with concentrations ranging from 15–25 µg/dL. The guidance was rescinded by the NHMRC on 31/12/2005. NHMRC (2009) notes that the value of 10 µg/dL was never intended as a 'safe' level of exposure of a 'level of concern', however they still recommend that goal of <10 µg/dL for all Australians.
NEPM (2003)	Air Quality Goal = 0.5 $\mu g/m^3$	Air guideline (based on an annual average) set by NEPM. Basis of the value is not stated; however it is the same as that set by WHO (2000).

Source	Value	Basis/Comments
International		
JECFA (WHO 1993)	PTWI = 0.025 mg/kg	In 1972 the JECFA set a PTWI of 0.05 mg/kg. The current PTWI was established in 1986 for infants and children based on metabolic studies showing a mean daily intake of 3–4 µg/kg was not associated with an increase in blood lead levels or in the body burden of lead. An intake of 5 µg/kg was associated with an increase in lead retention. The PTWI was reconfirmed in 1993 and extended to all age groups. The PTWI was estimated to be responsible for a blood lead concentration of 5.6 µg/dL for a 10 kg child, which is thought to be below that associated with effects on intellectual performance. This PTWI was withdrawn by JECFA in 2010 (WHO 2010) as the committee could no longer consider the value to be health-protective. The committee estimated that the previous PTWI is associated with a decrease of at least 3 intelligence quotient (IQ) points in children and an increase in systolic blood pressure of approximately 3 mm Hg in adults. Both these effects were considered important within a population. The committee did not provide any indication of a suitable threshold for the key adverse effects of lead and no alternate PTWI was established.
WHO (2011)	No value provided	WHO has adopted a provisional guideline of 0.01 mg/L based on treatment performance and analytical achievability. The WHO evaluation notes the withdrawal of the JECFA PTWI (WHO 1993) and that no new value is available. The review notes that there does not appear to be a threshold for the key effects of lead.
WHO (2000)	TC = 0.5 µg/m^3	Air guideline (based on an annual average) established for lead, based on an objective of 98% of the general population having a blood lead concentration of <10 µg/dL, where the median blood lead levels would be no more than 5.4 µg/dL.
RIVM (2001)	PTWI = 0.025 mg/kg	Adopted the JECFA (WHO 1993) evaluation.
DEFRA & EA (2002)	PbB goal <10 µg/dL	Guideline established for adults and children associated with exposures from all routes and sources. It is considered that neurotoxicity effects associated with lead exposure have no threshold and therefore an additional requirement to keep exposures from all sources as low as practically possible is noted.
ATSDR (2007)	No MRLs derived	No MRLs derived as some health effects associated with exposure to lead occur at blood lead levels as low as to be essentially without a threshold.

Source	Value	Basis/Comments
US EPA (IRIS 2012)	No RfD derived	No threshold values derived by the US EPA as it is noted that 'It appears that some of these effects, particularly changes in the levels of certain blood enzymes and in aspects of children's neurobehavioral development, may occur at blood lead levels so low as to be essentially without a threshold'.

The available goals reflect a blood lead goal of <10 µg/dL from all sources, which is considered relevant for all exposures and sources.

8.5 Calculated HILs

The HILs for lead have been previously established using both the JECFA (WHO 1993) PTWI and the blood lead model. Given that the PTWI has now been withdrawn and is no longer considered adequately protective, the HIL has been established on the basis of the blood lead model, on the basis of the blood lead goal of <10 µg/dL for all routes of exposure and all sources.

The most commonly used (and recommended) blood lead model relevant to the most sensitive age group, infants and young children, is the IEUBK model (win 32, Model 1.1). On the basis of the assumptions presented in Appendix C (consistent with the pathway-specific assumptions outlined in this review and reviewed in line with the use of the IEUBK model in Port Pirie (South Australia)), HIL A = 306 mg/kg. A value of around 300 mg/kg can also be confirmed using the model LeadSpread available from the California Department of Toxic Substances Control.

8.5.1 HILs

On the basis of the above, the previous soil HIL of 300 mg/kg for lead has been reaffirmed. HILs B, C and D have also been reaffirmed on the basis of the blood lead model.

HIL Scenario	HIL (mg/kg)
Residential A	300
Residential B	1200
Recreational C	600
Commercial D	1500

8.6 References

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9 Manganese

9.1 General

Several comprehensive reviews of manganese in the environment and its toxicity to humans are available and should be consulted for more detailed information (ATSDR 1997 and 2008; WHO 1999 and 2004; Health Canada 2008). The following provides a summary of the key aspects of manganese that are relevant to the derivation of a soil HIL.

Manganese (Mn) is the 12th most abundant element and comprises approximately 0.01% of the Earth's crust. Manganese does not occur naturally in its elemental state and is most commonly found in mineral form as oxides, carbonate and silicates. Elemental manganese is a steel-gray coloured solid at room temperature. Manganese can exist in a relatively wide range of oxidation states from -3 to +7. The most common oxidation state of manganese is Mn (IV), the form associated with manganese dioxide (MnO_2) (ATSDR 2008).

Manganese is used to increase stiffness, hardness and strength in a range of alloys including carbon steel, stainless steel, high-temperature steel, cast iron and super-alloys. Manganese is additionally used in the manufacture of dry cell batteries, matches, fireworks, porcelain, brick colourant, glass, animal feed, and plant fertilisers. Strongly oxidising forms of manganese, such as potassium permanganate are used as a disinfectant, an anti-algal agent, a water purifying agent, for metal cleaning, tanning and as bleach (ATSDR 2008).

Manganese is a dietary essential element that is required in several important processes including bone mineralisation, energy metabolism, metabolic regulation, and the formation of glycosaminoglycans (ATSDR 2008). As it is an essential element ,adverse effects can occur as a result of deficiency as well as toxicity associated with excess intake from contamination.

9.2 Previous HIL

The derivation of the previous HIL (HIL A = 1500 mg/kg) for manganese is presented by Lindon & Sabordo (1996). In summary, the HIL was derived on the basis of the following:

- Intakes of manganese from other sources were estimated with dietary intakes considered most significant for the general population. Intakes presented were based on data from WHO, where dietary intakes for young children were approximately 2.2–2.5 mg/day. Intakes from water were estimated to be low, less than 2% of total manganese intake.
- No toxicity threshold was identified for inorganic compounds of manganese and hence the HIL was derived on the basis of an incremental flux of manganese associated with ingestion of soil. The value of 1500 mg/kg was based on an incremental exposure of 10% over an adequate manganese intake received from food and water.

9.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed, as noted below.

9.3.1 Oral Bioavailability

Bioavailability has not been considered in the previous HIL, as insufficient data is available to adequately define the bioavailability of copper from soil. On this basis, a default approach of assuming 100% oral (and inhalation) bioavailability has been adopted in the derivation of an HIL. It is noted that a site-specific assessment of bioavailability can be undertaken where required.

9.3.2 Dermal absorption

Limited data is available on the dermal absorption of manganese. Absorption of inorganic manganese is not considered to occur to any great extent (Lindon & Sabordo 1996). While no studies relating to dermal absorption of inorganic manganese by ATSDR (2008) are available, the review noted that for inorganic manganese compounds, dermal exposure is not a typical pathway of exposure because manganese does not penetrate the skin readily. However, for organic manganese, dermal exposure is a possibility. The HIL derived relates to inorganic manganese and hence organic compounds have not been considered further.

On the basis of the above, there is no data available to suggest that dermal absorption of manganese is significant and hence it has been assumed to be negligible in the derivation of HILs.

9.3.3 Inhalation of Dust

Manganese is not volatile however WHO (1999) notes the following: 'Little is known about the relative toxicity of different manganese compounds. Inhaled manganese compounds tend to produce more severe toxicity than ingested manganese compounds. This is probably attributable to the difference in route-specific uptake of manganese from the lung (often assumed at 100%) compared with the gastrointestinal tract (3–5%). Studies have shown that a greater proportion of a manganese dose appears in the blood and brain of rats exposed via inhalation or intranasal instillation than when the same dose is given orally.'

Inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil, however, due to the toxicity of inhaled manganese, it is relevant to include this pathway in the derivation of soil HILs.

9.3.4 Plant Uptake

Manganese is a micronutrient required by plants for metabolism. Plant growth is affected by manganese deficiency as well as toxicity associated with excess levels of manganese. In general, natural levels of manganese in soil are sufficiently high to address deficiencies but where plant deficiencies occur it is typically due to manganese being present in a form not available for plant uptake. Hence the potential for plant uptake and toxicity will be dependent on the form present. While a comprehensive review of plant uptake has not been conducted in this review, the potential for manganese uptake into plants has been considered in the derivation of HIL A.

Based on the above, the uptake of manganese into all crops has been considered in the derivation of the HIL A. Limited plant uptake data is available, and translocation into above-ground crops is assumed to be negligible, hence the value presented by RAIS (2010) of 0.068 mg/kg fresh produce per mg/kg soil produce has been considered for root and tuber crops only.

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce (also included in background intakes). To address this in the derivation of HIL A, half the intake estimated to be derived from home-grown produce is assumed to be already accounted for in the total background intake (noted below).

9.3.5 Intakes from Other Sources – Background

Review of current information from Australia indicates the following:

- Review of manganese by FSANZ (2011) indicates that for young children aged 2–3 years, intakes range from a mean of 0.19 mg/kg/day to a 90th percentile of 0.26 mg/kg/day. These intakes are higher than estimated in the previous HIL evaluation and by ATSDR. Dietary intakes of manganese reported by WHO are summarised by Lindon & Sabordo

(1996) and are approximately 0.06 mg/kg/day for young children. Estimates provided by ATSDR (2008) suggest that adult intakes of food are 3.8 mg/day (or 0.05 mg/kg/day).

- Typical concentrations of manganese reported in the ADWG (NHMRC 2011) are less than 0.01 mg/L, resulting in an intake (1 L/day and body weight of 15.5 kg) by toddlers of 0.00076 mg/kg/day.
- Based on the above background intakes for young children, it has been assumed that background oral intakes comprise 50% of the recommended oral TRV.
- Manganese was reported in ambient air data collected in NSW (DEC 2003) where concentrations (24-hour averages) in urban, regional and industrial areas assessed ranged from 3.7–119 ng/m^3 (average of 18 ng/m^3). Typical concentrations in air have been reported by ATSDR (2008) to be 23 ng/m^3, consistent with that reported by DEC (2003). These background concentrations comprise (based on average concentrations) approximately 15% of the recommended inhalation TRV. A conservative background of 20% of the inhalation TRV could be assumed for intakes from air.

9.4 Identification of Toxicity Reference Values

9.4.1 Classification

The International Agency for Research on Cancer (IARC) has not classified manganese. US EPA has classified manganese as Group D—not classifiable.

9.4.2 Review of Available Values/Information

Insufficient data is available to assess wither manganese is carcinogenic to humans. Some in vitro and in vivo assays are available for manganese, with studies providing conflicting results. Overall review of the data shows that some chemical forms of manganese have mutagenic potential, but most results are inconsistent and hence no overall conclusion as to the genotoxic potential associated with exposure to manganese can be determined (ATSDR 2008). On this basis, a threshold approach is considered appropriate, based on the most sensitive effect associated with manganese exposure (CNS effects).

The following threshold values are available from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011)	Safe level of 10 mg/day	The ADWG (NHMRC 2011) derived a health based guideline of 0.5 mg/L based on a level of 10 mg/day, which is the amount of manganese that can be safely consumed from all sources, referenced from WHO 1973 evaluation.
International		
WHO (2011)	TDI = 0.05 mg/kg/day	The current WHO DWG (2011) has not established a guideline for drinking water, as the compound is not considered to be of health concern at the levels found in drinking water. The review notes that a health-based guideline of 0.4 mg/L can be derived based on the upper range value of manganese intake of 11 mg/day from dietary studies (IOM 2002) and an uncertainty factor of 3 (to allow for the increased bioavailability of manganese from water), which results in a TDI of 0.05 mg/kg/day for a 70 kg adult. The guidance also notes that the presence of manganese in drinking water will be objectionable (water discolouration) above 0.05 mg/L.
WHO (1999)	TC = 0.00015	Tolerable concentration or guideline value derived by WHO

Source	Value	Basis/Comments
	mg/m^3	on the basis of the same study considered by the US EPA (IRIS 2012) and ATSDR (2008), with the guideline value derived on the basis of a NOAEL of 0.03 mg/m^3 for neurotoxicological effects from a benchmark dose (BMD) analysis, adjustment for continuous exposure (5/7 x 8/24) and an uncertainty factor of 50. The value derived is similar to that from ATSDR (2008) with the main difference being the application of the BMD model. No oral guideline value was provided.
Health Canada (2008)	RfC = 0.00005 mg/m^3	RfC derived based on most sensitive benchmark dose analysis associated with neurotoxicological effects in an occupational inhalation study. A range of RfCs were derived that varied from 0.00005–0.00014 mg/m^3. The range derived is consistent with values derived from ATSDR and WHO.
ATSDR (2008)	Interim oral value of 0.16 mg/kd/day Inhalation MRL = 0.0003 mg/m^3	No oral MRLs have been derived by ATSDR; however they provide an interim guidance value of 0.16 mg/kg/day based on a tolerable upper intake level of 11 mg/day. Chronic inhalation MRL derived on the basis of a benchmark concentration (at the lower 95% confidence limit for the level of manganese exposure expected to result in 10% response rate) $BMCL_{10}$ (adjusted for continuous exposure) of 0.03 mg/m^3 associated with neurobehavioural effects in an occupational study and an uncertainty factor of 100.
US EPA (IRIS 2012)	RfD = 0.14 mg/kg/day RfC = 0.00005 mg/m^3	RfD (last reviewed in 1993) based on a NOAEL of 0.14 mg/kg/day associated with CNS effects in a number of dietary human studies and an uncertainty factor of 1. US EPA also notes that individual requirements for and effects associated with manganese exposure may be highly variable and that some individuals may consume more than 10 mg/day of manganese without any cause for concern. RfC (last reviewed in 1993) based on the same study considered by ATSDR (2008), however US EPA considered the LOAEL (HEC) of 0.05 mg/m^3 and applied an uncertainty factor of 1000.

