EVIDENCE EVALUATIONS FOR AUSTRALIAN DRINKING WATER GUIDELINE CHEMICAL FACT SHEETS

Lead Evaluation Report

Prepared for:

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BASIS OF REPORT

This report has been prepared by SLR Consulting Australia Pty Ltd (SLR) with all reasonable skill, care and diligence, and taking account of the timescale and resources allocated to it by agreement with National Health and Medical Research Council (the Client). Information reported herein is based on the interpretation of data collected, which has been accepted in good faith as being accurate and valid.

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EXECUTIVE SUMMARY

The National Health and Medical Research Council (NHMRC) have contracted SLR Consulting Australia Pty Ltd (SLR) to evaluate the existing guidance and evidence for 11 chemical factsheets in the 2011 *Australian Drinking Water Guidelines* (the Guidelines). The evidence reviews underpinning the evaluations have been undertaken in line with a new methodological framework which employs a pragmatic, systematic adopt/adapt approach for reviewing health advice.

This Evaluation Report summarises the evaluation undertaken for lead (Pb). The methodology of the review is also provided in more detail in an accompanying Technical Report.

The targeted screening of existing health-based guidance identified only one candidate health-based guidance/guideline value for potential adoption/adaptation from the Office of Environmental Health Hazard Assessment (OEHHA). Several other agency reviews summarised health-based information for Pb, but none considered it appropriate to derive a health-based guidance or guideline value for Pb. Two guidance/guideline values from the World Health Organization (WHO) and NHMRC were also identified in the literature which are not strictly health-based. The guidance/guideline documents assessed were found to be suitable to adopt/adapt based on an assessment of their administrative and technical characteristics, however NHMRC (2015a, b) met the highest number of overall criteria. The identified guidance/guidelines values are:

- OEHHA (2009): A health-based guidance value of 0.95 µg/day and a guideline value or Public Health Goal (PHG) in drinking water of 0.2 µg/L.
- WHO (2011): A provisional Drinking Water Guideline (DWG) of 10 µg/L, designated as provisional on the basis of treatment performance and analytical achievability.
- NHMRC (2015a, b): Although no guidance value was derived, NHMRC (2015a, b) concluded if a person has a BPb level > 5 µg/dL, their exposure to Pb should be investigated and reduced. This BPb level is currently referenced by public health services and applied in risk assessments of Pb exposure undertaken in Australia. It is termed a 'target' BPb level in this report.

The OEHHA (2009) PHG of 0.2 µg/L is much lower than the current Australian DWG of 10 µg/L. Based on current measured Pb concentrations in Australian drinking water supplies, it would be unlikely to be readily achievable. It is also at the current commercial laboratory limit of detection. Similarly, the relevant reviews identified from other jurisdictions and in the evidence scan provide indirect support for not recommending the OEHHA (2009) guideline value for adoption/adaptation in Australia, particularly since the technical rationale is underpinned by defining a blood lead (BPb) level of concern which is inconsistent with science policy in Australia.

Although it is acknowledged the latter 'target' BPb does not necessarily represent a threshold for the lack of adverse effects to Pb, the weight of evidence is less certain for effects of Pb at BPb <5µg/dL than for effects between 5 and 10 µg/dL (NHMRC 2015a, b). It therefore seems reasonable to consider deriving a DWG for Pb with the general aim of reduction / minimisation of Pb exposures to a target of <5 µg/dL, consistent with current Australian science policy.

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If it is assumed, as per the assumption in the current Guidelines (NHMRC and NRMMC 2011) that 20% of total Pb intake can be attributable to water consumption, this translates to a BPb level of 1 µg/dL. Using the Integrated Exposure Uptake Biokinetic (IEUBK) model for Pb, a target geometric mean BPb of 1 µg/dL would be attained in children between the ages of 6 months and 2 years if the concentration of Pb in drinking water were 5 µg/L. Formula-fed infants would likely have a similar geometric mean BPb although it is noted IEUBK is not designed to model formula-fed infant exposures. Since an infant would likely receive 100% of its Pb intake from formula as opposed to only 20% used for young children, the exposure modelling done for young children is protective of infant exposures. Therefore, it is considered appropriate for the current Australian DWG for Pb be halved from 10 µg/L to 5 µg/L. This is to ensure consistency with Australian science policy to minimise Pb exposure so that BPb in the most sensitive population (i.e. young children) remains below 5 µg/dL. A DWG of 5 µg/L should be achievable with existing source treatment technologies up to the point of supply. It should also be readily measurable with current commercial analytical techniques. It is noted that Pb concentrations often increase past the point of supply due to leaching from in-premise plumbing products that contain Pb. This issue should be considered during decision-making.

The studies identified in the evidence scan undertaken for this report would support the potential adoption of a DWG of 5 µg/L. Critical assessment of the studies identified in the evidence scan is out of scope of this review. These should be evaluated in further detail before being included in any decision-making.

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Abbreviations/Definitions

Acronym	Definition
APVMA	Australian Pesticides and Veterinary Medicines Authority
ATSDR	US Agency for Toxic Substances and Disease Registry
BMD_{01}	Dose Associated with a Benchmark Response (BMR) of 1 IQ-point.
BMDL	Lower one-sided 95% confidence limit of the BMD.
BPb	Blood lead
BW, bw	Body Weight
CDC	Centre for Disease Control (in United States)
DW	Drinking Water
DWG	Drinking Water Guideline
EFSA	European Food Safety Authority
FSANZ	Food Standards Australia New Zealand
IARC	International Agency for Research on Cancer
IEUBK	Integrated Exposure Uptake Biokinetic Model (for Pb)
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LOAEL	Lowest Observed Adverse Effect Level
LOR	Limit of Reporting
MRL	Minimal Risk Level (ATSDR terminology)
NHMRC	National Health and Medical Research Council
NOAEL	No Observed Adverse Effect Level
OEHHA	Californian Office of Environmental Health and Hazard Assessment
Pb	Lead
PBPK	Physiologically Based Pharmacokinetic Model
PHG	Public Health Goal (in drinking water) (OEHHA terminology)
PPRTV	Provisional Peer-Reviewed Toxicity Value (US EPA terminology)
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PTWI	Provisional Tolerable Weekly Intake (JECFA and EFSA terminology)
RfD	Reference Dose (US EPA terminology)
RSC	Relative Source Contribution
The Guidelines	NHMRC and NRMMC (2011). Australian Drinking Water Guidelines 6 2011; Version 3.6 updated March 2021, National Health and Medical Research Council and Natural Resource Management Ministerial Council, Commonwealth of Australia, Canberra.
US EPA	United States Environmental Protection Agency
WHO	World Health Organization
WQAC	Water Quality Advisory Committee

1 Introduction and Background

The National Health and Medical Research Council (NHMRC) have contracted SLR Consulting Australia Pty Ltd (SLR) to evaluate the existing guidance and evidence for 11 chemical factsheets in the 2011 *Australian Drinking Water Guidelines* (the Guidelines). The evidence reviews undertaken by SLR were governed by a newly designed methodological framework intended to increase transparency and quality control in the process of adopting or adapting existing guidance/guideline[1] values. For each of the 11 chemicals, SLR was asked to:

- Customise and apply a Research Protocol provided by NHMRC to answer research questions. The research questions varied slightly according to the chemical being evaluated.
- Produce a Technical Report and an Evaluation Report for each chemical factsheet.
    - The Technical Report is to capture the details and methods used to undertake each review.
    - The Evaluation Report is to interpret, synthesise and summarise the existing guidance and evidence pertaining to the research questions.

