Australian Government
National Health and Medical Research Council

NHMRC

Evidence evaluation for *Australian Drinking Water Guidelines* chemical factsheet – Lead (Research Protocol)

Organisation

SLR Consulting Australia Pty Ltd

Team

Ms Tarah Hagen

Mr Giorgio De Nola

Dr Slavica Kandic

Dr Roger Drew

Contact

Tarah Hagen; Level 11, 176 Wellington Parade, East Melbourne, VIC 3002; thagen@slrconsulting.com; Mob: 0428 363 897

Date protocol completed

1 July 2021

IMPORTANT: This Research Protocol template is designed for reviews commissioned by NHMRC to inform the update of *Australian Drinking Water Guidelines* (the Guidelines) chemical factsheets. The Research Protocol should be finalised in collaboration with the NHMRC Water Quality Advisory Committee before commencing work to conduct the search or make eligibility decisions.

A separate Research Protocol should be developed for each chemical (or closely related group of chemicals) for which an updated guidance review is to be conducted, as the current state of knowledge, health outcomes of interest and sources of evidence will vary.

This template was developed to maximise quality and efficiency in the review process, and has been adapted from an existing template developed for rapid reviews by Cochrane.[5] All sections should be completed. Rationales should be provided throughout for all methodological decisions in the final Technical Report, including any decisions to vary the recommended approaches noted in this template.

Contents

Background

Lead is a metal that is found concentrated in lead ore deposits and in the past was commonly used as an antiknock agent in petrol, in lead-based paints, pigments and glazes, electrical shielding, plumbing, storage batteries, solders, welding fluxes and lead-containing pesticides [1,2]. Due to the phasing out of lead in petrol and solder, concentrations in the air and food are relatively low. Exposure to lead by the general public primarily occurs via the diet; however, exposure can also occur via drinking water primarily from corrosive water effects on household plumbing systems containing lead pipes, solder or fittings [1,2,3].

Lead can be absorbed via inhalation, ingestion and placental transfer. Approximately 10% of ingested soluble lead in adults is absorbed, while in children this is about 50% [1,3]. Lead is distributed via blood to soft tissues including liver, kidney, and bone marrow where it has a biological half-life of less than 40 days, and in skeletal bone lead can accumulate and remain for 20 to 30 years [3]. Exposure to lead has been associated with a range of health effects, primarily with neurodevelopmental effects, impaired renal function, hypertension, reduced fertility and adverse pregnancy outcomes [2]. The International Agency for Research on Cancer (IARC) evaluation of inorganic lead compounds concluded they are probably carcinogenic to humans (Group 2A) [4]. There is currently little evidence that lead interacts directly with DNA at typically encountered blood lead concentrations [4].

Blood lead is used as a biomarker of lead exposure. The effects of concern (i.e. population shifts of IQ in children and blood pressure in adults) are due to chronic exposure. The WHO Provisional Tolerable Weekly Intake (PTWI) used in the 1996 derivation of the NHMRC[3] water quality guideline for lead has since been with withdrawn and is no longer considered to be health protective.

NHMRC (2015)[7] recently concluded a blood lead level greater than 5 µg/dL suggests a person has been, or continues to be, exposed to lead at a level that is above what is considered the average 'background' exposure in Australia, and that if a person has a blood lead greater than 5 µg/dL, their exposure to lead should be investigated and reduced. The NHMRC noted that research on the effects of low-level exposure to lead indicates there is not enough high-quality evidence to conclude that a blood lead level <10 µg/dL was the causing factor for any health effects observed. Thus it was not possible to make a definitive statement on what constitutes a 'safe level' or what should be considered as a 'level of concern' for blood lead concentrations in children. This arises because the tools of psychologists and psychiatrists used to investigate subtle impacts on intellectual performance and development are not precise, and the outcomes are influenced by such things as genetics, socio-economic status and early life experience/environment.

Objectives of the review

To identify existing sources of guidance or guidelines on the impact of exposure to lead in drinking water at levels higher or lower than 0.01 mg/L on human health outcomes. After discussion of initial findings with the Water Quality Advisory Committee (WQAC) or Chemical Subgroup, the currency of selected guidelines will also be assessed through a scan of recent literature to determine whether a more comprehensive review is required.

An evidence scan to inform an update to the supporting information (e.g. monitoring and treatment guidance) provided in the factsheet will also be undertaken.

The review will also seek to address whether recent data can better inform the lead dose response in sensitive groups of the general population.