As manganese toxicity via inhalation has been shown to be more significant than via oral intakes, it is reasonable that quantitative values for inhalation exposures are significantly lower than for oral exposures. Based on the available data, an oral threshold value of 0.16 mg/kg/day as derived by ATSDR (2008) is based on the most recent detailed review of manganese toxicity. It is noted that the basis for the value is consistent with the upper range of manganese intake considered by US EPA (IRIS 2012), NHMRC (2011) and WHO (2011, if the additional uncertainty factor of 3 were not considered for exposures from soil (based on increased bioavailability from water)).

The quantitative values available for the assessment of inhalation exposures are all essentially based on the same critical study (with the exception of Health Canada), with the main difference being the approach used to quantify a threshold value from the study data (using different benchmark dose models or not using a benchmark dose model), and consideration of uncertainty factors. The air guideline value derived by WHO (1999) is recommended based on the use of a benchmark dose analysis which is also within the range of threshold values derived by Health Canada (2008) using a number of benchmark dose approaches using a different study. The value is also similar to that derived by ATSDR (2008).

9.4.3 Recommendation

On the basis of the discussion above, the following toxicity reference values (TRVs) have been adopted for manganese in the derivation of HILs:

Recommendation for Manganese

Oral TRV (TRV_O) = 0.14 mg/kg/day (ATSDR 2008)

Dermal absorption factor (DAF) = negligible (0%)

Inhalation TRV (TRV_I) = 0.00015 mg/m^3 (WHO 1999)

Background intakes from other sources (as % of TRV):

BI_O = 50% for oral and dermal intakes

BIi = 20% for inhalation

Uptake in home-grown produce considered in derivation of HIL A.

9.5 Calculated HILs

On the basis of the above, the following HILs have been derived for manganese (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	3800	32	49	--	19
Residential B	14 000	29	--	--	71
Recreational C	19 000*	80	--	--	20
Commercial D	60 000	18	--	--	82

-- Pathway not included in derivation of HIL

* HIL is higher than HIL B (contrary to other HILs derived) due to the more significant influence of the dust inhalation pathway in the derivation of HILs A and B, and lower contribution for HIL C.

9.6 References

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FSANZ 2011, *The 23rd Australian Total Diet Study*, Food Standards Australia and New Zealand.

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10 Mercury

10.1 General

This review considered both inorganic mercury and methyl mercury. The derived HILs are not relevant to the assessment of elemental mercury, which should be addressed on a site-specific basis.

Several comprehensive reviews of mercury in the environment and its toxicity to humans are available and should be consulted for more detailed information (ATSDR 1999; WHO 1989, 1990, 1991, 2000a, 2003, 2004; DEFRA & EA 2002; EA 2009). The following provides a summary of the key aspects of mercury that are relevant to the derivation of a soil HIL.

Mercury is a heavy metal that exists in three oxidation states: 0 (elemental), +1 (mercurous) and +2 (mercuric). As well as the common mercurous and mercuric inorganic salts, mercury can also bind covalently to at least one carbon atom. Thus the most commonly encountered exposures associated with mercury are with elemental mercury, inorganic mercuric compounds and methyl mercury.

Mercury occurs naturally as a mineral and is widely distributed by natural and anthropogenic processes. The most significant natural source of atmospheric mercury is the degassing of the Earth's crust and oceans and emissions from volcanoes. Man-made sources such as mining, fossil fuel combustion and industrial emissions generally contribute less on a global scale, but more on a local scale. Wet and dry deposition to land and surface water result in mercury sorption to soil and sediments.

Uses of mercury include use in the electrical and chlor-alkali industry (lamps, batteries and as cathodes in the electrolysis of sodium chloride to produce caustic soda and chloride), industrial and domestic instruments, laboratory and medical instruments and dental amalgam (mixed in proportion of 1:1 with a silver-tin alloy).

Mercury in the environment, including groundwater, exhibits complex behaviour that affects both its mobility and potential toxicity. Mercury has a low solubility in water; however, it also has the potential to form multiple species in the environment, which can lead to increased total mercury concentrations in aqueous systems. The relative toxicity of mercury is also dependent on the form in which it occurs, which is dependent on biogeochemical processes, partitioning between solids, and complexation with dissolved organic and inorganic ligands.

On the basis of the potential for long-range transport, persistence in water, soil and sediment, bioaccumulation, toxicity and ecotoxicity, mercury is considered persistent and is addressed in the 1998 UN-ECE Convention on Long-Range Transboundary Air Pollution on Heavy Metals (UN-ECE 1998). The United Nations Environment Programme (UNEP) Governing Council concluded, at its 22nd session in February 2003, after considering the key findings of the Global Mercury Assessment report, that there is sufficient evidence of significant global adverse impacts from mercury to warrant further international action to reduce the risks to humans and wildlife from the release of mercury to the environment.

10.2 Previous HIL

The derivation of the previous HIL (HIL A for inorganic mercury = 15 mg/kg and for methyl mercury = 10 mg/kg) is presented by Imray & Neville (1996). In summary, the HILs were derived on the basis of the following:

- Intakes of mercury were considered based on available data that showed dental amalgams and dietary intakes (based on data from FSANZ from 1992) as most significant. The total intake of inorganic mercury (derived from inorganic or elemental sources, both of which add to the body burden of mercury) estimated for a 2-year-old

child was 2.1 µg/day. The most significant exposures were derived from dietary intakes and dental amalgams. For methyl mercury, the total intake was estimated to be 2.4 µg/day (approximately 50% of the adopted TI of 5 µg/day, which was based on methyl mercury). The most significant exposures were derived from dietary intakes of seafood. Based on the available data, 20% of the PTWI was considered for intakes derived from soil.

- A provisional tolerable weekly intake (PTWI) of 300 µg for total mercury, of which no more than 200 µg should be methyl mercury, referenced from the JECFA evaluation, was adopted as the toxicity reference value.
- Ingestion of both soil and dust has been considered assuming 100% is bioavailable.

10.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed, as noted below.

10.3.1 Oral Bioavailability

The bioavailability of different forms of mercury, by different routes of exposure, is expected to vary considerably (Imray & Neville 1996) with oral bioavailabilities reported in the range 2–15% for inorganic mercury and 80–100% for methyl mercury. Bioavailability has not been considered in the previous HIL, as insufficient data is available to adequately define the bioavailability of the different forms of mercury from soil. On this basis, a default approach of assuming 100% oral (and inhalation) bioavailability has been adopted in the derivation of an HIL. It is noted that site-specific assessment of bioavailability can be considered where required.

10.3.2 Dermal absorption

Review of dermal absorption by MfE (2011) has noted that 'Mercury reacts with skin proteins, and as a result penetration does not increase commensurably with increasing exposure concentration but rather approaches a plateau value. Mercury has a permeability coefficient in the order of 10^{-5} cm/h (Guy et al. 1999), which compares to permeability coefficients in the order of 10^{-4} cm/h for lead.' As dermal absorption for lead has not been considered to be negligible, the potential for dermal absorption of mercury has been considered.

ATSDR (1999) notes that absorption of mercurous salts in animals can occur through the skin, though no quantitative data is available, hence a default value of 0.1% has been adopted based on the lower end of the range for metals presented by US EPA (1995).

ATSDR (1999) also noted no information was identified for absorption of methylmercury via dermal absorption. The Environment Agency (EA 2009) notes that dermal absorption of methyl mercury is reported to be similar to that of inorganic mercury. Hence the value adopted for inorganic mercury has also been adopted for methyl mercury. It is noted that dermal absorption of dimethylmercury has been reported to be of potential significance and may need to be considered in a site-specific assessment if identified as the key form of mercury in soil.

US EPA (2004) has recommended the use of a gastrointestinal absorption factor (GAF) of 7% for inorganic mercury based on mercuric chloride and other soluble mercury salt studies used in the derivation of the oral RfD. The GAF is used to modify the oral toxicity reference value to a dermal value in accordance with the US EPA (2004) guidance provided.

10.3.3 Inhalation of Dust

Inorganic mercury and methyl mercury are not volatile and inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, potential inhalation exposures associated with dust have been considered in the HIL derived. Note that if elemental mercury is present then vapour phase issues need to be considered on a site-specific basis.

10.3.4 Plant Uptake

A detailed review of the plant uptake of mercury (primarily elemental and inorganic mercury) is presented in EA (2009). This review considered studies that are based on the uptake of mercury into green vegetables, root vegetables, tuber vegetables, herbaceous fruit, shrub fruit and tree fruit. The review provides recommendations on soil-to-plant uptake factors that are relevant for these types of produce. The recommendations from this review have been considered in the derivation of a residential A HIL and are summarised below for the range of crops considered:

Produce Group	Plant Uptake Factors (mg/kg produce fresh weight per mg/kg soil) (EA, 2009)
Green vegetables	0.0038
Root vegetables	0.0069
Tuber vegetables	0.0042
Tree fruit	0.001

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce (also included in background intakes). To address this in the derivation of HIL A, half the intake estimated to be derived from home-grown produce is assumed to be already accounted for in the total background intake (noted below).

No plant uptake values are reviewed or recommended for methyl mercury. EA (2009) notes that methylated mercury compounds are likely to be more toxic to plants compared with ionic forms, though no specific data is provided. Review by US EPA (1997) suggests that methyl mercury complexes in soil are available for plant uptake and translocation. In addition, plants have some mercury methylation ability and hence the percentage of methyl mercury in plants may not originate from methyl mercury uptake from soil. Due to the level of uncertainty involved in the estimation of plant uptake of methyl mercury from soil, including the potential for phytotoxicity, it is expected that the conservative approach to the consideration of intakes from dietary sources adequately addresses potential intakes that may be derived from the consumption of 10% home-grown produce.

10.3.5 Intakes from Other Sources – Background

For inorganic mercury, review of current information from Australia indicates the following:

- Mercury levels are reported in the *20th Australian Total Diet Survey* (FSANZ 2003). Dietary intakes of total mercury (which includes organic mercury in seafood) ranged from 0.01–0.2 µg/kg/day for toddlers (aged 2 years). This is consistent with intakes reported in the more recent survey (FSANZ 2011).
- Typical concentrations of mercury reported in the ADWG (NHMRC 2011) are less than 0.0001 mg/L, resulting in an intake (1 L/day and body weight of 15.5 kg) by toddlers of 0.0073 µg/kg/day.
- Review (NHMRC 1999) of intakes associated with amalgam fillings in Australian children and adults (based on average number of fillings of 0.5 and 8 respectively) provides an reasonable estimate of daily mercury absorption per person of about 0.3 µg

for children and 3.5 µg for adults. The estimate for children is expected to be conservative as the use of mercury dental amalgams is declining.

- Based on the above, background intakes by young children may be up to 0.23 µg/kg/day from oral intakes (dietary, dental and water). This is slightly higher than intakes of 0.1 µg/kg/day from RIVM (2001) and 0.037 µg/kg/day from the UK (EA 2009, for 20kg child). These intakes comprise approximately 40% of the recommended oral TRV.
- Levels of inorganic mercury in air are not available for Australia with estimates from WHO (2003) for mercury in air ranging from 10–20 ng/m^3 from the US (no indication on speciation between elemental and inorganic). These concentrations comprise up to 10% of the recommended inhalation TRV.

For methyl mercury, review of current information from Australia indicates the following:

- Mercury levels are reported in the *20th Australian Total Diet Survey* (FSANZ 2003). Dietary intakes of total mercury (which is dominated by organic mercury in seafood) ranged from 0.01–0.2 µg/kg/day for toddlers (aged 2 years). This is consistent with intakes reported in the more recent survey (FSANZ 2011).
- The most recent review of methyl mercury by JECFA (WHO 2004) included a review of estimated dietary intakes from a number of countries. The review references previous total diet surveys (from 1992 and 1995) and indicates that the mean intake of methyl mercury for the population is approximately 0.7 µg/kg/week. It is noted that the 95th percentile intake estimated exceeds the recommended PTWI adopted by JECFA (WHO 2004). This is a conservative estimate but it suggests intakes may be a significant proportion of the recommended PTWI.
- Reviews of background intakes of methyl mercury by EA (2009) and RIVM (2001) suggest intakes ranging from 8–20% of the adopted TDI (similar to the recommended TRV). Data from Australia suggests intakes may be higher and hence a value of 80% is recommended to address the potential for a significant proportion of the recommended oral TRV to be derived from background intakes.