These tasks were performed in collaboration with the Water Quality Advisory Committee (WQAC) and NHMRC.

The report herein is the Evaluation Report for Lead (Pb).

1.1 Objectives

The factsheet for Pb within the Guidelines was last updated in 1996. The overarching objective of this review is to identify existing sources of guidance or guidelines on the impact of exposure to Pb in drinking water at levels higher or lower than the current Australian drinking water guideline (DWG) of 0.01 mg/L (i.e. 10 µg/L) on human health outcomes. The intention is to identify candidate health-based guidance/guideline values for potential adoption/adaptation into the Guidelines.

Other objectives of the review are:

- To assess the currency of selected guidance/guidelines through a brief scan of recent literature to determine whether a more comprehensive review is required; and
- To undertake an evidence scan to inform an update to the supporting information (e.g. monitoring and treatment guidance) provided in the factsheet.

2 Research Questions

Research questions for this review were drafted by SLR and peer reviewed and agreed upon by the WQAC and NHMRC prior to conducting the literature searches. The research questions guiding the review are provided in **Table 1**.

[1] A guidance value in this report refers to a health-based oral intake which can be ingested daily without adverse health effects; examples are Tolerable Daily Intakes (TDIs), Acceptable Daily Intakes (ADIs), Reference Doses (RfDs), Minimal Risk Levels (MRLs) etc. A guideline value transforms the health-based guidance value into a 'tolerable' concentration in various exposure media, e.g. a drinking water guideline (DWG). For derivation of a DWG, factors such as assumed intake of water by a person per day, body weight, and assumed percentage contribution of drinking water to the overall intake of a chemical are taken into account.

Table 1 Research Questions for Evidence Evaluation of Lead Factsheet Review

#	Research Questions
Health-based	
1	What is the critical human health endpoint for lead (if any)? Therefore, what are the key adverse health hazards from exposure to Lead in Australian drinking water?
2	What are the justifications for choosing this endpoint/health hazard?
3	What is the toxicological mode of action of lead for the critical human health endpoint?
4	Is lead an oral genotoxic carcinogen of relevance to humans?
5	What is the most appropriate dose metric for derivation of a drinking water guideline for lead?
6	What dose(s) (internal and/or external) are associated with the critical human health endpoint?
7	Is the proposed health-based guideline value relevant to the Australian context?
8	What is the guidance value?
9	Are there groups of people in the general population who may be more sensitive to lead exposure?
10	Is there a knowledge gap from the time at which existing guideline values were developed?
11	Does any recent literature change the guideline value? (e.g. demonstrating a new critical endpoint?)
Exposure-based	
12	What are the typical lead levels in Australian drinking water? Do they vary around the country or under certain conditions e.g. source of water, drought?
13	Do Australian levels differ considerably from elsewhere?
14	What are the principal routes of exposure to lead in the Australian general population?
15	What are the typical levels of Australian exposure? (e.g. 'background' lead levels)?
Risk-based	
16	What are the risks to human health from exposure to lead in Australian drinking water?
17	Is there evidence of any emerging risks that are not mentioned in the current factsheet that require review?
Supporting Information on Factsheet	
18	Is the general description current?
19	What are the indicators of the risks? How can we measure exposure? Is the information on measurement/analytical methods current?
20	Are there commercial analytical methods available that can measure at or below the guideline value?
21	Is the information for treatment options current in terms of current practices in Australia?
22	Can treatment technologies treat to the suggested level of the guideline value?
23	Is there any new information which should be added? Should anything be removed?

3 Methodology Overview

As part of the review, a number of literature searches were undertaken to target specific information relevant to answering the research questions. They consisted of the following:

- A targeted literature search of existing health-based guidance/guidelines. Jurisdictions included in this search were those previously identified by ToxConsult (2019) as providing reliable information and meeting a large proportion of pre-determined technical and administrative criteria. They included the World Health Organization (WHO) including the Joint FAO/WHO Expert Committee on Food Additives (JECFA), European Food Safety Authority (EFSA), United States Environmental Protection Agency (US EPA), US Agency for Toxic Substances and Disease Registry (ATSDR), Californian Office of Health and Hazard Assessment (OEHHA), Food Safety Australia New Zealand (FSANZ), and the Australian Pesticides and Veterinary Medicine Authority (APVMA).
- Where eligible guidance/guideline values existed, a brief evidence scan of published reviews and/or primary studies published after the guidance/guideline search date, with a view to determining whether a full systematic review is required.
- Consultation of identified existing guidance/guideline documents for supporting information in the factsheet (e.g. general description, uses, measurement techniques and limits of reporting in drinking water, treatment options, etc).
- An additional evidence scan of recent publicly available literature for supporting information in the factsheet.

Results were subjected to the following steps in order to identify the most relevant information:

- A preliminary title screen where titles of results were scanned by a researcher and a decision recorded regarding relevance of the result; and
- A content screen where full text content of reports/reviews/articles selected to be included from the preliminary title screen step were reviewed in relation to the research questions by a subject expert to determine which to include in data extraction.

Relevant data were extracted by populating various pre-constructed tables which focused on data needed to answer the research questions. Synthesis was conducted by presenting extracted data side-by-side in tabular format for each individual research question. Expert judgement was used to highlight areas of uncertainty or areas where an organisation's methods/interpretations may differ from Australian science policy. In addition, each candidate jurisdiction's guideline/guidance value for Pb considered for potential adoption/adaptation into the Guidelines was evaluated with respect to defined list of administrative and technical criteria (previously defined by ToxConsult 2019 and NHMRC). The reader is referred to the accompanying Technical Report for the detailed methodology, records of the literature screening process (including all records that were excluded) and all data extraction tables.