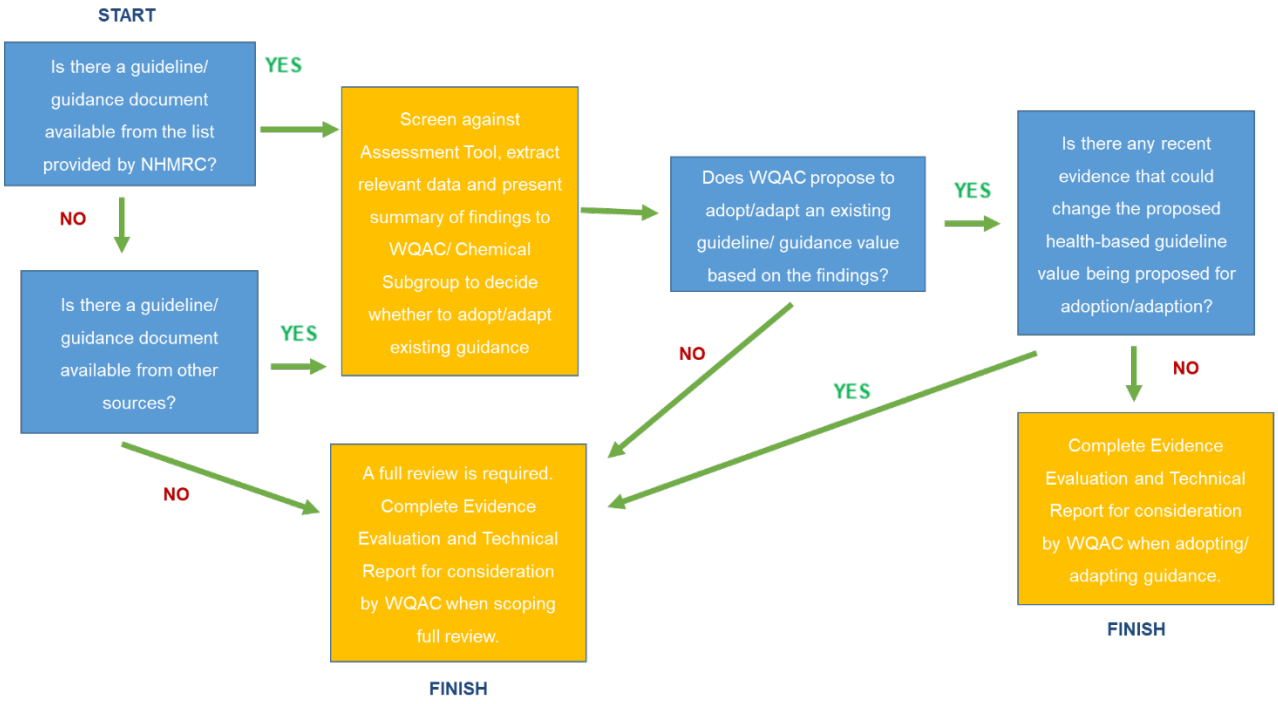
Methods

This review will be conducted using different approaches depending on the factsheet sections being updated.

For the health-based guideline value and health-related advice in the factsheet:

- A targeted review of existing advice will be conducted (includes existing health-based guideline values and associated recommendations in guidelines for drinking water and/or appropriate guidance values that can be used to derive drinking water guideline values).
- If no suitable guidance is found from these sources, an expanded search and review of other relevant guidance will be undertaken.
- Where an eligible guideline exists, a brief evidence scan of published reviews and/or primary studies published after the guideline search date will be undertaken, with a view to determining whether a full systematic review is required.

The process for reviewing health-based advice is summarised in the following flowchart:



For supporting information in the factsheet (e.g. monitoring, treatment information) an evidence scan will be conducted to assess the currency of the existing information in the factsheet.

The overall approach to reviewing different sections of the factsheet is summarised in the table below:

Section of factsheet	Key steps
Health-related advice in chemical factsheet including: • Health-based guideline value • Health considerations • Typical Australian exposure levels • Risk summary • Derivation of guideline value	• Targeted review: screen and assess quality of existing guidance for health-based guideline values or other relevant guidance values that can be adopted/adapted for drinking water • If required, check for currency by scanning literature for any evidence that might change existing guidance • Present summary of findings on each of these topics • Report details of methods used to search and evaluate existing guidance and other sources
Supporting information in chemical factsheet including: • General description • Measurement (analytical methods) • Treatment options	• Review information for currency • Scan evidence that could be used to update existing information • Present summary of findings • Report details of literature search

The methods outlined below will govern the searching, selecting, assessment and reporting of the evidence used to inform the update to the chemical factsheet.