It is noted that the potential for intakes in excess of the recommended oral TRV may occur in populations with high intakes of seafood. This may need to be considered on a site-specific basis.

10.4 Identification of Toxicity Reference Values

10.4.1 Classification

The International Agency for Research on Cancer (IARC) has classified methyl mercury as Group 2B—possibly carcinogenic to humans. IARC has classified metallic mercury and inorganic mercury compounds as Group 3—not classifiable.

It is noted that US EPA has classified methyl mercury as Class C—possible human carcinogen. In addition, US EPA has classified mercuric chloride as Group C—possible human carcinogen, based on increased incidence of squamous cell papillomas of the forestomach and marginally increased incidence of thyroid follicular cell adenomas and carcinomas from long-term oral studies in rats.

10.4.2 Review of Available Values/Information

10.4.2.1 Inorganic Mercury

Most information on the toxicity of inorganic mercury compounds comes from studies of mercuric chloride. As the water solubility and bioavailability of many other inorganic compounds, notably mercurous compounds, are much less than those of mercuric chloride, such compounds are likely to be less toxic. These issues should be considered further in a site-specific assessment, where relevant.

Carcinogenicity studies in experimental animals are available for mercuric chloride where no carcinogenic effect was observed in mice or female rats, though marginal increases in the incidence of thyroid follicular adenomas and carcinomas and forestomach papillomas were observed in male rats exposed orally. Mercuric chloride binds to DNA and induces clastogenic effects in vitro; in vivo, both positive and negative results have been reported, without a clear-cut explanation of the discrepancy. The overall weight of evidence is that mercuric chloride possesses weak genotoxic activity but does not cause point mutations (WHO 2011b). US EPA (IRIS 2012) evaluation of mercuric chloride indicates that a linear low-dose extrapolation is not appropriate as kidney tumours seen in mice occurred at doses that were also nephrotoxic.

On this basis, a threshold approach is considered appropriate, based on the most sensitive effect associated with mercury exposure. The following threshold values are available from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011)	Guideline established on the basis of methyl mercury	
FSANZ (2003)	PTWI = 0.003 mg/kg/week	Value for total mercury referenced from JECFA 1989, based on methyl mercury.
International		
WHO (2011b)	TDI = 0.002 mg/kg/day	The current WHO DWG (2011a, consistent with the review conducted in 2003) has derived a guideline of 0.006 mg/L, based on a TDI of 0.002 mg/kg/day derived from a NOAEL of 0.23 mg/day associated with kidney effects in a 26-week study in rats and an uncertainty factor of 100. A similar TDI was derived on the basis of a LOAEL of 1.9 mg/kg/day associated with renal effects in a 2-year rat study and an uncertainty factor of 1000.
JECFA (WHO 2011a)	PTWI = 0.004 mg/kg (equivalent to PTDI = 0.0006 mg/kg/day)	Review of mercury by JECFA indicated that the predominant form of mercury indoors, other than fish and shellfish, is inorganic mercury and, while data on speciation is limited, the toxicological database on mercury (II) chloride was relevant for establishing a PTWI for foodborne inorganic mercury. A PTWI was established on the bases of a benchmark dose approach, where the $BMDL_{10}$ of 0.06 mg/kg/day for relative kidney weight increases in male rates was considered as the point of departure. A 100 fold uncertainty factor was applied.
WHO (2000b)	TC = 0.001 mg/m^3	TC or guideline value derived on the basis of a LOAEL derived from occupational studies on elemental vapour. WHO notes that this value is expected to be adequately protective of renal effects associated with exposure to inorganic mercury.
WHO (2003)	TDI = 0.002 mg/kg/day TC = 0.0002 mg/m^3	TDI derived as noted in the DWG above. A TC in air was also derived for elemental mercury in air (0.0002 mg/m^3) associated with CNS effects in workers exposed to elemental mercury. The relevance of this value to inorganic compounds is not discussed. The TC is considered relevant to inhalation exposures to elemental vapour.
EA (2009)	TDI = 0.002	TDI referenced from WHO (2003) and WHO DWG (2011).

Source	Value	Basis/Comments
	mg/kg/day TC = 0.0002 mg/m^3	Inhalation value (converted to a dose by the EA) is based on the WHO (2003) value and has been assumed to be relevant to inorganic mercury in air.
RIVM (2001)	TDI = 0.002 mg/kg/day	Derived on the same basis as WHO. No inhalation value is derived for inorganic mercury.
ATSDR (1999)	No chronic MRLs derived	No chronic duration MRLs have been derived for inorganic mercury. An intermediate duration oral MRL of 0.002 mg/kg/day was derived.
US EPA (IRIS 2012)	RfD = 0.0003 mg/kg/day	RfD (last reviewed in 1995) based on a LOAEL of 0.226 mg/kg/day associated with autoimmune effects in a subchronic rat feeding study and an uncertainty factor of 1000. No RfC is available for inorganic mercury. An RfC of 0.0003 mg/m^3 is derived for elemental mercury.

The PTWI derived for inorganic mercury available from JECFA (WHO 2011a) is considered to provide the most current review of the available studies in relation to exposure to inorganic mercury and has been used in the derivation of a soil HIL.
Inhalation values for mercury are derived from occupational studies associated with elemental mercury vapour. While WHO (2000b) provides some comment on the potential relevance of the guideline value derived to the assessment of inorganic mercury in air, the available toxicity data does not specifically relate to the inhalation of inorganic mercury compounds likely to be present in soil contamination. EA (2009) has adopted the lower guideline value (TC) available from WHO (2003) assuming its relevance to the assessment of inorganic mercury. This approach has been adopted, though it is noted that the derived HIL is essentially the same if the WHO TC value is adopted, compared with the HIL derived if the TDI for all routes of exposure is used.

10.4.2.2 Methyl Mercury

Long-term exposure to methyl mercury has induced renal tumours in mice, but only at doses at which significant nephropathy was also evident (WHO 2004). Review by the US EPA (IRIS) concluded that methyl mercury is not a potent genotoxic agent and that methyl mercury -nduced tumours in mice were likely to have a non-genotoxic mode of action. On this basis, a threshold approach is considered appropriate based on the most sensitive effect associated with methyl mercury exposure. The following threshold values are available from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011)	TDI = 0.00047 mg/kg/day	Current ADWG (NHMRC 2011) derived a guideline of 0.001 mg/L on the basis of a PTWI of 0.0033 mg/kg derived from the older JECFA evaluation (see below).
FSANZ (2003)	PTWI = 0.003 mg/kg/week (PTDI = 0.00047 mg/kg/day)	Value for total mercury referenced from older JECFA 1989, based on methyl mercury.
International		
WHO (2011b)	Not established for methyl mercury	The current WHO DWG (2011b) has derived a guideline for inorganic mercury in drinking water only.

Source	Value	Basis/Comments
JECFA (WHO 2004)	PTWI = 0.0016 mg/kg/week (PTDI = 0.00023 mg/kg/day)	The most current evaluation by JECFA (WHO 2004) derived a PTWI of 0.0016 mg/kg based on a steady state intake of 1.5 µg/kg/day (from review of mercury in hair and blood, a benchmark dose approach to assess the relationship between maternal hair concentrations and foetal neurotoxicity and a pharmacokinetic model). This intake is estimated to represent the exposure that would be expected to have no appreciable adverse effects on children and applying an uncertainty factor of 6.4. The PTWI was considered to be sufficient to protect developing foetuses, the most sensitive subpopulation identified. The previous evaluations by JECFA (WHO 2000a) identified a PTWI of 0.0033 mg/kg methyl mercury based on review of oral intakes of mercury and hair and blood mercury levels. Subsequent reviewed of the PTWI by JECFA in 2000 identified that the value may not be adequately protective of foetuses and infants, who are more sensitive than adults.
EA (2009)	PTWI = 0.0016 mg/kg/week (PTDI = 00023 mg/kg/day)	Value adopted is referenced from JECFA for all routes of exposure.
RIVM (2001)	TDI = 0.0001 mg/kg/day	Derived on the basis of a NOAEL of 1.3 µg/kg/day for developmental effects in humans (and hair concentrations), and an uncertainty factor of 10.
ATSDR (1999)	MRL = 0.0003 mg/kg/day	Chronic oral MRL derived on the basis of a NOAEL of 0.0013 mg/kg/day (adjusted) associated with CNS effects in humans (and hair concentrations), and an uncertainty factor of 4.5.
US EPA (IRIS 2012)	RfD = 0.0001 mg/kg/day	RfD (last reviewed in 2001) based on a BMD of 0.0009 to 0.0015 mg/kg/day (adjusted) based on CNS effects in humans (and blood concentrations), and an uncertainty factor of 10.

The PTWI derived for methyl mercury from JECFA (WHO 2004) is considered to be based on the most recent detailed review of available studies in relation to exposure to methyl mercury. The TRV established by JECFA is within the same range of values previously established by US EPA and ATSDR and is recommended for use in the derivation of a soil HIL for methyl mercury. No dermal or inhalation specific data is available and hence the PTWI is recommended to be adopted for all routes of exposure.

10.4.3 Recommendation

On the basis of the discussion above, the following toxicity reference values (TRVs) have been adopted for mercury in the derivation of HILs:

Recommendation for Mercury

Inorganic Mercury:

Oral TRV (TRV_O) = 0.0006 mg/kg/day (WHO 2011a) for oral and dermal routes of exposure

Gastrointestinal absorption factor (GAF) = 0.07 (US EPA 2004)

Dermal absorption factor (DAF) = 0.001 (or 0.1%) (US EPA 1995)

Inhalation TRV (TRV_I) = 0.0002 mg/m^3 (WHO 2003) – note this is for elemental mercury

Background intakes from other sources (as % of TRV):

BI_O = 40% for oral and dermal intakes

BIi = 10% for inhalation

Uptake in home-grown produce considered in derivation of HIL A.

Methyl Mercury:

Oral TRV (TRV_O) = 0.00023 mg/kg/day (WHO 2004 and EA 2009) for all routes of exposure

Dermal absorption factor (DAF) = 0.001 (0r 0.1%) (as for inorganic mercury)

Background intakes from other sources (as % of TRV):

BI_O = 20% for oral and dermal intakes

BIi = 20% for inhalation

10.5 Calculated HILs

On the basis of the above, the following HILs have been derived for mercury (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

10.5.1 Inorganic Mercury

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	40	66	21	13	<1
Residential B	120	56	--	44	<1
Recreational C	80	72	--	28	<1
Commercial D	730	48	--	52	1

-- Pathway not included in derivation of HIL

10.5.2 Methyl Mercury

The previous HIL A for methyl mercury was 10 mg/kg. Direct calculation of the revised HIL on the basis of the above assumptions results in the calculation of an HIL A of 7 mg/kg. Given the level of uncertainty and variability in the estimation of intakes from other sources (background, particularly from fish) and the difficulty in obtaining reliable analytical data, the existing HIL A of 10 mg/kg has been retained. The HILs for other exposure scenarios have been calculated directly on the basis of the assumptions outlined in this document.

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	10	99	--	1	<1
Residential B	30	95	--	5	<1

Recreational C	13	97	--	3	<1
Commercial D	180	93	--	7	<1

-- Pathway not included in derivation of HIL

It is noted that the analysis of methyl mercury in soil can be difficult and hence the reliability/quality of the data collected should be considered in any assessment of methyl mercury.

10.6 References

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11 Nickel

11.1 General

Several comprehensive reviews of nickel in the environment and its toxicity to humans are available and should be consulted for more detailed information not presented in this summary (ATSDR 1997; ATSDR 2005; WHO 1991; EA 2009a). The following provides a summary of the key aspects of nickel that are relevant to the derivation of a soil HIL.

Nickel is a silvery white metal that is stable under environmental conditions. It occurs naturally in the Earth's crust. It is the 24th most abundant element and is primarily found as oxides or sulfides (ASTDR 1997). Nickel is extracted from mined ore via pyro- and hydrometallurgical refining processes. Most nickel is used for the production of stainless steel and other nickel alloys with high corrosion and temperature resistance. The primary sources of nickel emissions into the atmosphere are the combustion of coal and oil for heat or power generation, the incineration of waste and sewage sludge, nickel mining and primary production, steel manufacture, electroplating and cement manufacturing (WHO 1991).

The chemistry of nickel is complex, and the toxicological properties of the various compounds depend on physicochemical characteristics, surface chemistry, solubility, geological history. Hence it is important that any site specific assessment of nickel consider these issues.