Figure 1 shows an overview of the literature search process followed for Pb. This is presented as a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram that describes the study selection process and numbers of records at each stage of screening (Moher et al. 2009).

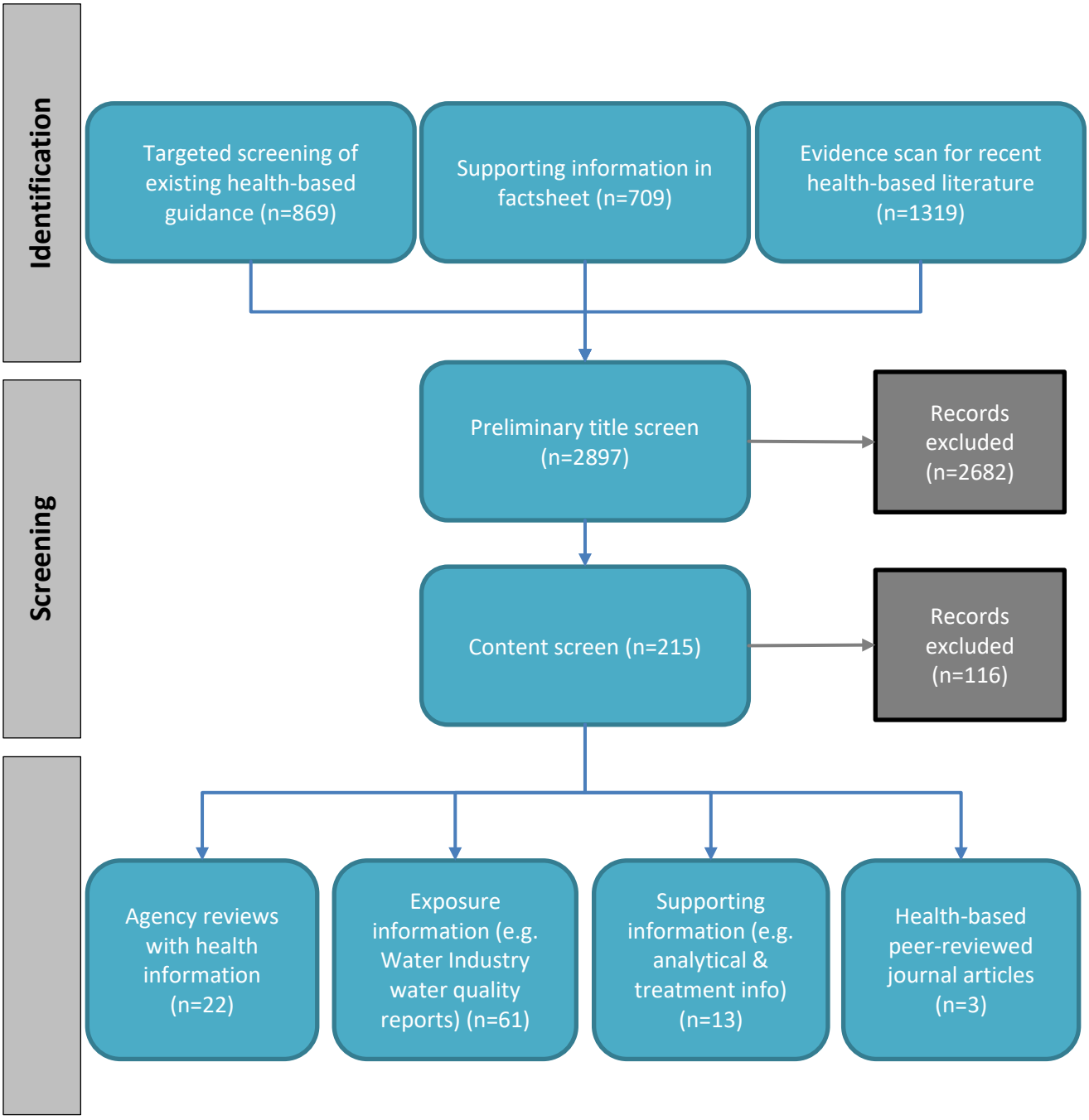

Figure 1 Overview of literature search process followed for Lead

This report provides the summary of the findings (**Section 4**), a discussion of the results (**Section 5**), and conclusion and recommendations (**Section 6**). Where health-based guidance values were considered reasonable for potential adaptation into the Guidelines, calculations of prospective DWGs were undertaken using the methodology and assumptions outlined in the Guidelines (NHMRC and NRMMC 2011).

The default equation is outlined in NHMRC and NRMMC (2011, Section 6.3.3) and has been adapted below as **Equation 1**. In this instance units have been added in to show how they cancel out and the 'animal dose' in the Equation can in fact be an animal or human dose, since both data types may be used to derive DWGs. In some instances, where adaptation of existing guidance values was considered, these guidance values may already incorporate the safety factor shown in the denominator of **Equation 1**.

Guideline value (µg/L) =

$$\frac{animal\ or\ human\ dose\ (\mu g/kg\ bw/d)\ x\ human\ weight\ (kg\ bw)\ x\ proportion\ of\ intake\ from\ water\ (fraction)}{volume\ of\ water\ consumed\ (L/d)\ x\ safety\ factor\ (unitless)}$$

……**Equation 1**

Default assumptions typically used in the Guidelines are 70 kg bw for adult human body weight (or 13 kg bw for 2-year old child, 5 kg for an infant), 10% (0.1) for the proportion of intake from drinking water, and 2 L/day of water consumption by an adult (1 L/day by a child, 0.75 L/day by an infant).

4 Results

The targeted screening of existing health-based guidance identified 22 agency reviews with health information on Pb. Upon further assessment, one candidate health-based guidance/guideline value for Pb for potential adoption/adaptation was found. This value was the following:

- OEHHA (2009): A guidance value of 0.95 µg/day and a guideline value or Public Health Goal (PHG) in drinking water of 0.2 µg/L.

Several other agency reviews summarised health-based information for Pb (e.g. ATSDR 2020, EFSA 2012, JECFA 2011a, b; NHMRC 2015a, b; US EPA 2004, WHO 2011), but none of these considered it appropriate to derive a health-based guidance or guideline value for Pb. The following guidance/guideline values were also identified in the literature which are not strictly health-based:

- WHO (2011): A provisional DWG of 10 µg/L, which is consistent with having been derived using a Provisional Tolerable Weekly Intake (PTWI) of 25 µg/kg bw for Pb which has since been withdrawn. WHO (2011) indicate the DWG is designated as provisional on the basis of treatment performance and analytical achievability.
- NHMRC (2015a, b): Although no guidance value was derived, NHMRC (2015a, b) concluded if a person has a blood Pb (BPb) level > 5 µg/dL, their exposure to Pb should be investigated and reduced. This BPb level is currently referenced by public health services and applied in risk assessments of Pb exposure undertaken in Australia. It is termed a 'target' BPb level in this report.