Any changes to the Research Protocol once finalised on the advice of the Water Quality Advisory Committee will be recorded and documented in the Technical Report.

Health-related advice in factsheet

Research questions

Health-related advice	Research questions to consider *
Health-based guidance value/ Health considerations	Is there evidence of any emerging risks that are not mentioned in the current factsheet that require review?Therefore, what are the key adverse health hazards from exposure to lead in Australian drinking water? What are the justifications for choosing this endpoint/health hazard? What is the toxicological mode of action of lead for the critical human health endpoint?

Health-related advice	Research questions to consider *
	Is lead an oral genotoxic carcinogen of relevance to humans? What is the most appropriate dose metric for derivation of a drinking water guideline for lead? What dose(s) (internal and/or external) are associated with the critical human health endpoint? Is the proposed health-based guideline value relevant to the Australian context? What is the guidance value? Is the health-based guidance value expressed in the best way? Are there groups of people in the general population who may be more sensitive to lead exposure? Is there a knowledge gap from the time at which existing guideline values were developed? Does any recent literature change the guideline value? (e.g. demonstrating a new critical endpoint?)
Typical Australian drinking water levels or exposure profile	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? Do Australian levels differ considerably from elsewhere? What are the principal routes of exposure to lead in the Australian general population? What are the typical levels of Australian exposure (e.g. 'background' blood lead levels)?
Risk summary	What are the risks to human health from exposure to lead in Australian drinking water? Is there evidence of any emerging risks that are not mentioned in the current factsheet that require review?
* Additional research questions may arise after examination of the candidate guidelines.	

Targeted screening of existing health-based guidance

Criteria for considering existing guidelines/guidance

Study designs for adopt/adapt approach	In the first instance, guidelines/guidance on lead developed by the following agencies will be considered: • 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) • Australian Pesticides and Veterinary Medicine Authority (APVMA) In the absence of existing guidance/guidelines from the sources listed above, other sources may be screened for relevant guidance/ guidelines and assessed against the applicable criteria outlined in **Appendix C**.
Population	Humans, including the general population as well as specific populations who may be at higher risk of adverse health outcomes such as: • Infants and children • People who are pregnant • Aboriginal and Torres Strait Islander peoples • People with iron deficiency • People with pre-existing health conditions such as renal, neurological, haematological or cardiovascular disease • People who ingest higher than average amounts of water (e.g. tropical locations, outdoor workers) • People with certain genetic polymorphisms
Exposure	Exposure parameters that will be considered for lead include: • Exposure during critical time periods (e.g. pregnancy, foetal) • Exposure over a lifetime • Exposure through drinking, cooking, washing • Combination or interaction with other substances
Comparator(s)	Comparisons will be presented for:

	• Value, critical study, critical health effect etc, of existing drinking water guideline for lead and other values identified in the search. • Threshold doses (internal and/or external) of lead (if possible) associated with no adverse effects and critical adverse health effect. • Percentage compliance with criteria in **Appendix C** by the agencies identified.
Outcome(s)	The human health outcomes of concern from exposure to lead include: • Mortality • Severe human health outcomes, including incidence of life-threatening illness, disability or chronic disease with ongoing impact on quality of life. • Subtle human health outcomes which may only be recognisable at a population level (e.g. increased blood pressure, IQ decrements). Consideration regarding these outcomes will be given to: • The level of lead in drinking water considered to be safe or acceptable to human health over a lifetime (if possible, to be delineated from the information available).

Search methods

Expertise	The searches will be: ☒ conducted by a researcher [SK] and verified by a content expert [TH] ☐ conducted by an information specialist [initials] ☐ independently peer reviewed.
Sources initially screened	The following sources will be screened initially: ☒ 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)

	☒ Australian Pesticides and Veterinary Medicine Authority (APVMA)
Other sources	If no suitable* guidance is found from initial screening above the following sources will be screened for existing guidance: ☒ Australian agencies [National Environmental Protection Council, National Health and Medical Research Council (Nutrient Reference Values)] ☒ International agencies [Dutch National Institute for Public Health and the Environment, European Commission, Health Canada, Minnesota Department of Health, New Zealand Ministry of Health, South African Department of Water Affairs and Forestry, UK Government] ☒ Other [Industry reports from water providers for exposure information: e.g. Melbourne Water, Sydney Water, SA Water, TasWater, Water Corporation of Western Australia, Power and Water Corporation NT, Seqwater, Icon Water, Water Services Association of Australia] Note these water provider sources will be included in the literature search regardless of whether suitable guidance is found from the agencies identified above.
Limits:	Guidance/guidelines that will be included: ☒ Publicly available documents (near publication drafts will be accepted if available). ☐ Guidance/guidelines in languages other than English ☐ Other [please specify]
Dates:	The search for existing guidance/guidelines will be conducted from 1996 to the present date.
Key search terms to be used**:	Lead
Excluded guidance/ guidelines	All decisions taken during screening will be documented and outlined in the final report with a list of excluded guidance/guidelines and justification for their exclusion.
* It is recognised ‘suitability’ of existing guidance is somewhat subjective, but will be judged based on age and comprehensiveness of identified existing guidance from the sources initially screened, as well as through an evaluation using the criteria for assessing existing guidance (see Appendix C).	