11.2 Previous HIL

The derivation of the previous HIL (HIL A = 600 mg/kg) is presented by Turczynowicz & Sabordo (1996). In summary, the HILs were derived on the basis of the following:

- Based on available information from Australia, background intakes for a 2 ½-year-old child were estimated to comprise up to 179.88 µg/day.
- A reference dose (RfD) of 0.02 mg/kg/day, referenced from a study by Hall & Rumack (1995) was adopted as the toxicity reference value.
- Dermal absorption was considered to be negligible.
- Based on potential intakes via ingestion, inhalation and intake derived from home-grown produce, a soil criterion in the range of 200 mg/kg (with produce) to 800 mg/kg (no produce) was suggested.
- A soil criterion was also derived on the basis of hypersensitivity with the target population being those that have been sensitised in the community. Based on an oral provocation threshold of 0.0083 mg/kg/day, referenced from NHMRC/ARMCANZ (1994), and consideration of nickel leachability (83%), a soil HIL of 600 mg/kg was derived.
- The calculated soil HIL was considered to also be adequately protective of carcinogenic risks associated with inhalation exposures.

11.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed, as noted below.

11.3.1 Oral Bioavailability

Bioavailability has not been considered in the previous HIL, as insufficient data is available to adequately define the bioavailability of the different forms of nickel from soil. On this basis, a default

approach of assuming 100% oral (and inhalation) bioavailability has been adopted in the derivation of an HIL.

It is noted that the rate of nickel absorption from the gastrointestinal tract is dependent on its chemical form. While soluble nickel compounds (e.g. $NiSO_4$) are better absorbed than relatively insoluble ones, the contribution of the poorly soluble compounds to total nickel absorption may be more significant, since they are more soluble in the acidic gastric fluids. In human volunteers who ingested nickel sulfate in the drinking water or food, at doses of between 12 and 50 µg/kg body weight (one treatment), the amount of nickel absorbed averaged 27±17% of the dose ingested in water compared with 0.7±0.4% of the same dose ingested in food (WHO 1991). These issues should be addressed in a site-specific assessment.

11.3.2 Dermal absorption

Nickel is a potent skin sensitiser, and as many as 1–4% of men and 8–20% of women in the general population may be nickel-sensitive. Both oral and dermal exposures to nickel can cause hypersensitivity reactions of the skin. There has been a limited number of studies on the dermal absorption of nickel through human skin and even fewer examining uptake from soil. The Environment Agency (EA 2009a) reviewed the available studies and recommended the use of a value of 0.005 (0.5%), based on a study by Moody et al. (2009).

Moody et al. (2009) measured in vitro dermal absorption of radioactive nickel chloride through human breast skin over a 24-hour period with and without a spiked commercial soil. It is noted that several studies have noted that most nickel applied as a soluble salt is bound within the skin and does not reach systemic circulation though, until this effect is better documented, the dermal absorption value from Moody et al. (2009) has been adopted in the derivation of a soil HIL.

It is noted that US EPA (2004) has recommended the use of a gastrointestinal absorption factor (GAF) of 4% for nickel based on a diet study in rats used in the derivation of the oral RfD. Little supporting information is available on the basis for the GAF recommended by US EPA. The recommended oral TRV is derived from WHO (2008) as used in the derivation of the guidelines for drinking water. The TRV is based on drinking water studies in (fasted) nickel-sensitised humans, consistent with the TRV derived from a two-generation drinking water rat study. As the study basis for the GAF differs from that relevant to the TRV adopted, and insufficient data is available on the GAF to determine its relevance to the oral TRV recommended, the application of the GAF has not been considered in the derivation of the soil HIL.

11.3.3 Inhalation of Dust

Nickel is not volatile and inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, potential inhalation exposures associated with dust have been considered in the HIL derived.

11.3.4 Plant Uptake

A detailed review of the plant uptake of nickel is presented in EA (2009b). This review considered studies that are based on the uptake of nickel into green vegetables, root vegetables, tuber vegetables, herbaceous fruit, shrub fruit and tree fruit. The review provides recommendations on soil-to-plant uptake factors that are relevant for these types of produce. The recommendations from this review have been considered in the derivation of a residential HIL A and are summarised below for the range of crops considered:

Produce Group	Plant Uptake Factors (mg/kg produce fresh weight per mg/kg soil) (EA, 2009b)
Green vegetables	0.0038
Root vegetables	0.0043

Produce Group	Plant Uptake Factors (mg/kg produce fresh weight per mg/kg soil) (EA, 2009b)
Tuber vegetables	0.0019
Tree fruit	0.0034

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce (also included in background intakes). To address this in the derivation of HIL A, half the intake estimated to be derived from home-grown produce is assumed to be already accounted for in the total background intake (noted below).

11.3.5 Intakes from Other Sources – Background

Review of current information from Australia indicates the following:

- Dietary intakes of nickel have been assessed in the *22nd Australian Total Diet Survey* (FSANZ 2008), where mean intakes for children aged 2–3 years were reported to be 83–91 µg/day, or 6.2–6.9 µg/kg/day. Estimates provided by ATSDR (2005) and EA (2009b) suggest that adult intakes from food are 69–162 µg/day (up to 2.3 µg/kg/day) and 130 µg/day (1.9 µg/kg/day) respectively. Intakes for children (ATSDR 2005) range from 6.9 µg/kg/day (6–11 months old) to 9.5 µg/kg/day (children aged less than 18).
- Typical concentrations of nickel reported in the ADWG (NHMRC 2011) are less than 0.01 mg/L, resulting in an intake (1 L/day and body weight of 15.5 kg) by toddlers of 0.6 µg/kg/day.
- Based on intakes estimated from Australian data, background intakes by young children are approximately 7 µg/kg/day, up to 60% of the recommended oral TRV.
- Nickel was reported in ambient air data collected in NSW (DEC 2003) where concentrations (24-hour averages) in urban, regional and industrial areas assessed ranged from 0.86–20 ng/m^3 (average of 3.5 ng/m^3). Typical background concentrations in air reported in (EA (2009b) range from 0.3–4.5 ng/m^3, consistent with that reported by DEC (2003). These background concentrations comprise (based on average concentrations) approximately 17% of the recommended TC. A conservative background of 20% of the recommended inhalation TRV has been assumed for intakes from air.

11.4 Identification of Toxicity Reference Values

11.4.1 Classification

IARC (2012) classified nickel compounds a Group 1—carcinogenic to humans. The IARC working group noted that the overall evaluation of nickel compounds as a group was undertaken on the basis of the combined results of epidemiological studies, carcinogenicity studies in experimental animals, and several types of other relevant data supported by the underlying assumption that nickel compounds can generate nickel ions at critical sites in their target cells.

It is noted that US EPA has classified nickel refinery dust as Group A—human carcinogenic.

11.4.2 Review of Available Values/Information

The toxicity of nickel is complex and appears to differ via the different routes of exposure and hence the following addresses oral exposures separately from inhalation exposures.

11.4.2.1 Oral

Review in WHO (2011) concluded that there was no substantial evidence that nickel compounds may produce cancers other than in the lung or nose in occupationally exposed persons. Limited animal studies on carcinogenic effects after oral exposures to nickel compounds did not show any significant increase in tumours. Review by EA (2009b) noted that while not all expert groups (WHO, US EPA, EU) have explicitly concluded that there is no carcinogenic concern from ingested nickel, none of those evaluating oral exposure concluded that a non-threshold approach should be undertaken. Hence the assessment of oral intakes on the basis of a threshold approach is reasonable. The following quantitative values are available from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011)	TDI = 0.005 mg/kg/day	The ADWG (NHMRC 2011) derived a health-based guideline of 0.02 mg/L based on NOEL of 5 mg/kg/day associated with organ-to-body-weight ratios in a 2-year rat study and an uncertainty factor of 1000. An additional factor of 10 was not included to address carcinogenicity as this was only relevant for inhalation exposures, not oral exposures.
International		
WHO (2011)	TDI = 0.012 mg/kg/day	The current WHO DWG (2011), based on a review conducted in 2005, derived a guideline of 0.07 mg/L based on a TDI of 0.012 mg/kg/day derived from a LOAEL of 0.012 mg/day established from a study associated with hand eczema in nickel-sensitised volunteers who had fasted prior to administration of the nickel salt (Nielsen et al. 1999). This study (using fasted patients) was considered conservative and an uncertainty factor of 1 was adopted. The review also noted that a general guideline value of 0.13 mg/L could also be derived from a TDI of 0.022 mg/kg/day on the basis of a two-generation study in rats where a NOAEL of 2.2 mg/kg/day could be determined for all end-points studied and an uncertainty factor of 100.
RIVM (2001)	TDI = 0.05 mg/kg/day	TDI derived on the basis of a NOAEL of 5 mg/kg/day (same study considered in the ADWG) and an uncertainty factor of 100.
EA (2009b)	TDI = 0.012 mg/kg/day	Adopted the WHO evaluation presented in the WHO DWG (2011).
TERA (1999)	RfD = 0.008 mg/kg/day	RfD derived for soluble nickel salts on the basis of a LOAEL of 7.6 mg/kg/day associated with kidney effects in rats and an uncertainty factor of 1000. The value derived was in addition to the diet rather than total intake.
ATSDR (2005)	No oral MRL derived	
US EPA (IRIS 2012)	RfD = 0.02 mg/kg/day	RfD (last reviewed in 1991) based on a NOAEL of 5 mg/kg/day (same study as considered in the ADWG (NHMRC 2011)) and an uncertainty factor of 300.

11.4.2.2 Inhalation

Inhalation exposures to nickel are complex, with the toxicity dependent on the form of nickel present. The most recent review of nickel toxicity by EA (2009b) indicates the following with respect to the consideration of inhalation exposures:

- Nickel and compounds are established carcinogens via the inhalation route with tumours of the respiratory tract a consequence of occupational exposure to both soluble and insoluble nickel salts.
- Nickel compounds are generally considered to be genotoxic; however the mechanism of action associated is not well understood. The lack of understanding has resulted in a conservative approach that genotoxicity is critical in the development of tumours and that a non-threshold may be appropriate.
- Non-threshold assessments of inhalation cancer risk have relied on occupational studies to derive a quantitative value (unit risk). These occupational studies relate to specific nickel compounds in the occupational environment including nickel subsulfide (WHO 2000) and nickel refinery dusts (US EPA IRIS 2012).
- WHO (1991) notes that very high concentrations of nickel are required to produce teratogenic and genotoxic effects.
- Review by RIVM (2001) suggested the mechanism of action suggests a cytotoxic effect and that a threshold was appropriate for inhalation exposure to nickel. Review by EPAQS (2008, as referenced by EA 2009b) also suggested a non-genotoxic threshold mechanism of action and that a threshold can be considered.
- A threshold value can be adopted for inhalation exposure that is protective of both carcinogenic and non-carcinogenic effects. However it is noted that the assessment of carcinogenic issues relies on the non-threshold values available and acceptance of a 1 in 100,000 excess lifetime cancer risk.

With respect to the derivation of a soil HIL, nickel is not volatile and hence inhalation exposures are only relevant to dust intakes. Carcinogenic end points are expected to be of particular importance if they are derived from nickel refinery dust of nickel subsulfide, but dust generated from soil contamination is not likely to be significant and hence the consideration of carcinogenic effects using a non-threshold approach may not be appropriate. It is therefore appropriate to consider intakes on the basis of a threshold approach associated with the most significant end point which includes both carcinogenic and non-carcinogenic effects. These issues were considered by EA (2009b), where a threshold value was recommended that was considered protective of both carcinogenic and non-carcinogenic effects.

The following quantitative threshold values (including guideline values derived to be protective of carcinogenic effects) are available for the assessment of inhalation exposures from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian – No guidelines derived		
International		
WHO (2000)	GV = 0.025 µg/m^3	Review by WHO (2000) established a range of air guideline values for nickel based on a non-threshold approach with a unit risk derived from occupation studies associated with nickel subsulfate. It has been assumed that the nickel ion is the active agent in the occupational studies and therefore the studies are relevant to all nickel exposures. The guideline value noted here is based on an excess lifetime cancer risk of 1 in 100,000.
TERA (1999)	RfC = 0.2 µg/m^3	RfC derived on the basis of a benchmark approach using a $BMCL_{10}$ (HEC) of 0.0017 mg/m^3 associated with lung fibrosis from soluble nickel salts in a rat study and an uncertainty factor of 10. This is the same study as considered by the ADTSR (2005).