Detailed summary findings tables for each research question are provided in the Technical Report. In this Evaluation Report, the research question tables have been condensed to highlight differences between the various jurisdictions and/or uncertainties where they have been identified.

4.1 Health-based aspects

Research questions 1-11 all cover health-based aspects of the review; this is considered to be the most important information in the factsheet. **Table 2** provides a synthesis of the results by showing where there is and is not agreement between different jurisdictions.

Table 2 Summary of findings from data extraction for health-based research questions

#	Research Questions	Is there agreement between different jurisdictions?	Any disagreement or things to note?
1	What is the critical human health endpoint for lead (if any)? Therefore, what are the key adverse health hazards from exposure to lead in Australian drinking water?	The jurisdictions generally agree that the evidence is strongest for adverse cognitive effects (including reduced IQ) in children and cardiovascular effects (including increased blood pressure) in adults being the most sensitive endpoints.	ATSDR (2020) indicates it is not possible to determine from the epidemiological studies which organ systems are the most sensitive targets for Pb toxicity however agrees that cognitive deficits in children occurring at the lowest BPbs are the best substantiated effects.
2	What are the justifications for choosing this endpoint/health hazard?	The agencies agree that the most significant health effects from a public health and regulatory point of view are the ones which occur at the lowest BPb levels, because these affect the greatest part of the population. For children these are the effects on intelligence and behaviour. For adults the most sensitive health effect is the increase in blood pressure and other cardiovascular effects. Both of these health effects are of concern from >5 to 10 µg/dL BPb.	
3	What is the toxicological mode of action of lead for the critical human health endpoint (if applicable)?	Mechanisms associated with Pb-induced toxicity (unclear if specific to critical health endpoint) include: • Perturbations of ion homeostasis & transport. • Perturbations of protein binding. • Oxidative stress. • Inflammation. • Interference with neurotransmitters in brain. • Inhibition of δ-aminolevulinic acid dehydratase. • Inhibition of pyrimidine-5'-nucleotidase.	
4	Is lead an oral genotoxic carcinogen of relevance to humans?	Most jurisdictions agree that it is unclear whether Pb is an oral genotoxic carcinogen due to mixed results in genotoxicity assays. Pb is probably carcinogenic to humans as classified by IARC.	IARC (2006) indicates there is little evidence that Pb interacts directly with DNA at environmentally relevant BPb. JECFA (2011a, b) indicates Pb is likely a non-DNA reactive carcinogen.
5	What is the most appropriate dose metric for derivation of a drinking water guideline for lead?	Although most jurisdictions did not derive a health-based guidance/guideline value for Pb, dose-response analysis of Pb is typically exclusively conducted using BPb to describe exposure, which is then converted back to an intake using physiologically based pharmacokinetic modelling.	
6	What dose(s) are associated with the critical human health endpoint (if any)?	Jurisdictions agree that cognitive deficits in children may occur at BPb ≤5 µg/dL but have not derived threshold values. NHMRC (2015a, b) indicates, however, that the evidence is weaker for IQ reductions at BPb <5 µg/dL than between 5 and 10 µg/dL. OEHHA (2009), on the other hand, consider a BPb 'level of concern' to be 1 µg/dL which is correlated with a decrease in 1 IQ point.	

#	Research Questions	Is there agreement between different jurisdictions?	Any disagreement or things to note?
7	Is the proposed health-based guideline value relevant to the Australian context?	Most jurisdictions did not derive a guidance value. NHMRC (2015a, b) concluded if a person has a BPb level >5 µg/dL, their exposure to Pb should be investigated and reduced. This BPb level is currently referenced by public health services and applied in risk assessments of Pb exposure undertaken in Australia. It therefore seems reasonable to use a similar and consistent approach for derivation of the Australian DWG.	It is noted OEHHA (2009) in their derivation of a PHG in drinking water have defined the BPb 'level of concern' to be 1 µg/dL as this is correlated with a decrease of 1 IQ point. Australia has not determined what would be considered a BPb level of concern; current science policy in Australia is to reduce Pb exposure and to manage individual Pb exposures if BPb is >5µg/dL.
8	What is the guidance/guideline value?	Only three jurisdictions derived guidance/guideline values: • OEHHA (2009): 0.95 µg/day and a PHG of 0.2 µg/L. • NHMRC (2015a, b): Target BPb <5 µg/dL. • WHO (2011): Provisional DWG 10µg/L (not health-based).	
9	Are there groups of people in the general population who may be more sensitive to Lead exposure?	All jurisdictions agree that children have higher vulnerability to the neurotoxic effects of Pb due to their developing nervous system. In addition, ATSDR (2020) indicates additional groups of people may be more susceptible to Pb (e.g. elderly due to declining physiological functions, pregnant women due to increasing bone demineralisation and subsequent potential mobilisation of Pb from bone reserves, people with low dietary calcium, and people with genetic polymorphisms which can alter kinetics of Pb such as δ-ALAD).	
10	Is there a knowledge gap from the time at which existing guideline values were developed?	Potentially. Latest available health-based review is ATSDR (2020) which included literature up to February 2015. Therefore, an evidence scan was undertaken for 2015-2021.	
11	Does any recent literature change the guideline value? (e.g. demonstrating a new critical endpoint?)	The relevant reviews identified in the evidence scan provide indirect support for not recommending the OEHHA (2009) guideline value for adoption/adaptation in Australia, and instead basing the recommended DWG for Pb on a reduction/ minimisation of Pb exposures to <5 µg/dL, consistent with current Australian science policy.	

NOAEL = No Observed Adverse Effect Level. LOAEL = Lowest Observed Adverse Effect Level.

4.2 Exposure-related aspects

Another important aspect of the factsheet covers the exposure-related considerations. This is important for considerations of whether exposures by Australians to the chemicals evaluated are approaching the health-based guidance value used for deriving a DWG (it is noted that for lead, only one health-based guidance/guideline value was identified). It is also important for considerations of whether typical levels of the chemicals considered in Australian drinking water supplies would currently adhere to any revised DWG. Research questions 12-15 cover exposure-related aspects of the review. For these aspects, drinking water quality reports from various water corporations around Australia were consulted in addition to the agency reviews identified in the targeted search.

Table 3 provides a synthesis of the results by showing where there is and is not agreement between different sources.