** Search terms may need to be modified depending on the website queried. Any modification to search terms will be recorded.

Data collection and analysis

Expertise	Data extraction will be performed by content expert [TH].
Data to be extracted from existing guidance/ guidelines	☒ Guideline details (e.g. developing organisation, citation information, date of publication, date of evidence search used for underpinning review). ☒ Information on administrative/technical criteria as outlined in the Assessment Tool for each guidance document/ guideline under consideration (see **Appendix C**). ☒ Health-based guideline values or equivalent guidance value for lead (including any formulae or safety margins incorporated into the calculation of the values). ☒ Outcomes/critical health effects used to inform the recommendation, including any thresholds for acceptable risk used. ☒ An assessment of the certainty of the evidence on which each recommendation is based (drawn from the guideline or briefly summarised by the providers). [If applicable this will be undertaken consistent with the GRADE approach considering: risk of bias, imprecision, inconsistency, indirectness, publication bias, size of effect, dose response effect and direction of residual confounding. This will allow WQAC to assess the extent to which new evidence would be likely to modify the existing recommendations, see https://www.nhmrc.gov.au/guidelinesforguidelines/develop/assessing-certainty-evidence.] ☒ Information relevant to decision making (e.g. community values and preferences, resources or cost, analytical achievability, impacts on equity, acceptability and feasibility). [This will allow WQAC to identify areas where the existing recommendations may or may not be applicable to the Australian context and the ADWG[6]]. ☒ Information on the applicability of the guideline to the Australian context (e.g. setting and population, any issues with supporting evidence such as geographical or infrastructure differences, including to remote and tropical areas). [This will allow WQAC to assess whether there are barriers or adaptations required before the recommendations could be adopted in Australia, see https://www.nhmrc.gov.au/guidelinesforguidelines/plan/adopt-adapt-or-start-scratch.]

	☒ Any considerations or health outcomes noted in the guideline that appear not to be addressed in the current version of the ADWG ☐ Other [please specify]
Data extraction methods	☒ Single, no second reviewer ☐ Dual; second reviewer checks all data ☐ Dual; second reviewer checks [add proportion] ☐ Dual; independent screen and cross check
Analysis	Results will be tabulated for each eligible guideline. The following tables will be presented: ☒ Table to compare guideline characteristics e.g. developing organisation, setting, context, PECO characteristics / study design features. ☒ Table of health-based guideline values (or equivalent) for each guideline for each specific PECO question, and associated additional considerations. ☒ Table or Figure summarising findings of Assessment Tool against all included guidelines [e.g. bar chart or heat map comparing performance of each guidance document against the assessment criteria to demonstrate areas of uncertainty] ☐ Other [please specify]
Reporting	Following assessment of the existing guidance/ guidelines, a summary of findings will be provided to the Water Quality Advisory Committee or Chemical Subgroup to consider for adopting/adapting. If existing guidance is selected for further consideration, a brief evidence scan from the date of review will be required to ensure that no further review is needed (see *Evidence scan for recent studies*).

Evidence scan for recent studies

Criteria for considering recent evidence

Study designs	☒ Existing systematic reviews or literature reviews ☒ Human epidemiological studies ☒ Animal studies ☒ In vitro studies, but only if they inform the mode of action for the critical health effect of concern

	☐ Other [please specify]
Population	☒ Humans, including the general population as well as specific populations who may be at higher risk of adverse health outcomes such as: • Infants and children • People who are pregnant • Aboriginal and Torres Strait Islander peoples • People with iron deficiency • People with pre-existing health conditions such as renal, neurological, haematological or cardiovascular disease • People who ingest higher than average amounts of water (e.g. tropical locations, outdoor workers) • People with certain genetic polymorphisms ☒ Animals or cells as surrogates for human exposure (the latter only if the studies inform the mode of action for the critical health effect of concern)
Exposure	Exposure parameters that will be considered for lead include: • Exposure during critical time periods (e.g. pregnancy, foetal) • Exposure over a lifetime • Exposure through drinking, cooking, washing • Combination or interaction with other substances
Comparator(s)	Comparisons will be presented for: • Value, critical study, critical health effect etc, of existing drinking water guideline for lead and other values identified in the search. • Threshold doses (internal and/or external) of lead (if possible) associated with no adverse effects and critical adverse health effect.
Outcome(s)	The human health outcomes of concern from exposure to lead include: • Mortality • Severe human health outcomes, including incidence of life-threatening illness, disability or chronic disease with ongoing impact on quality of life. • Subtle human health outcomes which may only be recognisable at a population level (e.g. increased blood pressure, IQ decrements).