Source	Value	Basis/Comments
RIVM (2001)	TC = 0.05 µg/m^3	Tolerable concentration (TC) derived on the basis of a threshold approach from a NOAEC (HEC) of 0.005 mg/m^3 associated with respiratory effects in rats, and an uncertainty factor of 100.
Health Canada (1994)	TC = 0.0035 µg/m^3 TC_{05} = 0.07 mg/m^3	Tolerable concentration (TC) derived on the basis of a threshold approach from a LOAEC (HEC) of 0.0035 mg/m^3 associated with respiratory effects from nickel sulfate in rats, and an uncertainty factor of 1000. Health Canada also derived a tumorigenic concentration of 5%, TC_{05}, based on epidemiology studies of exposed workers at two nickel refineries (based on nickel sulphate and nickel chloride), and derived from the non-threshold dose–response curves.
EPAQS (2008)	TC = 0.02 µg/m^3	TC derived assuming a threshold approach is appropriate, based on a LOAEL of 0.02 mg/m^3 associated with respiratory tract tumours in occupational nickel exposures, and an uncertainty factor of 1000. TC derived is similar to but slightly lower than that derived on the basis of inflammatory response in experimental animals.
EA (2009b)	TC = 0.02 µg/m^3	Adopted evaluation of EPAQS (2008), noting the value derived is protective of carcinogenic and non-carcinogenic effects.
OEHHA (2009)	REL = 0.05 µg/m^3	Chronic inhalation reference exposure level (REL) for nickel and nickel compounds (except nickel oxide where a higher REL is derived) based on a NOAEL (HEC) of 0.0016 mg/m^3 associated with respiratory/lung effects in a 104-week rat study, and an uncertainty factor of 30. OEHHA also provide a non-threshold unit risk for nickel and compounds.
ATSDR (2005)	Inhalation MRL = 0.09 µg/m^3	Chronic inhalation MRL derived on the basis of a NOAEL (HEC) of 0.0027 mg/m^3 associated with lung effects in rats, and an uncertainty factor of 30.
US EPA (IRIS 2012)	GV = 0.04 µg/m^3	Review by the US EPA (last reviewed in 1991) established a range of air guideline values for nickel based on a non-threshold approach with a unit risk derived from occupation studies associated with nickel refinery dust. The guideline value noted here is based on an excess lifetime cancer risk of 1 in 100,000.

11.4.2.3 Identified TRVs

With respect to oral exposures, the more recent review by WHO (2011) is considered appropriate (and most current) and adequately protective of the most critical health effects. The threshold value recommended is considered adequately protective of hypersensitivity responses that may be associated with oral (and dermal) exposures.

With respect to inhalation exposures a number of evaluations are available that consider LOAELs/NOAELs that are similar, with the application of different uncertainty factors. It is recommended that the evaluation provided by EA (2009b) be adopted, where the lower threshold value of 0.02 µg/m^3 is adopted, and is consistent with guidelines derived using a non-threshold approach (at an excess lifetime cancer risk level of 1 in 100,000).

11.4.3 Recommendation

On the basis of the discussion above, the following toxicity reference values (TRVs) have been adopted for nickel in the derivation of HILs:

Recommendation for Nickel

Oral TRV (TRV_O) = 0.012 mg/kg/day (WHO 2011) for oral and dermal routes of exposure

Dermal absorption factor (DAF) = 0.005 (or 0.5%) (EA 2009a)

Inhalation TRV (TRV_I) = 0.00002 mg/m^3 (EA 2009b)

Background intakes from other sources (as % of TRV):

BI_O = 60% for oral and dermal intakes

BIi = 20% for inhalation

Uptake in home-grown produce considered in derivation of HIL A.

11.5 Calculated HILs

On the basis of the above, the following HILs have been derived for nickel (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	400	55	26	4	15
Residential B	1200	42	--	11	47
Recreational C	1200	80	--	11	9
Commercial D	6000	30	--	11	59

-- Pathway not included in derivation of HIL

11.6 References

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12 Selenium

12.1 General

Several comprehensive reviews of selenium in the environment and its toxicity to humans are available and should be consulted for more detailed information not presented in this summary (ATSDR 2003; WHO 1987; CCME 2007; NHMRC 2006; EA 2009a; EA 2009b). The following provides a summary of the key aspects of selenium that are relevant to the derivation of a soil HIL.

Selenium is a non-metal that is widely but unevenly distributed in the Earth's crust. In its elemental form selenium forms metallic grey to black crystals but in nature it primarily occurs as sulfide minerals or with silver, copper, lead, and nickel minerals. Selenium's physical and chemical properties are similar to those of sulfur (ATSDR 2003).

Selenium is manufactured as a by-product of copper refining. It is widely used in electronics and photography because of its semiconductor and photoelectric properties. A variety of selenides, selenates and selenium salts are used in pigments, some pharmaceutical products (sodium selenide in anti-dandruff shampoo) and in dietary supplements (ATSDR 2003).

Selenium is considered an essential element and is important for an extensive range of biochemical functions within the body. As such, adverse effects are associated with both deficiency and toxicity associated with excess intake.

12.2 Previous HIL

No previous HIL has been established for selenium in soil.

12.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed, as noted below.

12.3.1 Oral Bioavailability

Insufficient data is available to adequately define the bioavailability of selenium from soil. On this basis, a default approach of assuming 100% oral (and inhalation) bioavailability has been adopted in the derivation of an HIL. It is noted that a site-specific assessment of bioavailability can be undertaken where required.

12.3.2 Dermal absorption

ATSDR (2003) notes that there is little or no information available on the dermal absorption of selenium sulfides, but selenium disulfides are not believed to be absorbed through intact skin. This is consistent with reviews provided by CCME (2007) and EA (2009a), where dermal absorption of selenium through intact skin has been considered negligible. Based on the limited data available, dermal absorption has been considered negligible in the derivation of soil HIL.

12.3.3 Inhalation of Dust

Selenium is not volatile and inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, potential inhalation exposures associated with dust have been considered in the HIL derived.

12.3.4 Plant Uptake

A detailed review of the plant uptake of selenium is presented by EA (2009b). This review considered studies that are based on the uptake of selenium into green vegetables, root vegetables, tuber vegetables and herbaceous fruit. No data was available on plant uptake into shrub fruit and tree fruit. The review provides recommendations on soil-to-plant uptake factors that are relevant for these types of produce. The recommendations from this review have been considered in the derivation of a residential A HIL and are summarised below for the range of crops considered:

Produce Group	Plant Uptake Factors (mg/kg produce fresh weight per mg/kg soil) (EA, 2009b)
Green vegetables	0.0108
Root vegetables	0.0036
Tuber vegetables	0.00083
Tree fruit	0.003

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce (also included in background intakes). To address this in the derivation of HIL A, half the intake estimated to be derived from home-grown produce is assumed to be already accounted for in the total background intake (noted below).

12.3.5 Intakes from Other Sources – Background

Background intakes of selenium have been estimated by EA (2009a), where intakes from food dominated the total intake. Oral intakes by adults from background sources were estimated to be 34 µg/day from food and 1 µg/day from water. Inhalation intakes were estimated to be 0.06 µg/day based on an average ambient air concentration of 3 ng/m^3.

Review of current information from Australia indicates the following:

- Selenium in dietary intakes has been assessed most recently in the *20th, 22nd* and *23rd Total Diet Surveys* (FSANZ 2003, 2008 and 2011). The *22nd Total Diet Survey* considered a wider range of food sources where estimated mean dietary intakes for children aged 2–3 were 2.8 µg/kg/day. Mean dietary exposures reported in the earlier 20th TDS were 2.6–3 µg/kg/day for toddlers aged 2 years.
- Typical concentrations of selenium reported in the ADWG (NHMRC 2011) are less than 0.005 mg/L, resulting in an intake (1 L/day and body weight of 15.5 kg) by toddlers of 0.32 µg/kg/day.
- Selenium was reported in ambient air data collected in NSW (DEC 2003) where concentrations (24-hour averages) in urban, regional and industrial areas assessed ranged from 0.10–0.65 ng/m^3 (average of 0.2 ng/m^3). These concentrations are lower than those reported in EA (2009a). Based on the mean concentration reported in Australian air, intake by young children is approximately 0.15 ng/kg/day, significantly less than intakes from food and water.
- Based on the above, background intakes by young children are estimated to be 3 µg/kg/day, approximately 60% of the recommended TRV.

12.4 Identification of Toxicity Reference Values

12.4.1 Classification

The International Agency for Research on Cancer (IARC 1987) has classified selenium as Group 3—not classifiable.

It is noted that US EPA has classified selenium as Group D—not classifiable.

12.4.2 Review of Available Values/Information

Insufficient information is available to adequately assess selenium for carcinogenicity. Review by CCME (2007) notes that the available carcinogenicity studies with selenates, selenites and organic selenium compounds have shown negative results. The only selenium compound found to be carcinogenic to experimental animals is selenium sulphide, noted to be not readily present in food and the environment. Selenium supplementation has been shown to significantly inhibit tumours induced by chemicals, viruses and UV radiation.

Reviews on genotoxicity are mixed. Review by CCME (2007) and ATSDR (2003) suggests the available data on genotoxicity of selenium compounds is inconclusive, with studies showing inorganic selenium compounds having both genotoxic and anti-genotoxic effects, with anti-genotoxic effects generally occurring at lower exposure levels than the genotoxic effects. Review by EA (2009a) suggests that some selenium compounds have given indications of genotoxic effects when administered orally to laboratory animals. However, there is evidence that selenium compounds have given rise to genotoxicity by the production of reactive oxygen species; thus, it has been concluded that the genotoxic effect of selenium is likely to have a threshold.

On the basis of the available information, the consideration of a threshold approach for the quantification of selenium intakes is considered reasonable. It is noted that since selenium is an essential element, a number of the threshold values available are associated with recommended dietary intakes (RDIs) or adequate intake (AI) and associated upper limits (ULs) based on available studies. It is noted that in reviewing the available information, threshold values such as ADIs or RfDs should lie between the RDI or AI and the UL established for selenium intakes. ADIs or RfDs that are lower than the RDI or AI are considered overly conservative and may lead to deficiency. The following provides a summary of quantitative values are available from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011)	ADI = 0.24 mg/day or 0.003 mg/kg/day for 70 kg adult	The ADWG (NHMRC 2011) derived a health-based guideline of 0.01 mg/L based on an ADI of 0.24 mg/day derived from review of toxic effects from a 2-year study on 140 people (1991 study). For an adult this is equivalent to an ADI of 0.003 mg/kg/day.
FSANZ (2003 & 2008)	TL = 0.0125 mg/kg/day UL (infants) = 0.007 mg/kg/day UL (adults) = 0.4 mg/day equivalent to 0.006 mg/kg/day for 70 kg adult	Tolerable limit (TL) for selenium considered in the evaluation of dietary exposures to selenium in 20th ATDS (FSANZ 2003). Upper limit for infants and adults considered in the 22nd ATDS (FSANZ 2008) based on the evaluation provided by NHMRC (2006). Also note RDI and AI noted below from NHMRC (2006).
NHMRC (2006)	AI = 0.012–0.015 mg/day for infants RDI = 0.025–0.06 mg/day for children UL = 0.045–0.06 mg/day for infants and 0.09–0.4 mg/day for infants and children, based on 0.007 mg/kg/day. RDI = 0.065–0.075 mg/day for adults	Upper limit (UL) for infants based on a NOAEL from studies showing human milk concentrations are not associated with adverse effects, and an uncertainty factor of 1. There is no evidence of increased toxicity in older children and adolescents and hence the UL derived for infants is adopted for these age groups. UL for adults is based on a NOAEL of 0.8 mg/kg/day associated with brittleness and loss of hair and nails, gastrointestinal disturbances, skin rash, fatigue and effects on the nervous system from a population study,

Source	Value	Basis/Comments
	UL = 0.4 mg/day for adults (including pregnant women) equivalent to 0.006 mg/kg/day for 70 kg adult	and an uncertainty factor of 2 to address sensitive individuals and because of data gaps.
International		
WHO (2011)	UL = 0.4 mg/day	The WHO (2011) review has derived a provisional guideline of 0.04 mg/L based on an upper tolerable intake of 0.4 mg/day. The guideline is considered to be provisional due to uncertainties in the scientific database, however the review notes that it is important to balance recommended intakes with undesirable intakes in setting any guideline level.
CCME (2007)	UL = 0.0055 mg/kg/day for infants	For potential risks posed at contaminated sites in Canada by exposure to contaminants that are also considered to be essential trace elements, Health Canada recommends the use of 'Tolerable Upper Intake Levels' (ULs) as the reference exposure levels for risk assessment. Since selenium is an essential trace element in human health and selenium compounds do not appear to be carcinogenic, the ULs for all life stage groups are proposed for use in the derivation of the human health soil quality guidelines for selenium. The UL noted here is the lower value relevant to infants (the most sensitive age group).
EA (2009a)	UL = 0.45 mg/day or 0.006 mg/kg/day for a 70 kg adult	A Safe Upper Level of 450 μg of total selenium ('ionic selenium') per day was established. This was derived from a LOAEL of 910 μg Se day^{-1} for mild signs of selenosis (changes in the hair and nails) indicated in an exposed Chinese population, and the use of an uncertainty factor (UF) of 2 to convert the LOAEL for 'slight effects' to a NOAEL (no observed adverse effect level). As the LOAEL was from a population study, a UF to take into account inter-individual variation was said not to be required.
ATSDR (2003)	MRL = 0.005 mg/kg/day	Chronic oral MRL derived for selenium based on a NOAEL of 0.015 mg/kg/day for disappearance of symptoms of selenosis in recovering individuals, and an uncertainty factor of 3 to account for sensitive individuals.
US EPA (IRIS 2012)	RfD = 0.005 mg/kg/day	RfD (last reviewed in 1991) based on a NOAEL of 0.015 mg/kg/day (same study as considered by ATSDR), and an uncertainty factor of 3.