Table 3 Summary of findings from data extraction for exposure-related research questions

#	Research Questions	Findings
12	What are the typical lead levels in Australian drinking water? Do they vary around the country or under certain conditions e.g. source of water, drought?	Mean (range) concentrations of lead in drinking water: • ACT: 0.3 µg/L (<0.2-8.1 µg/L) • VIC: (<1-4 µg/L) • Tas: 0.2-2 µg/L (<0.1-2.7 µg/L) • NT: <1-20 µg/L (range not reported) • QLD: <1 µg/L (<1-<1 µg/L) • Rainwater tanks around Australia: Mean 3.8 µg/L (0.3 µg/L-13 µg/L) • SA (stored rainwater for drinking): 0.6 µg/L (max 22.4 µg/L). Main source of Pb in DW is household plumbing systems, therefore Australian Department of Health recommends flushing taps used for drinking and cooking for about 30 seconds first thing in the morning or after periods of absence. This will draw fresh water into the tap and reduce potential exposure to Pb. Pb is not detected from most water samples taken around Australia. However, where the sample site plumbing has started to corrode Pb can be detected. In addition, due to soft and sometimes acidic nature of rainwater, when used in hot water systems, it leads to increases in Pb concentrations in the hot water.
13	Do Australian levels differ considerably from elsewhere?	Mean levels in drinking water in Australia appear to be lower than or similar to those in other developed countries (e.g. USA, Canada, Europe, Japan) (ATSDR 2020, EFSA 2012, IARC 2006).
14	What are the principal routes of exposure to lead in the Australian general population?	The principal route of exposure is oral intake. The vast majority (i.e. more than 80%) of the daily intake of Pb is derived from ingestion of food, dirt and dust. Intake from drinking water (at 5 µg/L, for example) forms a relatively small proportion of the total daily intake for children and adults, but a significant one for bottle-fed infants.
15	What are the typical levels of Australian exposure? (e.g. 'background' lead levels)?	Australia has not undertaken a recent national BPb survey, however background BPb levels are likely similar to other developed countries. In USA geometric mean BPb levels in 2015-2016 were 0.47 – 0.92 µg/dL depending on the age range. In 1-5 year olds it was 0.76 µg/dL. In 2011-2014, the 97.5th percentile BPb in children aged 1-5 years was 3.5 µg/dL. Mean and 90th percentile (respectively) estimated dietary Pb exposures in Australia (µg/kg bw/d): ○ Lower bound: 0.016-0.048 and 0.032-0.1 ○ Upper bound: 0.16-0.38 and 0.23-0.56 ○ Highest in 2-5 yr old children: 0.048-0.38 and 0.1-0.56.
DW = Drinking Water.		

4.3 Risk-based aspects

Research questions 16 and 17 are risk-based considerations. The jurisdiction reviews subjected to detailed data extraction mentioned at the start of **Section 4** were also consulted to answering the questions. **Table 4** presents a summary of the findings.

Table 4 Summary of findings from data extraction for risk-based research questions

#	Research Questions	Findings
16	What are the risks to human health from exposure to lead in Australian drinking water?	None identified for drinking water *per se*.
17	Is there evidence of any emerging risks that are not mentioned in the current factsheet that require review?	JECFA (2011a,b) concluded that, in populations with prolonged dietary exposures to Pb that are at the higher end of the ranges identified (~9 µg/kg bw/day), measures should be taken to identify major contributing sources and foods and, if appropriate, to identify methods of reducing dietary exposure that are commensurate with the level of risk reduction. The evidence scan revealed associations of Pb exposure with ototoxicity in one review and preeclampsia in another. However, these associations are considered unlikely to alter the recommendation from the NHMRC (2015a, b) to reduce BPb exposures to <5 µg/dL.
DW = Drinking Water.		

4.4 Supporting information

The Pb factsheet contains a range of supporting information, including a brief general description (i.e. uses of Pb, sources in drinking water), typical values in Australian drinking water, treatment of drinking water, and measurement (i.e. analytical) considerations. The remaining Research questions 18-23 cover the supporting information of the review. For these aspects, in addition to consulting the previously mentioned sources (e.g. the drinking water quality reports from various water corporations around Australia, the agency reviews identified in the targeted search), additional targeted searches were undertaken (for details, refer to Technical Report). **Table 5** provides a summary of the results.

Table 5 Summary of findings from data extraction for supporting information

#	Research Questions	Findings
18	Is the general description current?	Yes.
19	What are the indicators of the risks? How can we measure exposure? Is the information on measurement/analytical methods current?	Current fact sheet indicates Pb in DW can be measured with graphite furnace absorption spectroscopy with a limit of detection of 0.005 mg/L. ICP-MS (US EPA 6010, 6020, APHA 3010 and 3030) now appears to be the more common method of choice in Australian laboratories, with standard limits of reporting ranging from 0.0002 to 0.05 mg/L and trace ranging from 0.0002 to 0.002 mg/L, depending on the laboratory.
20	Are there commercial analytical methods available that can measure at or below the guideline value?	Commercial analytical methods can measure at or below the current Australian DWG value of 0.01 mg/L (with the lowest standard limit of determination available of 0.0002 mg/L).

#	Research Questions	Findings
21	Is the information for treatment options current in terms of current practices in Australia?	Yes, it appears to be, although additional studies were identified in the literature search which described mostly commercially used water treatment techniques with small adjustments in order to improve Pb removal efficiency. The approaches include aggregation, stabilisation, gravitation filtration, adsorption, phosphate treatment, etc. Pb is exceptional in that most Pb in DW arises from plumbing in buildings, and the remedy consists principally of removing plumbing and fittings containing it, which requires both time and money. According to WHO (2011), in the interim, all practical measures to reduce total exposure to Pb, including corrosion control, should be implemented.
22	Can treatment technologies treat to the suggested level of the guideline value?	Conventional treatment technology appears to be able to reduce mean Pb concentrations of source water to 0.0002 to 0.002 mg/L (i.e. 0.2 to 2 µg/L) most of the time. However occasional instances of higher concentrations (e.g. 20 µg/L) have been recorded. Mean concentrations in rainwater tanks appear to be similar (e.g. 0.8 to 3.8 µg/L). However, the concentrations in water exiting the tap may be higher in older buildings if Pb-soldered pipes are present. According to WHO (2011), it is extremely difficult to achieve a concentration below 10 µg/L in such buildings by central conditioning, such as phosphate dosing.
23	Is there any new information which should be added? Should anything be removed?	Update Limit of Reporting (LOR) in measurement section, treatment section can be expanded to include reference to difficulties in treating Pb concentrations in older houses without replacement of Pb-soldered plumbing, and typical values in Australian drinking water can be updated.