	Consideration regarding these outcomes will be given to: • The level of lead in drinking water considered to be safe or acceptable to human health over a lifetime (if possible, to be delineated from the information available).

Search methods

Expertise	The searches will be: ☒ verified by a content expert [TH] ☐ conducted by an information specialist [initials] ☐ independently peer reviewed.
Electronic databases	☒ MEDLINE/PubMed/TOXLINE ☐ Scopus ☐ SciFinder ☐ Trials registers [please specify] ☐ Other [please specify]
Other sources	☐ Citation tracking of primary studies identified in existing reviews ☐ Systematic review references ☐ Data from government/ intergovernmental agencies [please specify] ☐ Data from industry [please specify] ☐ Contact experts for references ☐ Other [please specify]
Limits:	We will include: ☒ Peer reviewed, published, in press, unpublished and ongoing studies will be included. ☐ Abstracts and conferences proceedings ☐ Studies in languages other than English [please specify]
Dates:	The search will be conducted from the date of the last search supporting eligible guidelines (to be confirmed) to the present date.
Key search terms to be used:	Lead AND toxicity AND oral

	Lead AND health AND oral Lead AND toxicity AND drinking water Lead AND health AND drinking water Lead AND exposure AND Australia
Search strategy:	☐ The complete search strategy for [at least one database] is provided in [Appendix X]. ☒ Complete search strategies for all electronic sources will be documented in sufficient detail to enable reasonable replication, and will be provided in the final report. ☐ If available, the search strategies used to underpin an eligible guideline will be replicated.
Screening search results:	☒ Screening of titles will be performed by researcher [SK] in Excel and verified by content expert [TH]
Abstracts	☒ Single reviewer screens relevant records identified in screening step. ☐ Dual; second reviewer checks all excluded records ☐ Dual; second reviewer checks [X%] of excluded records ☐ Dual; independent screen and cross check
Full text	☒ Single reviewer screens relevant records identified in abstract screening step. ☐ Dual; second reviewer checks all excluded records ☐ Dual; second reviewer checks [X%] of excluded records ☐ Dual; independent screen and cross check
Discrepancy resolution	☐ Consensus and/or third reviewer ☐ Other (please specify)
Excluded studies	☒ All decisions taken during screening will be documented and outlined in the final report with a list of excluded studies and brief justification of exclusion. ☐ Studies that are found to be relevant but not included in the final list of studies evaluated are to be listed with a brief justification of why they were excluded.

Data collection and analysis

Expertise	Data extraction will be performed by researcher [SK] and verified by content expert [TH].
Data to be extracted from recent literature	☒ Details on the review/study [including citation information, publication status, type of study, sample size, and summary of methods] ☒ Population, setting, exposure, comparison and outcome characteristics (PECO) of the study ☒ Data relevant to answering the research questions, along with definitions of outcomes measured, measurement instruments/tools used, and the main conclusions of the study. Where multiple numerical results are presented, all will be extracted. ☐ Other [please specify]
Data extraction methods	☒ Single, no second reviewer ☐ Dual; second reviewer checks all data ☐ Dual; second reviewer checks [add proportion] ☐ Dual; independent screen and cross check
Analysis	☒ Results will be tabulated across studies, grouping together studies of relevance to each research question, and by study design. ☒ Synthesis will not be conducted. The following tables will be presented: ☒ Table to compare PECO characteristics/ study design features ☒ Table of extracted numerical data for compilation of meta-analyses (if applicable). Where multiple eligible numerical results are reported from a single study, all will be reported. ☐ Other [please specify]
Reporting	A summary of relevant studies will be tabulated for consideration by the Water Quality Advisory Committee.

Supporting information in factsheet

Research questions

Supporting information	Research questions to consider

General description	Is this information current?
Measurement	Is this information current? What are the indicators of the risks? How can we measure this exposure? Analytical methods – current? Are there commercial analytical methods available that can measure at or below guideline value?
Treatment options	Is this information current in terms of current practices in Australia? Can treatment technologies treat to the suggested level of the guideline value?
Are there any new sections that should be added? Should anything be removed?	