There is unanimity among the expert groups that the heavily exposed population within mainland China offers the best opportunity of defining the toxicological consequences of long-term oral exposure to 'selenium'—a term which would appear to include all selenium compounds other than the sulphides. The available threshold values for selenium are based on these studies and typically relate to an upper limit (UL); that is, an intake that can be consumed daily over a lifetime without significant risk to human health on the basis of available evidence. The values derived by ATSDR and US EPA are based on a UL from the same studies and they have both considered an uncertainty factor of 3. Review by EA (2009a) suggested that, given the large population group considered in the studies, the

use of the uncertainty factor may not be required. There are differences in the interpretation of the various studies used to derived ULs with variability in assumed body weights most significant. Hence there is some variability in the threshold values derived by different organisations.

The value of 0.006 mg/kg/day, the lower UL value recommended/endorsed by NHMRC (2006), is consistent with that derived from CCME (2007) and EA (2009a) and is similar to that derived by ATSDR (2003) and US EPA (IRIS 2012). Hence the UL from NHMRC is considered reasonable for the quantification of oral intakes associated with selenium and is recommended as a TDI for the derivation of a soil HIL.

There are no dermal or inhalation specific values available for selenium therefore the TDI adopted is considered relevant for all intakes.

12.4.3 Recommendation

On the basis of the discussion above, the following toxicity reference values (TRVs) have been adopted for selenium in the derivation of HILs:

Recommendation for Selenium

Oral TRV (TRV_O) = 0.006 mg/kg/day (NHMRC 2006 and EA 2009a) for all routes of exposure

Dermal absorption factor (DAF) = negligible (0%)

Background intakes from other sources (as % of TRV):

BI_O = 60% for oral and dermal intakes

BIi = 60% for inhalation

Uptake in home-grown produce considered in derivation of HIL A.

12.5 Calculated HILs

On the basis of the above, the following HILs have been derived for selenium (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	200	62	38	--	<1
Residential B	1400	100	--	--	<1
Recreational C	700	100	--	--	<1
Commercial D	10 000	100	--	--	<1

-- Pathway not included in derivation of HIL

12.6 References

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13 Zinc

13.1 General

Several comprehensive reviews of zinc in the environment and its toxicity to humans are available and should be consulted for more detailed information not presented in this summary (ATSDR 2005; WHO 2001; NEHF 1997). The following provides a summary of the key aspects of zinc that are relevant to the derivation of a soil HIL.

Zinc is ubiquitous in the environment and occurs in the Earth's crust at an average concentration of about 70 mg/kg. Zinc is not found in elemental form in nature, and occurs in the +2 oxidation state primarily as various minerals such as sphalerite (zinc sulfide), smithsonite (zinc carbonate), and zincite (zinc oxide). Fifty-five zinc-containing minerals are known to exist. In its pure elemental (or metallic) form, zinc is a bluish-white shiny metal (WHO 2001).

Most rocks and many minerals contain zinc in varying amounts. Commercially, sphalerite (ZnS) is the most important ore mineral and the principal source of the metal for the zinc industry (WHO 2001). Inorganic zinc salts have numerous commercial uses. Zinc oxide is used in the rubber industry as a vulcanisation activator and accelerator and to slow down oxidation, and also as a reinforcing agent, heat conductor, pigment, UV stabiliser, supplement in animal feeds and fertilisers, catalyst, chemical intermediate, and mildew inhibitor. Zinc sulfate is used in rayon manufacture, agriculture, zinc plating, and as a chemical intermediate and mordant. Zinc chloride is used in smoke bombs, in cements for metals, in wood preservatives, in flux for soldering, in the manufacture of parchment paper, artificial silk, and glues, as a mordant in printing and dye textiles, and as a deodorant, antiseptic and astringent. Zinc chromate is used as a pigment in paints, varnishes, and oil colours. In addition, zinc phosphide is used as a rodenticide while zinc cyanide is used in electroplating.

Zinc is an essential element for all living things, including man. Zinc-containing proteins and enzymes are involved in every aspect of metabolism, including the replication and translation of genetic material. Hence adverse effects are associated with deficiency and toxicity associated with excess intake. Zinc deficiency has been reported to affect children of many countries while other groups identified at particular risk are women of child-bearing age and the elderly. The main cause of human zinc deficiency is consumption of diets that contain little highly bioavailable zinc (NEHF 1997).

13.2 Previous HIL

The derivation of the previous HIL (HIL A = 7000 mg/kg) for zinc is presented by Imray & Neville (1996). In summary, the HIL was derived on the basis of the following:

- Based on data from the US, background intakes for adults were estimated to be 0.23 mg/kg/day, 77% of the adopted threshold TDI of 0.3 mg/kg/day.
- A tolerable daily intake (TDI) of 0.3 mg/kg/day, referenced from ATSDR, relevant for soluble zinc salts was adopted. It was noted that insoluble salts and metallic zinc may have a lower bioavaiability.
- Dermal absorption was considered to be negligible.
- An HIL was derived on the basis of soil ingestion by a 2-year-old child, assuming 100% bioavailability.

13.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed, as noted below.

13.3.1 Oral Bioavailability

Insufficient data isavailable to adequately define the bioavailability of zinc from soil as it will be dependent on the form present. On this basis a default approach of assuming 100% oral (and inhalation) bioavailability has been adopted in the derivation of an HIL.

The toxicokinetic properties of ingested zinc have been extensively studied. The bioavailability of zinc from specific foods ranges from 10–40%. Absorption from the gastrointestinal tract is homeostatically controlled. Under normal physiological conditions 20–30% of ingested zinc is absorbed (Imray & Neville 1996). It is expected that bioavailability from soil will depend on the form present and may be considered further in a site-specific assessment.

13.3.2 Dermal absorption

Imray & Neville (1996) note that dermal absorption of zinc occurs, but the mechanism is undefined and studies are limited. Certain zinc compounds (such as acetate and chloride) are skin irritants, though zinc oxide is a common constituent in many topical skin creams, such as sunscreen/block. Data presented by WHO (2001) shows some (low) dermal absorption of zinc in animal studies. Based on the limited data available, it is reasonable to consider that dermal absorption may be more than negligible. Limited data is available regarding the dermal absorption of zinc from soil and hence a default value of 0.1% has been considered. The default value of 0.1% is the lower end of the range considered relevant for metals, as presented by US EPA (1995).

13.3.3 Inhalation of Dust

Zinc is not volatile and inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, potential inhalation exposures associated with dust have been considered in the HIL derived.

13.3.4 Plant Uptake

An important aspect of the potential for plant uptake of zinc is the potential for zinc to be present in soil water. The concentration of zinc in soil solution is dependent on the form and amount of zinc present in the soil, solubility of the particular zinc compound, and the extent of adsorption. Zinc compounds vary significantly in solubility (CCME 1999).

Geochemical differences in zinc concentrations in soil and autonomic selection processes during the evolution of plants result in a great variation in zinc demand and zinc content between plant species and between plant genotypes of the same species. As a general rule, plants from environments poor in zinc are characterised by low zinc concentrations, those from zinc-enriched environments by high concentrations (WHO 2001).

Zinc toxicity to plants affects general physiological processes, e.g. transpiration, respiration and photosynthesis, and plant development in general can be visibly inhibited. The critical leaf tissue concentration of zinc at which growth is affected was found for many plant species to be between 200 and 300 mg/kg dry matter (WHO 2001). However, zinc phytotoxicity in leaves can depend to a large extent on the plant species, the age of the leaf and other factors such as exposure period and exposure concentration.

An extensive literature review of plant uptake of zinc has not been undertaken, and few quantitative values are available that are specifically relevant to different types of edible produce, but the potential for plant uptake has been considered in the derivation of the HIL A. The approach adopted by MfE (2011) in the derivation of a soil guideline where plant phytotoxicity may be of importance has been adopted in the derivation of an HIL. This approach considered potential intakes associated with

consumption of home-grown produce in soil concentrations that are not phytotoxic (based on the lower limit of phytotoxicity) as part of the overall intake from other sources.

For zinc, plant growth is considered to be affected at concentrations between 200–300 mg/kg tissue concentration. To estimate the additional background intake, a child's produce consumption (0.048 kg DW[3]/day) was multiplied by 200–300 mg/kg and divided by the child body weight of 15.5 kg to obtain the maximum additional background daily intake for 100 % of produce being home-grown. For the consumption of 10% home-grown produce this results in an additional intake of 0.06 to 0.09 mg/kg/day was considered.

It is noted that the inclusion of home-grown produce in the calculations presented for HIL A results in some double counting of intakes from fruit and vegetable produce. The amount of double counting cannot be easily determined; however, to partially address this issue, the lower intake value calculated for zinc from home-grown produce has been included in the derivation of HIL A.

13.3.5 Intakes from Other Sources – Background

Review of current information from Australia indicates the following:

- Zinc in dietary intakes has been assessed most recently in the *20th* and *23rd Total Diet Survey* (FSANZ 2003 and 2011) where mean dietary exposures ranged from 0.627 mg/kg/day for infants and 0.5 mg/kg/day for toddlers aged 2–3 years to 0.128 mg/kg/day for adult females. These intakes were higher than the recommended daily intakes (RDI) established by NHMRC (as noted by FSANZ 2003) for adult males, boys, toddlers and infants and lower than the RDI for adult females and girls. The RDI for zinc (NHMRC 2003 and 2006) ranges from 3 mg/day for breastfed infants, 3–6 mg/day for formula-fed infants to 4–5 mg/day for children aged 7 months to 3 years, 6 mg/day for 4–7-year-olds, 9 mg/day for 8–11-year-olds and 12 mg/day for 12–18-year-olds. The mean intake by infants was considered to comprise up to 63% of the tolerable limit of 1 mg/kg/day established by WHO.
- Typical concentrations of zinc reported in the ADWG (NHMRC 2011) are up to a maximum 0.26 mg/L with typical concentrations less than 0.05 mg/L. Based on typical and maximum concentrations, these result in intakes (1 L/day and body weight of 15.5 kg) by toddlers of 3–20 µg/kg/day.
- Zinc was reported in ambient air data collected in NSW (DEC 2003) where concentrations (24-hour averages) in urban, regional and industrial areas assessed ranged from 11–71 ng/m^3 (average of 33 ng/m^3). These concentrations are consistent with those reported in New Zealand and Canada (HSDB) but lower than those reported in the US and Germany (from older data) (WHO 2001) and the UK (HSDB). Based on the mean concentration reported in Australian air, intake by young children is approximately 25 ng/kg/day, significantly less than intakes from food and water.
- Based on the above, background intakes by young children (2 years) are estimated to be approximately 0.4 mg/kg/day (dominated by dietary intakes), which is above the RDI of 0.32 mg/kg/day and approximately 80% of the recommended TDI. Intakes estimated by WHO (2001) for infants and children aged 2 months to 19 years range from 5.6–13 mg/day (from dietary intakes). For a 2-year-old child these intakes range from 0.4–0.9 mg/kg/day (80% to greater than 100% of the recommended TD). Based on mean intakes from Australian data, background intakes can be assumed to comprise up to 80% of the recommended oral TRV.

[3] It has been assumed that fruit and vegetable crops contain at least 80% moisture. This value has been used to convert wet weight consumption rates into dry weight consumption rates.

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13.4 Identification of Toxicity Reference Values

13.4.1 Classification

The International Agency for Research on Cancer (IARC) has not evaluated zinc with respect to human carcinogenicity.

It is noted that US EPA has evaluated zinc in the more recent 2005 review (available on IRIS). The evaluation notes '*there is inadequate information to assess carcinogenic potential of zinc*' because studies of humans occupationally-exposed to zinc are inadequate or inconclusive, adequate animal bioassays of the possible carcinogenicity of zinc are not available, and results of genotoxic tests of zinc have been equivocal.

13.4.2 Review of Available Values/Information

Insufficient information is available to adequately assess zinc for carcinogenicity. WHO (2001) notes that the weight of evidence supports the conclusion that zinc is not genotoxic or teratogenic. At high concentrations zinc can be cytotoxic. More recent reviews of genotoxicity studies for zinc by EU (2003) and US EPA (2005) are equivocal. The EU (2003) review concluded that in vitro tests indicated that zinc has a genotoxic potential, while the in vivo studies as presented are inconclusive, with sometimes contradictory results. However, there are indications of some weak clastogenic, and possibly aneugenic effects following zinc exposure. The relevance of these findings needs to be clarified.