5 Discussion

This section provides a discussion of the strengths and limitations of the identified guidance/guideline values from OEHHA (2009), WHO (2011) and NHMRC (2015a,b) for possible adoption/adaptation into the Guidelines.

5.1 Suitability of candidate health-based guidance for adoption/adaptation

Candidate guidance/guideline values for Pb shown in **Section 4** and **5.2** for possible adoption/adaptation in Australia have been evaluated using the Assessment Tool provided in Appendix C in the Technical Report. This tool evaluates each document against administrative and technical criteria that demonstrate transparent and robust guideline development and evidence review processes that meet NHMRC standards for guidelines. The overall suitability of the guidance/guideline values for adoption/adaption can be gauged at least partially by examining the percentage of 'must-have', 'should-have', and 'may-have' criteria met by each jurisdiction.

Figure 2 presents the percentage of criteria (combined technical and administrative criteria) met by each jurisdiction. It is evident from the figure that OEHHA (2009) and WHO (2011) met similar percentages of criteria (i.e. 68-73% of 'must-have' and 60% of 'should-have' criteria), whereas NHMRC (2015a, b) met the highest number of criteria (100% of all criteria met). Most of the instances where the criteria were not met by WHO (2011) or OEHHA (2009) were related to lack of reporting of literature search and review details. Whilst all three jurisdictions provided comprehensive bibliographies of the information relied upon, none apart from NHMRC (2015a, b) reported any detail of the literature searches.

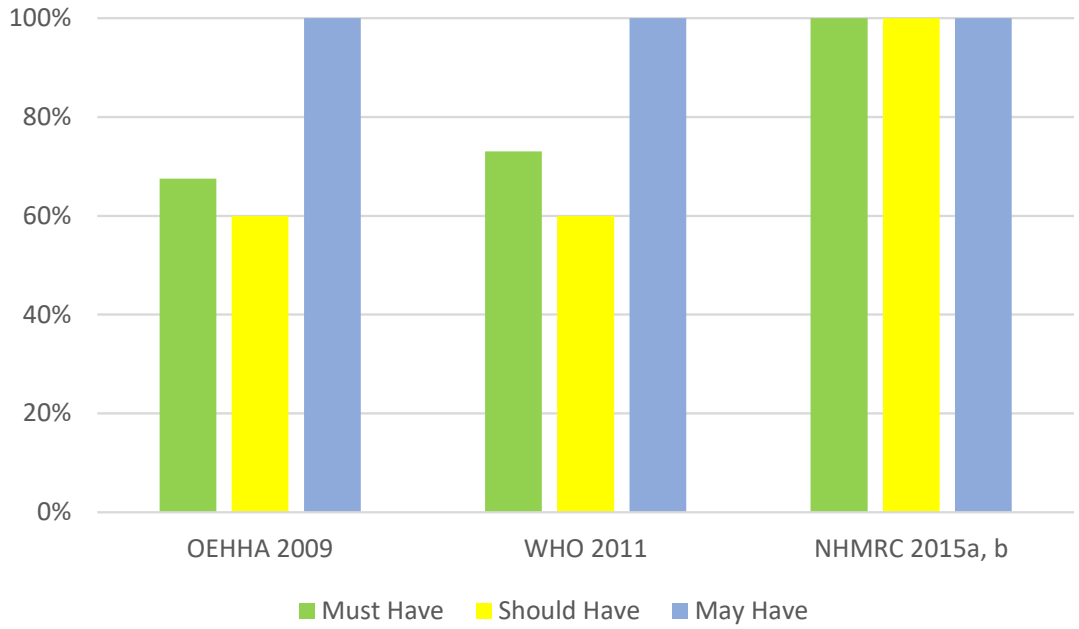

Figure 2 Overall proportion of 'must-have', 'should-have' and 'may-have' technical/administrative criteria met by jurisdictions who have derived candidate guidance/guideline values for lead for possible adoption/adaptation in Australia

This analysis indicates that the assessment undertaken by NHMRC (2015a, b) meets the highest proportion of criteria compared to other jurisdictions assessed. This is followed by similar performance by WHO (2011) and OEHHA (2009).

5.2 Overall Evaluation

The analysis in **Section 5.1** indicated the suitability of the candidate guidance/guideline values for adoption/adaption based on an assessment of their administrative and technical characteristics. Further analysis of the toxicological basis for deriving the guidance/guideline was also undertaken.

The following summary comments are made with respect to the toxicological basis (if any) and methods used to derive the guidance values for Pb cited or derived by the jurisdictions shown in **Section 5.1:**

- As discussed in **Section 4**, the targeted screening of existing health-based guidance only identified one health-based guidance/guideline value for Pb. This was a guidance value of 0.95 µg/day and a guideline value or PHG in drinking water of 0.2 µg/L from OEHHA (2009). This PHG is much lower than the current Australian DWG of 10 µg/L and is lower than current measured Pb in Australian drinking water supplies. It would be unlikely to be achievable as it is at the current standard commercial laboratory limit of detection. It may also be unnecessary since intake from Pb in drinking water makes a relatively small contribution compared to intake from other sources (diet, soil and dust). Similarly, as noted in **Table 2,** the relevant reviews identified from other jurisdictions and in the evidence scan provide indirect support for not recommending the OEHHA (2009) guideline value for adoption/adaptation in Australia.

- The critical study relied upon by OEHHA (2009) is an unpublished conference paper by Carlisle and Dowling (2006) in which is understood to present an analysis of information from Lanphear et al. (2005). Given that the analysis by Carlisle and Dowling (2006) cannot be evaluated as part of this review (since it is unpublished) and the mean IQ (and 95% confidence interval) for pooled BPb levels in the lowest intervals (< 5 µg/dL and the 5–10 µg/dL) appear to be similar (refer to Figure 3, Lanphear et al. 2005), it is not possible at this time to support the use of the analysis by Carlisle and Dowling (2006) as a basis for setting a guideline value in Australia[2]. Other reasons for not adopting the analysis as a basis of an Australian guideline value is that it is very difficult to determine whether a small change in a health effect (such as a change in IQ of 1) was due to Pb exposure (either solely or as a contributor) given the change may simply be a result of natural variation or chance (NHMRC 2015a). Further, there may be other credible plausible explanations responsible for the differences observed in IQ (e.g. socioeconomic status) or other confounding factors associated with health effects that have not been accounted for (e.g. smoking, eating and drinking habits, body weight and physical activity) (NHMRC 2015a). Wilson and Wilson (2016), identified as part of the evidence scan undertaken for this report, examined why statistical tests and statistical models applied by previous researchers failed to identify confounding and concluded that effects of low Pb exposure (BPb <10 µg/dL) have likely been exaggerated.
- The current Australian DWG of 10 µg/L is based on a PTWI that has since been withdrawn, so its basis is indeed in need of a review. WHO (2011) retained a DWG of 10 µg/L, but designated it to be provisional on the basis of treatment performance and analytical achievability.