Evidence scan to assess currency of information

Criteria for considering evidence

All study types that are relevant to answering the research questions will be considered.

Search methods

Expertise	The searches will be: ☒ informed/verified by a content expert [TH or GDN] ☐ conducted by an information specialist [initials] ☐ independently peer reviewed.
Electronic databases	☐ MEDLINE/PubMed/TOXLINE ☒ Scopus ☐ SciFinder ☐ Other
Other sources	☐ Citation tracking of primary studies identified in existing reviews ☐ Systematic review references ☐ Data from government/ intergovernmental agencies [please specify] ☒ Data from industry [contact Australian laboratories: National Measurement Institute, SGS, ALS, Eurofins]

	☐ Contact experts for references ☒ Other [Water Services Association of Australia; Standard Methods for the Examination of Water and Wastewater (https://www.standardmethods.org/); US EPA Drinking Water Treatability Database (https://tdb.epa.gov/tdb/home); discussion/consultation with WQAC or Chemical Subgroup]
Limits:	Evidence to be considered will include: ☒ Peer reviewed, published, in press, unpublished and ongoing studies. ☐ Abstracts and conferences proceedings ☐ Studies in languages other than English [please specify] ☒ Other [Australian laboratory information sheets on measurement methods and limits of reporting, general correspondence with laboratories, grey literature]
Dates:	The search will be conducted from the date of the last search supporting eligible guidelines (to be confirmed) to the present date.
Key search terms to be used:	(Lead) AND (treatment) AND (drinking water) (Lead) AND (analysis) AND (drinking water) (Lead) AND (testing) AND (drinking water)
Search strategy:	Complete search strategies for all electronic sources will be documented in sufficient detail to enable reasonable replication, and will be provided in the final Technical Report.
Screening search results:	☒ Screening will be performed by researcher [SK] in Excel and verified by content expert [TH]
Excluded studies	All decisions taken during screening will be documented and outlined in the final report with a list of excluded studies and justification for exclusion.

Data collection and analysis

Expertise	Data extraction will be performed by researcher [SK] and verified by content expert [TH].
Data to be extracted	☐ Study design details (including citation information, publication status, sample size, summary of methods). [see **Appendix B** for example] ☐ Data relevant to answering the research questions, along with definitions of outcomes measured, measurement instruments/tools used and the main conclusions of the study. Where multiple relevant numerical results are presented, all will be extracted. ☒ Other [citation information, name of commercial treatment technology (as applicable), name of commercial analytical technique and associated reporting limit]
Data extraction methods	☒ Single, no second reviewer ☐ Dual; second reviewer checks all data ☐ Dual; second reviewer checks [add proportion] ☐ Dual; independent screen and cross check
Analysis	☐ Results will be tabulated across studies, grouping together studies of relevance to each research question, and by study design. ☒ Synthesis will not be conducted. The following tables will be presented: ☒ Table of relevant extracted data to answer research questions. ☐ Other [please specify]

Reporting

Evidence Evaluation and Technical Reports

Section	Description of content	Evaluation Report	Technical Report
Executive summary	Overarching statement about review and findings	☒	☐
Introduction and Background	Definitions (key terms, outcome measures, abbreviations), rationale for review and objectives.	☒	☐

Research question/s	Questions underpinning the review and factsheet update	☒	☒
Evidence Evaluation Methods	Brief overview of the approach taken for evidence search and evaluation (reference complete details in Technical Report)	☒	☐
	Approach used to identify and retrieve existing guidance or studies [see **Appendix A** for the type of information that can be included in a search strategy]	☐	☒
	Process for selecting studies (i.e. application of inclusion/exclusion criteria) and list of included studies (and excluded if available).	☐	☒
	Methods for data extraction and completed table of extracted data for each piece of evidence	☐	☒
	Methods of assessing quality of existing guidance/ guidelines (i.e. use of Assessment Tool). Completed copy of Assessment tool for each guidance/guideline document.	☐	☒
	Methods used to analyse/synthesise/summarise or compare data from different sources. Summary of findings tables directly comparing data from different sources and uncertainty.	☒	☒
	Methods used for any calculations and explanatory text for any assumptions if used (can have different levels of information about this in each Report)	☒	☒
Results	Summary of findings tables for each research question or section of factsheet. Easy to compare different guidelines/studies in Evaluation Report, more detailed information in Technical Report	☒	☒
Discussion	Strengths and limitations of the studies/guidance, comparison of existing literature, a discussion of gaps in the evidence (if identified during the evaluation of the evidence) and a suggestion of areas for further research	☒	☐
Conclusion	Summary of option/s to adopt/adapt existing guidance, including whether recent evidence	☒	☐

	indicates that a health-based guideline value needs to be comprehensively reviewed		
Review team	List members of Review Team	☒	☐
Declared interests	Documentation of the declared interest(s) of reviewers	☒	☐
Acknowledgements	Documentation of any inputs from individuals not on the Team	☒	☐
References	Included references	☒	☒
Appendices	Additional technical detail or examples of templates used in methods to be provided as required	☐	☒