On the basis of the available information, the consideration of a threshold approach for the quantification of zinc intakes is considered reasonable. It is noted that since zinc is an essential element, a number of the threshold values available are associated with recommended dietary intakes (RDIs) or adequate intake (AI) and associated upper limits (ULs) based on available studies. It is noted that in reviewing the available information, threshold values such as TDIs or RfDs should lie between the RDI or AI and the UL established for zinc intakes. TDIs or RfDs that are lower than the RDI or AI are considered overly conservative and may lead to deficiency. The following quantitative values are available from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011)	No health-based guideline established	The ADWG (NHMRC 2011) has not derived a health-based guideline for zinc, with the current guideline based on aesthetic considerations (taste).
FSANZ (2003)	TDI = 1 mg/kg/day	TDI noted to be derived from WHO (refer to comments provided below from JECFA).

Source	Value	Basis/Comments
NHMRC (2006)	Infants: AI = 2-3 mg/day UL = 4–5 mg/day 1-3 years: RDI = 3 mg/day UL = 7 mg/day Children 4–18 yrs: RDI = 4–13 mg/day UL= 12–35 mg/day Adults: RDI = 8–14 mg/day UL = 35–40 mg/day including during pregnancy and lactation	The upper limit (UL) applies to total zinc intake from food, water and supplements (including fortified food). The UL for infants is based on a NOAEL at a level of 5.8 mg zinc/L of infant formula fed for 6 months, equal to a NOAEL of 4.5 mg/day at 0.78 L milk per day. A UF of 1 was applied, given the length and quality of the study and the fact that there is no evidence of harm from intakes of formula at 5.8 mg zinc/L. Rounding down, a UL of 4 mg was therefore set for infants of 0–6 months. As there was no data for older children and adolescents, this figure was adjusted on a body weight basis, for older infants, children and adolescents and values rounded down. The adverse effect of excess zinc on copper metabolism has been identified as the critical effect on which to base the adult UL. This is based on the consistency of findings from a number of studies where the sensitivity of the marker used (erythrocyte copper–zinc superoxide dismutase) and the quality and completeness of the database for this end point. A LOAEL of 60 mg/day was adopted (and is supported by other studies). A UF of 1.5 is applied to account for inter-individual variability in sensitivity and for extrapolation from a LOAEL to NOAEL. As reduced copper status is rare in humans, a higher UF was unjustified. The adult UL was therefore set at 40 mg/day.
International		
WHO DWG (2011)	No health-based guideline established	The current WHO DWG (2011) derived a guideline of 3 mg/L based on aesthetic issues. The review notes that in 1982, JECFA proposed a daily dietary requirement of zinc of 0.3 mg/kg of body weight and a provisional maximum tolerable daily intake (PMTDI) of 1.0 mg/kg of body weight. The daily requirement for adult humans is 15–22 mg/day. Hence it was concluded that the derivation of a health-based guideline value is not required.
JECFA (WHO 1982)	TDI = 1 mg/kg/day	Provisional maximum tolerable daily intake estimated to be 1 mg/kg/day based on the evaluation that there is a wide margin between nutritionally required amounts of zinc and toxic levels. Clinical studies in which up to 600 mg of zinc sulfate (equivalent to 200 mg elemental zinc) has been administered daily in divided doses for a period of several months, provides a basis for the evaluation.
RIVM (2001)	TDI = 0.5 mg/kg/day	TDI derived on the basis of a LOAEL (adjusted) of 1 mg/kg/day associated with haematological effects in a 1989 human study (from supplements) and a UF of 2.
ATSDR (2005)	MRL = 0.3 mg/kg/day	Chronic oral MRL derived based on a NOAEL of 0.83 mg/kg/day from the same study considered by RIVM (however interpretation of the study differed) and a UF of 3.
US EPA (IRIS 2012)	RfD = 0.3 mg/kg/day	RfD (last reviewed in 2005) based on a LOAEL of 0.91 of 0.015 mg/kg/day, identified as the point of departure associated with haematological effects from a number of oral human studies published from 1984 to 2000 (including the study considered by ATSDR and RIVM) and a UF of 3.

It would be relevant and consistent to consider potential exposures to zinc in soil on the same basis as considered by FSANZ (also noted in WHO 2011) where dietary intakes are addressed. However it is noted that the upper limit of zinc intakes identified for children by NHMRC (2006) is lower than that considered in the *20th Australian Total Diet Survey* (FSANZ 2003), where an upper limit of 7 mg/day for children aged 1–3 years, equivalent to 0.5 mg/kg/day (based on a 15.5 kg child) is identified. This is the same as derived by RIVM (2001) and is lower than the upper limit recommended for adults of 40 mg/day, equivalent to 0.57 mg/kg/day (based on 70 kg adult). It is recommended that the lower value for children of 0.5 mg/kg/day recommended by NHMRC (2006) be adopted.

It is noted that for the derivation of a soil HIL, where young children are most sensitive, background intakes of zinc for young children (aged 2 years) of 0.4 mg/kg/day exceeds the threshold value derived by US EPA and ATSDR. Hence it would not be appropriate to adopt these threshold values for the derivation of a soil HIL.

There are no dermal or inhalation specific values available for zinc, so the TDI adopted is considered relevant for all intakes.

13.4.3 Recommendation

On the basis of the discussion above, the following toxicity reference values (TRVs) have been adopted for zinc in the derivation of HILs:

Recommendation for Zinc

Oral TRV (TRV_O) = 0.5 mg/kg/day (NHMRC 2006) for all routes of exposure

Dermal absorption factor (DAF) = 0.001 (or 0.1%) (US EPA 1995)

Background intakes for the general population = 0.4 mg/kg/day = 80% of the oral TRV (adopted for HIL B, C and D)

Background intakes including plant uptake = 0.46 mg/kg/day = 90% of oral TRV (adopted for HIL A)

Background intake assumed relevant for all pathways of exposure (BI_O and BIi)

13.5 Calculated HILs

On the basis of the above the following HILs have been derived for zinc (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	7400	98	--	1	<1
Residential B	60 000	95	--	5	<1
Recreational C	30 000	98	--	2	<1
Commercial D	400 000	93	--	7	<1

-- Pathway not included in derivation of HIL

13.6 References

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14 Cyanide (free)

14.1 General

Several comprehensive reviews of cyanide in the environment and its toxicity to humans are available and should be consulted for more detailed information not presented in this summary (ATSDR 2006; WHO 2004 and 2011; RIVM 2001; DEFRA & EA 2002; NICNAS 2010). The following provides a summary of the key aspects of cyanide that are relevant to the derivation of a soil HIL.

Cyanide is a chemical group consisting of one atom of carbon connected to one atom of nitrogen by three molecular bonds. Cyanides can both occur naturally or be man-made and many are powerful and rapid-acting poisons. Hydrogen cyanide and the simple cyanide salts (sodium cyanide and potassium cyanide) are common examples of cyanide compounds. Certain bacteria, fungi, and algae can produce cyanide. In certain plant foods, including almonds, millet sprouts, lima beans, soy, spinach, bamboo shoots and cassava roots (which are a major source of food in tropical countries), cyanides occur naturally as part of sugars or other naturally-occurring compounds (ATSDR 2006).

Cyanide in soil and water predominantly comes from industrial processes. Major sources of cyanide in water includes discharges from metal mining processes, organic chemical industries, iron and steel plants or manufacturers, and publicly owned wastewater treatment facilities. Other cyanide sources include vehicle exhaust, releases from certain chemical industries, burning of municipal waste, and use of cyanide-containing pesticides. Much smaller amounts of cyanide may enter water through stormwater runoff where road salts containing cyanides are used.

Cyanide can be present in soil as cyanide complexes, free cyanide or as the gas hydrogen cyanide. The behaviour of cyanide is complex and the potential for free cyanide to be present should include some consideration of the former source. Review of cyanide in soil from a range of sources (RIVM 2001) identified little free cyanide (or hydrogen cyanide gas) present at former manufactured gasworks sites (with most cyanide in the form of Prussian blue), little free cyanide associated with former metallurgic and photographic industry wastes (where most cyanide present is complexed) and other waste materials.

The lifetime of dumped free cyanide and simple cyanides at high or low concentrations in the soil is limited. At high concentrations, leaching and emanation of free cyanide is dominant initially, together with the formation of metal hexacyanide complexes, generally with iron and/or manganese. Later and/or at low concentrations, free cyanide is reduced by biochemical breakdown. Little free cyanide is liberated from cyanide complexes found in soil (RIVM 2001).

14.2 Previous HIL

The derivation of the previous HIL (HIL A = 250 mg/kg) for cyanide is presented by Turczynowicz (1993) and NEPC (1999). In summary, the HIL was derived on the basis of the following:

- Background intakes of cyanide were not estimated due to a lack of data, hence it has been assumed that 25% of the adopted acceptable intake is relevant for exposures from soil.
- A tolerable daily intake (TDI) of 12 µg/kg/day referenced from WHO was considered for free cyanide.
- Ingestion of both soil and dust has been considered assuming 100% is bioavailable and is absorbed.
- Dermal absorption has been considered, with a dermal absorption rate of 5% assumed.
- Inhalation of cyanide in dust has been considered both outdoors and indoors.

14.3 Significance of Exposure Pathways

Ingestion of soil and dust is considered the most significant pathway of exposure for inorganics in soil. The consideration of bioavailability and inclusion of other exposure pathways in the derivation of a soil HIL has been further reviewed, as noted below.

14.3.1 Oral Bioavailability

Insufficient data is available to adequately define the bioavailability of free cyanide. On this basis, a default approach of assuming 100% oral (and inhalation) bioavailability has been adopted in the derivation of an HIL. It is noted that a site-specific assessment of bioavailability can be undertaken where required and relevant.

14.3.2 Dermal absorption

Turczynowicz (1993) noted that cyanides are moderately lipid soluble, which allows them to penetrate the epidermis. Some cyanide compounds, such as potassium cyanide, have a corrosive effect on the skin that increases the rate of absorption. In addition, hydrogen cyanide and soluble cyanide salts can be absorbed by the skin. The value of 5% adopted by Turczynowicz (1993) was estimated.

Limited information is available on dermal absorption of free cyanide, however DTSC (2005) has listed a dermal absorption of 0.1 for free cyanide in soil. Limited information is available to support the value of 0.1, though, as data is lacking, the value has been adopted in the derivation of HILs.

14.3.3 Inhalation of Dust

Inhalation exposures associated with particulates outdoors and indoors are expected to be of less significance than ingestion of soil. While likely to be negligible, potential inhalation exposures associated with dust have been considered in the HIL derived.

14.3.4 Inhalation of HCN Gas

The fate and partitioning of free cyanide in soil to hydrogen cyanide gas has been reviewed. Cyanide behaves somewhat differently in soil with respect to phase partitioning from volatile organics. Phase partitioning (and speciation) depends on the soil pH, ionic strength, complexation and the presence of sunlight (Larsen 2005). As noted by RIVM (2001), little HCN gas has been reported at sites where cyanide (free and/or complexed) is present, particularly sometime after disposal of cyanide wastes. In addition the validity of standard volatilisation models such as the Johnson & Ettinger model (J&E from US EPA 2003) for free cyanide needs to be determined. A more detailed review of free cyanide and relevance of standard vapour models was conducted by RIVM (2001), where the model VOLASOIL (similar to the J&E model) was reviewed in conjunction with field data. It was concluded that HCN gas concentrations in air due to soil contamination are too complex to predict as too many soil factors are involved. On the basis of the above, the generation of HCN gas has not been considered in the derived HILs. The potential presence of HCN gas (and potential inhalation exposures) should be addressed on a site-specific basis.

14.3.5 Plant Uptake

There is little information available on the presence of free cyanide and cyanide species in plants grown on cyanide-affected soil. Similarly, limited data is available on the concentration of free cyanide and cyanide species in different parts of plants. The most relevant information available relates to phytotoxic levels of cyanide. Based on the available information, RIVM (2001) estimated that the maximum concentration that may be present in plants grown in contaminated soil is 1 mg free cyanide/kg produce. At concentrations higher than this, plants are most likely to be unhealthy, hampered in their growth and not suitable for consumption. In addition, the maximum concentration of

free cyanide in soil not affecting seed emergence is 1–5 mg/kg soil, with laboratory studies showing 27 mg free cyanide/kg soil is phytotoxic to plants.

Free cyanide does not accumulate in healthy plants, with practically all free cyanide taken up by healthy plants converted to asparagines (provided phytotoxicity does not occur). Based on the above, plant uptake of free cyanide is not considered significant and has not been considered in the derivation of HIL A.

Note that there are some cyanogenic plants that release elevated concentrations of free cyanide upon damage to their plant cells (RIVM 2001). The presence of these plants and the phytotoxicity of free cyanide should be considered in any site-specific assessment.

14.3.6 Intakes from Other Sources – Background

Some levels of cyanide and free cyanide in the Australian environment are provided in the review undertaken by NICNAS (2010). In general, cyanides can occur naturally at low concentrations in ground and surface water with the ADWG (NHMRC 2011) noting that naturally occurring free cyanide in the water supply is usually less than 0.01 mg/L. Concentrations of free cyanide are available for areas near industrial emissions (including former manufacturing plants), mining operations and accidents. However, concentrations relevant to background intakes by the general public away from these areas are not readily available. While background exposure relevant to the general public is difficult to quantify based on limited information, it is not considered reasonable that the background intake is assumed to be negligible (0%).