Other jurisdictions (e.g. ATSDR 2020, EFSA 2012, JECFA 2011a, b; NHMRC 2015a, b; US EPA 2004, WHO 2011) did not derive a guidance or health-based guideline value. A recent review by NHMRC (2015a, b) concluded if a person has a BPb level >5 µg/dL, their exposure to Pb should be investigated and reduced. This BPb level is currently referenced by public health services and applied in risk assessments of Pb exposure undertaken in Australia. Although it is acknowledged this does not necessarily represent a threshold for the lack of adverse effects to Pb, the weight of evidence is less certain for effects of Pb at BPb <5µg/dL than for effects between 5 and 10 µg/dL (NHMRC 2015a, b).

It therefore seems reasonable to consider deriving a DWG for Pb with the general aim of reduction / minimisation of Pb exposures to a target of <5 µg/dL, consistent with current Australian science policy. If it is assumed, as per the assumption in the current Guidelines (NHMRC and NRMMC 2011) that 20% of total Pb intake can be attributable to water consumption, this translates to a BPb level of 1 µg/dL (i.e. 5µg/dL x 0.2 = 1 µg/dL).

[2] A co-author of the 2006 analysis is understood to be Jim Carlisle, an employee of OEHHA and thus may have relevant information on the validity of the analysis which is not readily apparent to parties outside of OEHHA.

The Pb concentration in drinking water that would result in a child BPb level of 1 µg/dL, assuming a drinking water intake of 1 L/day for children and 0.75 L/day for infants (as per the current Guidelines) can be estimated using a physiologically based pharmacokinetic (PBPK) model. A number of PBPK models have been developed that are able to predict BPb concentrations in children, e.g. O'Flaherty 1993, 1995 and Leggett 1993, IEUBK, AALM[3]. However only the Integrated Exposure Uptake Biokinetic (IEUBK) model developed by the US EPA is publicly available in a form amenable for use. Consequently, this is the predictive model used in this report; apart from being readily available and validated, the IEUBK model has the advantage of being maintained and updated, having an extensive user manual, being used in regulatory decision making in the US and in health risk assessments undertaken by the Centre for Disease Control (CDC). The model has also been used in Australia for risk assessments for Broken Hill (Toxikos 2010, ToxConsult 2017), an assessment undertaken in Mount Isa (Noller et al. 2017) and to inform deliberations in establishing a health investigation level (HIL) for Pb in soil (NEPM 2013).

Table 6 presents the inputs and results of the BPb modelling undertaken (output is attached as **Appendix A**).

Table 6 Inputs and results of BPb modelling at a target BPb of 1 µg/dL

Input Assumptions			Results	
Parameter		**Value (units)**	**Age Group (yr)**	**Predicted geometric mean BPb (µg/dL)**
Air, Diet, Soil/Dust, Alternate intake		All set to zero	0.5-1 (4)	1.0
Maternal BPb		0.88 µg/dL (1)	1-2	1.0
Drinking water intake	0-1 yr old	0.75 L/day (2)	2-4	0.9
	1-7 yr old	1 L/day (2)	4-6	0.8
Gastrointestinal absorption from water		50% (3)	6-7	0.7
Pb concentration in drinking water		5 µg/L		

1. The latest information for the Australian general population stems from the 2009-2010 Victorian Health Monitor. Sample selection in this study was based on a stratified cluster sample of Census Collection Districts within Victoria and involved individuals aged 18-75 years. BPb was obtained by venipuncture for 3,622 participants. The median BPb in women of child-bearing age (18-44) was 0.055 µmol/L (i.e. 1.1 µg/dL) (VIC DoH 2011, 2012). As a comparison, the median BPb for adults (males and females) aged 20+ for the year 2009-2010 in the US was similar at 1.2 µg/dL (CDC 2019). However, the US NHANES has kept monitoring BPb in the general population after this date. The most recent data for adults age 20+ in the US (year 2015-2016) indicates BPb has decreased to a median of 0.88 µg/dL (CDC 2019). Current BPb is likely even lower, and Australian BPb levels have likely mirrored those in the US. It is also noted adult females generally have lower BPb than adult males, so the median for female adults of child-bearing age in the US is likely to be lower than the median value for all adults. Overall this supports using a background BPb level of <0.88 µg/dL as an assumption for maternal BPb in the IEUBK model. A value of 0.88 µg/dL has conservatively been used for this exercise.
2. Consistent with default assumption for drinking water intake from the Guidelines (NHMRC and NRMMC 2021).
3. Default assumption in IEUBK model. This is consistent with the knowledge that soluble Pb is approximately 50% absorbed by the gastrointestinal tract of children (US EPA 1999, ATSDR 2020).
4. Although the IEUBK model does not model BPb for formula-fed infants, the daily intake of Pb by formula-fed infants at an assumed Pb concentration in drinking water of 5 µg/L using the uptake equations embedded into the model results in a similarly estimated Pb uptake (1.81 µg/d) compared with a 0.5-1 year old (1.837 µg/d)[4]. As the same biokinetic factors are likely applicable for converting Pb uptake to a BPb concentration in infants as in 0.5-1 year old children, this indicates a similar BPb would be expected to that estimated for 0.5-1 year olds. In addition, an infant would likely receive 100% of its Pb intake from formula as opposed to only 20% used for young children. Thus the exposure modelling done for young children is protective of infant exposures.

[3] Although the All Ages Lead Model (AALM) is an outgrowth of the IEUBK model, at the time of writing this report the latest available version of the AALM was still an external review draft (US EPA 2019). As the model is not yet available as a finalised version, it was not used in this evaluation report.

[4] Formula for Pb uptake in IEUBK model:
UPWATER(t) = INWATER(t) x ABSW x AVW x [PAF + (1-PAF) ÷ (1 + AVINTAKE ÷ SATINTAKE(t)]
[refer to IEUBK guidance documentation in US EPA (1994, 2007, 2009) for description and assumptions for parameters]

Using the input assumptions outlined in **Table 6**, a target geometric mean BPb of 1 µg/dL would be attained in children between the ages of 6 months and 2 years if the concentration of Pb in drinking water were 5 µg/L. As the same biokinetic factors are likely applicable for converting Pb uptake to a BPb concentration in infants as in 0.5-1 year old children, this indicates a similar BPb would be expected to that estimated for 0.5-1 year olds. Since an infant would likely receive 100% of its Pb intake from formula as opposed to only 20% used for young children, the exposure modelling done for young children is protective of infant exposures. Reducing the current DWG of 10 µg/L to 5 µg/L would ensure consistency with current Australian science policy which is to minimise Pb exposure so that BPb remains below 5 µg/dL (assuming a RSC of 20% as per the current Guideline).