Acknowledgements

The authors acknowledge Kristal Jackson from NHMRC for her indispensable contributions to the layout of the draft research protocol, as well as the Water Quality Advisory Committee for their insightful review comments.

Declaration of 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: • Conducted numerous health risk assessments for mining clients where lead was one of the chemicals of potential concern requiring assessment. • Determined appropriate hazard and dangerous goods classifications for lead-containing mineral products (e.g. concentrates) for clients in the mining industry. • Provided the report “Assessment of International and National Agency Processes for Deriving HBGVs and DWGs” to the NHMRC.
Mr Giorgio De Nola	As part day-to-day consulting activities at SLR Consulting, Mr De Nola has been involved in numerous health risk assessments as part of contaminated land audits as well as for developer clients where lead was one of the chemicals of potential concern requiring assessment.
Dr Slavica Kandic	No interest to declare.

Dr Roger Drew	As part day-to-day consulting activities at ToxConsult Pty Ltd and Drew Toxicology Consulting, Dr Drew has: • Reviewed numerous health risk assessments where lead was one of the chemicals of potential concern requiring assessment. • Provided the report "Assessment of International and National Agency Processes for Deriving HBGVs and DWGs" to the NHMRC.

References

1. ATSDR (2020). Toxicological Profile for Lead, Agency for Toxic Substances and Disease Prevention, U.S. Department of Human health and Services. Atlanta, US https://www.atsdr.cdc.gov/toxprofiles/tp13.pdf.

2. WHO (2017). Guidelines for drinking-water quality. Fourth edition incorporating the first Addendum, World Health Organization. Geneva. https://apps.who.int/iris/bitstream/handle/10665/254637/9789241549950-eng.pdf;jsessionid=8A179F96A66DD2F070E785831CAB3180?sequence=1.

3. NHMRC (2021). Australian Drinking Water Guidelines 6 2011- V 3.6 (March 2021 update) National Health and Medical Research Council . Canberra, Australia.

4. IARC (2006). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 87. Inorganic and Organic Lead Compounds. World Health Organization. International Agency for Research on Cancer Lyon France.

5. Cochrane (2021). COVID Rapid Review Protocol Template. Accessed 19 February 2021. Available from: https://covidreviews.cochrane.org/sites/covidreviews.cochrane.org/files/public/uploads/covid-19_rr_protocol_template_v4.docx

6. Alonso-Coello P, Schünemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, Treweek S, Mustafa RA, Rada G, Rosenbaum S, Morelli A, Guyatt GH, Oxman AD, Grade Working Group (2016). GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. *BMJ*. 353.

7. NHMRC (2015). NHMRC information paper: evidence on the effects of lead on human health. National Health and Medical Research Council. May 2015.

Appendix A – Search strategy and selection of evidence

Example template of documenting a search strategy and how evidence is selected (if required).

Outline specific steps that will be taken to search and select the evidence in enough detail that someone else could reasonably replicate the search, including details such as:

Search terms	[List and define keywords and suggested search string combinations that you will use to search for publications based upon the PECO elements and research questions (present in table if possible) – these will have to be used across all databases for consistency. If there are multiple research questions to answer, several different searches may need to be undertaken.]
Databases	[List at least two databases that will be searched using the agreed search terms (e.g. PubMed, Scopus, Scifinder).]
Publication date	[Specify the publication date range that will be searched across all databases including justifications for any specific date ranges (e.g. for a guideline update NHMRC usually searches from the date of the last literature search so there is no duplication of effort, but if some key pieces of evidence were not considered in the last review these may also be included with justification)]
Language	[Specify the language of publications that the search will be limited to (this is important when there are limited resources to translate publications)]
Study Type	[State what types of publications will be accepted to answer the research question, or what hierarchy will be used by the reviewer in the event that limited evidence is available. State what types of publications will not be accepted.]
Inclusion and exclusion criteria	[Define any other criteria that can be applied to the evidence to select studies for appraisal; and importance (priority rating) of outcomes to be considered as part of the review.]
Validation methods used (if any)	[Details on how you will validate the search strategy and check that it works before you undertake a full search, e.g. performing an initial search based upon the chosen search terms and checking against key publications as determined by the reviewer or expert committee. Include a description of how you will refine the process based on these initial results (e.g. adding/modifying criteria or filters)]
Screening methods	[Details on how you will efficiently screen the results of your search (which can sometimes retrieved thousands of publications). For example, will you only screen the titles or