WHO (2011) notes that even healthy individuals have a small amount of cyanide in their bodies (mainly associated with the breakdown of cyanogenic foods, vitamin B12 and heavy smoking). DEFRA & EA (2002) identified a range of potential intakes from food (4.2–28 µg/kg/day) and air (0.06 µg/kg/day). Estimates presented by CCME (1997) suggested intakes of free cyanide from air, water and soil may be greater than 0.11 µg/kg/day in infants, lower than estimated by the UK. These intakes vary significantly and have been assumed to comprise approximately 50% of the recommended oral TRV. Background concentrations in air are less than 2% of the recommended inhalation TRV, which are considered to be negligible.

14.4 Identification of Toxicity Reference Values

14.4.1 Classification

The International Agency for Research on Cancer (IARC) has not classified cyanide and US EPA has classified cyanide as Group D—not classifiable.

14.4.2 Review of Available Values/Information

The information on free cyanide toxicity should emphasise the high acute toxicity, which also complicates the interpretation of available data and studies relevant to the assessment of chronic effects and establishing quantitative values. While data is limited, the weight of evidence (WHO 2004, US EPA 2010 and ATSDR 2006) suggests that cyanide in not genotoxic and that it induces developmental effects only at doses or concentrations that are toxic to the mothers. Limited/insufficient information is available on carcinogenicity of cyanide. On this basis, consideration of a threshold dose–response approach is appropriate. The following threshold values are available from Level 1 Australian and International sources:

Source	Value	Basis/Comments
Australian		
ADWG (NHMRC 2011) and	TDI = 0.012 mg/kg/day	Derived from a NOEL of 1.2 mg/kg/day from a 6-month feeding study in pigs (Jackson et al. 1986 and Jackson 1988) and a 100-fold safety factor. The cyanide species is not

Source	Value	Basis/Comments
former WHO DWG (2003)		stated in the guidance provided. Review of the study by NICNAS (2010) and WHO (2004) suggested it was not appropriate as the test animals were experimentally compromised.
NICNAS (2010)	No ADI recommended	No ADI or TDI has been recommended. The review has identified that the most reliable repeated dose study available is from NTP (1993) where a NOAEL of 4.5 mg/kg/day was determined (same study as considered in the WHO (2011) review).
International		
JECFA (WHO 1965)	TDI = 0.05 mg/kg/day	ADI adopted for intakes of cyanide arising from the fumigation of food with HCN. Values derived on the same study as noted by US EPA (IRIS 2012) with consideration of a different uncertainty factor. The value was established in 1965 and has not been replaced.
WHO (2004)	No values derived	Review of hydrogen cyanide and cyanides by WHO indicated a number of limitations with the available data (particularly with respect to chronic assessments) were identified. A chronic inhalation TC could not be derived due to inadequate data.
WHO (2011)	TDI = 0.045 mg/kg/day for short term exposure	No drinking water guideline is established by WHO (2011) as cyanide is considered to occur in drinking water at concentrations well below those of health concern. However WHO has identified that cyanide is highly acutely toxic, where they note the following: '*It is detoxified in the liver by first-pass metabolism following oral exposure. As a consequence, exposure to a dose spread over a longer period, for example through a day, will result in lower toxicity, or higher tolerance, than the same dose given in a single bolus dose. Exposure to high doses can give rise to thyroid toxicity as a secondary effect of exposure due to the inhibition of iodine uptake from the thiocyanate generated through the detoxifying action of rhodanese*.' Hence it is appropriate to establish a short-term guideline rather than a chronic guideline. The review has noted data on acute exposures to cyanide is not suitable for the derivation of a short-term guideline due a high level of uncertainty. However a short-term guideline of 0.5 mg/L has been derived on the basis of NOAEL associated with reproductive effects of 4.5 mg/kg/day from a 90-day (13-week) drinking water study in male rats (NTP 1993), and an uncertainty factor of 100.
DEFRA & EA (2002)	TDIo = 0.012 mg/kg/day TDIi = 0.0009 mg/kg/day (=0.003 mg/m^3)	TDIo derived on the basis of the former WHO DWG, as currently referenced in the ADWG (NHMRC 2011). TDIi derived on the same basis as the current US EPA RfC (with different uncertainty factors).
RIVM (2001)	TDI = 0.05 mg/kg/day TC = 0.025 mg/m^3	TDI was derived on the basis of a NOAEL of 4.5 mg/kg/day associated with male reproductive effects from a 90-day rat study with well-soluble NaCN salt (which forms free cyanide readily after ingestion), and a 100-fold uncertainty factor (as considered by WHO 2011). This is rounded to the

Source	Value	Basis/Comments
		TDI of 0.05 mg/kg/day. TC was derived on the basis of a LOAEL (HEC) of 2.5 mg/m^3 based on critical effects to the CNS and thyroid in an occupational study of HCN, and a 100-fold uncertainty factor (same study as considered by US EPA).
ATSDR (2006)	No chronic MRL Intermediate MRL = 0.05 mg/kg/day	Intermediate MRL (exposures up to 1 year) based on same study and approach considered by WHO (2011).
OEHHA	RfC = 0.009 mg/m^3	Value based on same study considered by US EPA with consideration of a 300-fold uncertainty factor (less than adopted by US EPA).
US EPA (2010)	RfD = 0.0006 mg/kg/day RfC = 0.0008 mg/m^3	RfD based a point of departure ($BMDL_{10}$) of 1.9 mg/kg/day from a 13-week drinking water study in male rats (NTP 1993) and a 3000-fold uncertainty factor. RfC based on a LOAEL (HEC) of 2.5 mg/kg/day based on CNS and thyroid effects in an occupational study (1975) of HCN and application of a 3000-fold uncertainty factor.

In relation to the evaluations presented above for the assessment of oral exposures, the following can be noted:

- There are few good oral studies available for the assessment of chronic effects of exposure to cyanide.
- WHO evaluation considered that, in relation to cyanide exposures and toxicity, it is more relevant to establish a guideline for short-term exposures rather than chronic exposures. Hence the guideline established, from a NOAEL of 4.5 mg/kg/day from the NTP (1993) study was considered relevant to short-term exposures (rather than chronic exposures). The same key study has been considered as the most reliable repeated dose study by NICNAS, RIVM, ATSDR and US EPA, where the NOAEL has been used to derive short-term and chronic toxicity reference values. It is noted that the US EPA review has established a $BMDL_{10}$ of 1.9 mg/kg/day from the study, rather than use the NOAEL.
- The study considered in the derivation of the Australian Drinking Water Guideline (also adopted by the UK review), is based on a study (Jackson et al. 1986 and Jackson 1988) that has been considered to be deficient, though the NOEL of 1.2 mg/kg/day established is slightly lower than but similar to (in the same order of magnitude) as that established on the NTP (1993) study (noted above).
- Toxicity reference values established on the basis of the above studies have primarily incorporated uncertainty factors of 100-fold (10 for interspecies variations and 10 for intraspecies variations), with the exception of the US EPA review.
- The most recent detailed review by US EPA has considered all the available studies, including a range of end points determined in the NTP (1993) study, Jackson et al. (1988), Kamalu (1993) and more recent study by Manzano et al. (2007). The point of departure from these studies ranged from 0.7–14.6 mg/kg/day, with the NTP (1993) study identified as the most appropriate for establishing a toxicity reference value. This is consistent with reviews of other organisations.
- The key difference with the US EPA review (from reviews by other organisations) is the use of a significantly larger uncertainty factor of 3000 (10 for interspecies, 10 for intraspecies, 10 for extrapolating sub-chronic to chronic and 3-fold for database deficiencies). The use of uncertainty factors is based on expert judgement and differs from organisation to organisation. Review by WHO (2011) indicated that the use of a

sub-chronic study to establish a short-term guideline is adequately protective of the chronic effects of oral exposures to cyanide. Hence use of the additional 10-fold sub-chronic to chronic uncertainty factor is not considered warranted. Consideration of database deficiencies is relevant as the available studies for cyanide toxicity are limited. Hence use of a factor of 3-fold is appropriate. On this basis, it is reasonable that a 300-fold uncertainty factor be applied to the point of departure from the NTP (1993) study. If the $BMDL_{10}$ established by the US EPA were considered (1.9 mg/kg/day), this would result in an oral toxicity reference value of 0.006 mg/kg/day. This value is the same as the toxicity reference value adopted in the derivation of the Australian Drinking Water Guidelines of 0.012 mg/kg/day if an additional 2-fold factor were adopted to account for the limitations with the study.

- Consideration of use of an oral toxicity reference value of 0.006 mg/kg/day results in the derivation of an HIL A value of 200 mg/kg. This value is similar to (20% lower than) the existing HIL A of 250 mg/kg/day. Review of the available information in relation to cyanide does not indicate that the available science supports a change to the existing HIL, Hence the existing HIL A should be retained.

With respect to inhalation exposures to HCN, the value available from US EPA (2010) of 0.0008 mg/m^3 has been adopted. It is noted that, similar to the derivation of an oral value, the approach adopted by US EPA is conservative (using large uncertainty factors) as the available data in relation to HCN exposures is more limited. Where HCN is expected to be of significance at a site, it should be evaluated on a site-specific basis as vapour intrusion issues may be of importance (not included in the derivation of HILs)).

14.4.3 Recommendation

On the basis of the discussion above, the following toxicity reference values (TRVs) have been adopted for free cyanide in the derivation of HILs:

Recommendation for Free Cyanide

Oral TRV (TRV_O) = 0.006 mg/kg/day (NHMRC 2011 with inclusion of additional 2-fold uncertainty factor) for oral and dermal routes of exposure

Dermal absorption factor (DAF) = 0.1 (or 10%) (DTSC 2005)

Inhalation TRV (TRV_I) = 0.0008 mg/m^3 (US EPA 2010)

Background intakes from other sources (as % of TRV):

BI_O = 50% for oral and dermal intakes

BIi = 0% for inhalation

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14.5 Calculated HILs

On the basis of the above, the following HILs have been derived for free cyanide (refer to Appendix B for equations used to calculate the HILs and Appendix C for calculations):

HIL Scenario	HIL (mg/kg)	Percentage Contribution from Exposure Pathways			
		Ingestion of Soil/Dust	Ingestion of Home-grown Produce	Dermal Absorption of Soil/Dust	Inhalation (dust)
Residential A	200*	43	--	57	<1
Residential B	300	16	--	84	<1

Recreational C	240	27	--	73	<1
Commercial D	1500	12	--	88	<1

* Retained existing HIL A of 250 mg/kg in guideline

-- Pathway not included in derivation of HIL

14.6 References

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15 Shortened forms

ADI	acceptable daily intake
ADWG	Australian Drinking Water Guidelines
AI	adequate intake
ANZECC	Australia and New Zealand Environment and Conservation Council
APVMA	Australian Pesticides and Veterinary Medicines Authority
ATDS	Australian Total Diet Survey
ATSDR	Agency for Toxic Substances and Disease Registry
BA	bioavailability
BI	background intake
BMD	benchmark dose
BMDL	Benchmark dose lower confidence limit
CCME	Canadian Council of Ministers of the Environment
CICAD	Concise International Chemicals Assessment Document
CNS	central nervous system
DAF	dermal absorption factor
DW	dry weight
EA	Environment Agency (England and Wales)
EHC	Environmental Health Criteria
EPA	Environment Protection Authority
FSANZ	Food Standards Australia New Zealand
GAF	gastrointestinal absorption factor
HEC	human equivalent concentration
HED	human equivalent dose
HIARC	Hazard Identification Assessment Review Committee
HIL	health investigation level
HSDB	Hazardous Substances Data Bank
HSL	health screening level
IARC	International Agency for Research on Cancer
IEUBK	Integrated exposure uptake biokinetic model
IRIS	Integrated Risk Information System

JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	WHO/FAO Joint Meeting on Pesticide Residues
LOAEL	lowest observed adverse effect level
LOEL	lowest observed effect level
MF	modifying factor
MOA	mode (or mechanism) of action
MRL	minimal risk level
NEPC	National Environment Protection Council
NEPM	National Environment Protection Measure
NHMRC	National Health and Medical Research Council
NOAEL	no observable adverse effect level
NOEL	no observable effect level
NSW DECC	New South Wales Department of Environment and Climate Change
OCS	Office of Chemical Safety
PTDI	provisional tolerable daily intake
PTMI	provisional tolerable monthly intake
PTWI	provisional tolerable weekly intake
RAIS	Risk Assessment Information System
RDI	recommended daily intake
REL	reference exposure level
RfC	reference concentration
RfD	reference dose
RME	reasonable maximum exposure
SF	slope factor
TC	tolerable concentration
TDI	tolerable daily intake
TRV	toxicity reference value
UF	uncertainty factor
UL	upper limit
UR	unit risk
US EPA	United States Environmental Protection Agency

WHO	World Health Organization
WHO DWG	World Health Organization Drinking Water Guidelines