The various guidance values from the three agencies are summarised in **Table 7**. The current Australian DWG is also provided in the table for comparison.

Table 7 Potential drinking water guideline values (µg/L) resulting from adaptation of Pb guidance / guideline values from other jurisdictions

Parameter	NHMRC (2011) – Existing Aus DWG – last updated in 1996	OEHHA (2009)	WHO (2011)	NHMRC (2015a, b)
Critical study	Based on JECFA PTWI, which in turn is based on infant metabolic studies (Zeigler et al. 1978, Ryu et al. 1983)	Unpublished conference paper by Carlisle and Dowling (2006) in humans, reanalysis of Lanphear et al. (2005)	Not applicable (based on treatment achievability)	Various in children (systematic review)
Study duration	Not stated	Not stated	Not applicable	Various
Critical Effect	Does not result in increase in Pb retention	Decrease in 1 IQ point in children	Not applicable	If a person has a BPb level >5 µg/dL, their exposure to Pb should be investigated and reduced. Although it is acknowledged this does not necessarily represent a threshold for the lack of adverse effects to Pb, the weight of evidence is less certain for effects of Pb at BPb <5µg/dL than for effects between 5 and 10 µg/dL
Point of Departure (µg/kg bw/d)	3.5	BPb level of concern of 1µg/dL correlating with decrease in 1 IQ point (corresponds to Pb intake of 2.86 µg/day)	Not applicable	
Uncertainty factor	- (infant metabolic studies)	3 (UF_t)	Not applicable	
Health-based guidance value (µg/kg bw/d)	3.5	0.95 µg/day	Not applicable	
Resulting adaptation to a Health-Based Guideline Value or DWG[(1)] (µg/L)	10	0.25	10	5

UPWATER(infant) = (5 µg/L x 0.75 L/day) x 0.5 x 1 x [0.2 + (1-0.2) ÷ (1 + 1.875 µg/d ÷ 40.65 µg/d)]
UPWATER(infant) = 1.81 µg/d

Parameter	NHMRC (2011) – Existing Aus DWG – last updated in 1996	OEHHA (2009)	WHO (2011)	NHMRC (2015a, b)
Comments	PTWI has since been withdrawn, basis in need of review.	Unpublished study, cannot be evaluated; DWG is at LOR for Pb.	Retained previous guideline based on withdrawn PTWI, on basis of treatment achievability. Designates provisional.	Derived *de novo* in this report by adapting NHMRC BPb information (see **Table 6** and text preceding table).

DWG = Drinking Water Guideline; Aus = Australian; PTWI = Provisional Tolerable Weekly Intake. UF_t = Uncertainty factor to account for the lack of a threshold for Pb and extrapolation from the small sample size used in the main study of Lanphear et al. (2005).

1. Adaptation of guidance value has been undertaken using the default assumptions for derivation of DWGs in Australia using the following equation as outlined in NHMRC (2011); relative contribution as per current Guidelines for Pb:

   DWG (µg/L) = [Guidance value (µg/kg bw/d) x 13 kg bw x 0.2 (i.e. 20% relative contribution from DW)] ÷ 1 L/day

6 Conclusions

One existing health-based guidance/guideline value relevant to Pb was found suitable to adopt/adapt based on an assessment of the administrative and technical criteria described in Appendix C of the Technical Report. A DWG from WHO (2011) and blood lead level guidance from NHMRC (2015a,b) were also identified and considered for potential adaption/adoption in the Guidelines.

Potential adaption of the OEHHA (2009) guidance value would result in an Australian DWG of 0.2 µg/L. This is a significant decrease from the existing DWG of 10 µg/L and would have impacts on the treatment requirements for water suppliers. It would also be difficult to achieve using existing treatment and analytical techniques. In addition, the guidance value appears to be based on reanalysis of existing data in an unpublished conference paper which could not be evaluated in this report.

Potential adaption of the WHO (2011) provisional DWG of 10 µg/L based on treatment and analytical capabilities would result in no change to the current Australian DWG.

Potential adaption of the current NHMRC (2015 a,b) advice on BPb levels (with an aim to keep BPb levels under 5 µg/dL) would result in the current Australian DWG for Pb being halved from 10 to 5 µg/L. This would ensure consistency with Australian science policy to minimise Pb exposure so that BPb in the most sensitive population (i.e. young children) remains below 5 µg/dL, assuming that 20% of total Pb intake is derived from drinking water. Formula-fed infants would likely have a similar BPb as that modelled for young children. The concentration of 5 µg/L is achievable up to the point of supply with existing water treatment technologies and readily measurable with current commercial analytical techniques. It is noted that Pb concentrations often increase past the point of supply due to leaching from in-premise plumbing products that contain lead. This issue should be considered during decision-making.

The studies identified in the evidence scan undertaken for this report would support the recommendation made. Critical assessment of the studies identified in the evidence scan is out of scope of this review. These should be evaluated in further detail before being included in any decision-making.

7 Review Team

Name	Position	Responsibilities
Ms Tarah Hagen, MSc, DABT, RACTRA	Technical Discipline Manager – Toxicology & Risk Assessment, SLR	Report author and technical oversight of literature review
Dr Slavica Kandic, PhD	Project Consultant – Toxicology & Risk Assessment, SLR	Literature searching, preliminary title screen, compilation of Appendices
Mr Giorgio De Nola, MSc, RACTRA	Principal Consultant – Toxicology & Risk Assessment, SLR	Internal peer review

8 Declared Interests

Team Member	Declaration of Interest
Ms Tarah Hagen	As part day-to-day consulting activities at SLR Consulting and ToxConsult Pty Ltd, Ms Hagen has: • Provided the report "Assessment of International and National Agency Processes for Deriving HBGVs and DWGs" to the NHMRC. This has been used to inform the methodological framework for this review as described in the Research Protocol. • Written numerous risk assessments for public exposure to metals in dust, of which Pb was a principal metal of concern.
Dr Slavica Kandic	No interest to declare.
Mr Giorgio De Nola	No interest to declare.

9 Acknowledgements

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APPENDIX A

IEUBK Blood Lead Modelling Output

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