	abstracts for key words? What will you do with publications that you aren't sure about?]
Quality check	[Methods for checking that key publications have been picked up the search – are there any omissions or missed papers from the database searches?]
Grey literature	[Detail how you will search and retrieve any grey literature (e.g. define what kind of grey literature you will be looking for, what search engines or websites you will use, list any agencies/organisations that will be contacted for information and how this will be done).]
Documentation of search	[Explain how this process will be recorded (e.g. using a PRISMA diagram (Moher et al. 2009)). Explain how you will record which publications were found but excluded with justification.]
Retrieval of publications	[Describe how you will obtain publications, collate papers for review into a literature database (e.g. Endnote) and store in secure backup storage]

Appendix B – Data extraction template

General information	Study ID	
	Date template completed	
	Authors Publication date Publication type Peer reviewed Country of origin Source of funding Possible conflicts of interest	
Study characteristics	Aim/objectives of study Study type/design Study duration Type of water source (if applicable)	
Population characteristics	Population/s studied Selection criteria for population (if applicable) Subgroups reported Size of study	
Exposure and setting	Type of water source (if applicable) Exposure pathway Source of chemical/contamination Comparison group(s)	
Study methods	Water quality measurement used Water sampling methods (monitoring, surrogates)	
Results **(for each outcome)**	Definition of outcome How outcome was assessed Method of measurement Number participants (exposed/non-exposed, missing/excluded) (if applicable)	

Statistics **(if any)**	Statistical methods used Details on statistical analysis Relative risk/odds ratio, confidence interval?	
Author's conclusion	Interpretation of results Assessment of uncertainty (if any)	
Reviewer comments	Results included/excluded in review (if applicable) Notes on study quality e.g. gaps, methods	

Appendix C – Criteria for assessing existing guidance or guidelines

Administrative and technical criteria for assessing existing guidance or guidelines

Criteria have been colour-coded to assess minimum requirements as follows: 'Must have', 'Should have' or 'May have'

	Criteria	Y/N/?/NA	Notes
	Overall guidance/advice development process		
	Are the key stages of the organisation's advice development processes compatible with Australian processes?		
	Are the administrative processes documented and publicly available?		
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?		
	Are funding sources declared?		
	Was there public consultation on this work? If so, provide details.		
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?		
	Was the guidance/advice developed or updated recently? Provide details.		
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?		
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?		
	Does the organisation use or undertake systematic literature review methods to identify and select data underpinning the advice? Are the methods used documented clearly?		
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?		
	Are inclusion/exclusion criteria used to select or exclude certain studies from the review? If so, is justification provided?		

	Does the organisation use or adopt review findings or risk assessments from other organisations? What process was used to critically assess these external findings?		
	Can grey literature such as government reports and policy documents be included?		
	Is there documentation and justification on the selection of a toxicological endpoint for use as point of departure for health-based guideline derivation?		
	Evidence search		
	Are databases and other sources of evidence specified?		
	Does the literature search cover at least more than one scientific database as well as additional sources (which may include government reports and grey literature)?		
	Is it specified what date range the literature search covers? Is there a justification?		
	Are search terms and/or search strings specified?		
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?		
	Critical appraisal methods and tools		
	Is risk of bias of individual studies taken into consideration to assess internal validity? If so, what tools are used? If not, was any method used to assess study quality?		
	Does the organisation use a systematic or some other methodological approach to synthesise the evidence (i.e. to assess and summarise the information provided in the studies)? If so, provide details.		
	Does the organisation assess the overall certainty of the evidence and reach recommendations? If so, provide details.		
	Derivation of health-based guideline values		
	Is there justification for the choice of uncertainty and safety factors?		
	Are the parameter value assumptions documented and explained?		
	Are the mathematical workings/algorithms clearly documented and explained?		

	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?		
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?		
	What processes are used when expert judgement is required and applied? Is the process documented and published?		
	Is dose response modelling (e.g. BMDL) routinely used?		
	What is the organisation's policy for dealing with substances for which a non-threshold mode of action may be applicable in humans? Has the policy been articulated and recorded?		
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?		