

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

Organisation

CDM Smith

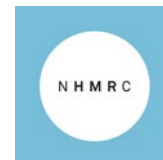
Team

Name	Qualification	Experience
John Frangos	MSc Toxicology, DABT, FACTRA	25+ years of experience in toxicology and risk assessment and regulatory advice to industry and government bodies (including GV development and health impacts of environmental exposure).
Dr Suzie Reichman	PhD Risk Assessment Expert	25+ years of experience
Dr Paolin Rocio Caceres Velez	PhD Ecotoxicology / Nanotoxicology	5 years of experience in ecotoxicity risk assessment
Dr Maryam Moslehi	PhD Molecular Biochemistry/Health Science	3 years of experience in risk assessment and literature review

[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]

Date protocol completed

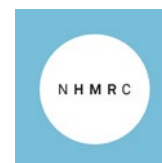
6th July 2021



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.

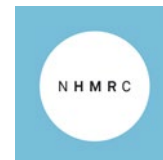
A separate Research Protocol should be developed for each chemical (or closely related group of chemicals) for which an updated guidance review is to be conducted, as the current state of knowledge, health outcomes of interest and sources of evidence will vary.

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.¹ 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.



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Background

Chlorate and chlorite are disinfection by-products resulting from the use of chlorine dioxide as a disinfectant and for odour/taste control in water. Chlorine dioxide rapidly decomposes into chlorite, chlorate and chloride ions in treated water, chlorite being the predominant species; this reaction is favoured by alkaline conditions. The major route of environmental exposure to chlorine dioxide, sodium chlorite and sodium chlorate is through drinking-water. Chlorate is also formed in sodium hypochlorite solution that is stored for long periods, particularly at high ambient temperatures (Asami, 2009).

With chlorine dioxide disinfection, the concentration of chlorate depends heavily on process conditions (in both chlorine dioxide generator and the water treatment plant) and applied dose of chlorine dioxide. As there is no viable option for reducing chlorate concentrations, control of chlorate concentration must rely on preventing its addition (from sodium hypochlorite) or formation (from chlorine dioxide) (WHO, 2004).

No guideline value (GV) for chlorate was set in Australian Drinking Water Guidelines (ADWG) due to insufficient data. WHO (2004) and Health Canada (endorsed 2008) established GV of 0.7 and 1 mg/L, respectively based on thyroid gland effects (colloid depletion).

GV derivation of 1 mg/L in Health Canada has not been specified.

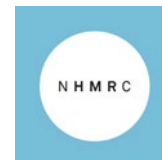
A provisional guideline value for chlorate of 0.7 mg/L was published by WHO in 2004 based on limited data from human volunteer studies and a short-term study in rats. Data from a long-term study in rats was subsequently published (NTP 2005) and has been used to derive a new TDI value (JECFA 2007). JECFA concluded that the most sensitive effects were changes to the thyroid gland of male rats (it was considered that humans are likely to be less sensitive than rats) thus an interspecies variation not required. However, JECFA noted deficiencies in the database, particularly with respect to the investigation of possible neurodevelopmental effects. This concern relates to reduced iodide transport to the thyroid in pregnant women who are seriously iodine deficient. Although JECFA (2007) set a health-based value of 0.3 mg/L, the previous GV of 0.7 mg/L was retained given that the control of chlorate concentrations must rely on preventing its formation and control of storage conditions is considered to be difficult in small, resource limited water supplies.

Given the importance of maintaining adequate disinfection of water supplies and limited options for reducing chlorate levels in supplies treated with hypochlorite, further information on the occurrence and sources of chlorate in Australian waters is needed before a guideline value can be developed.

Objectives of the review

The objective of this study is to identify existing sources of guidance or guidelines on the impact of exposure to chlorate in drinking water on human health outcomes. 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.



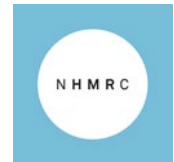
As well as characterising guidance and guidelines for chlorate, review toxicity studies and observation studies focussing on chlorate in drinking water systems will be conducted.

Methods

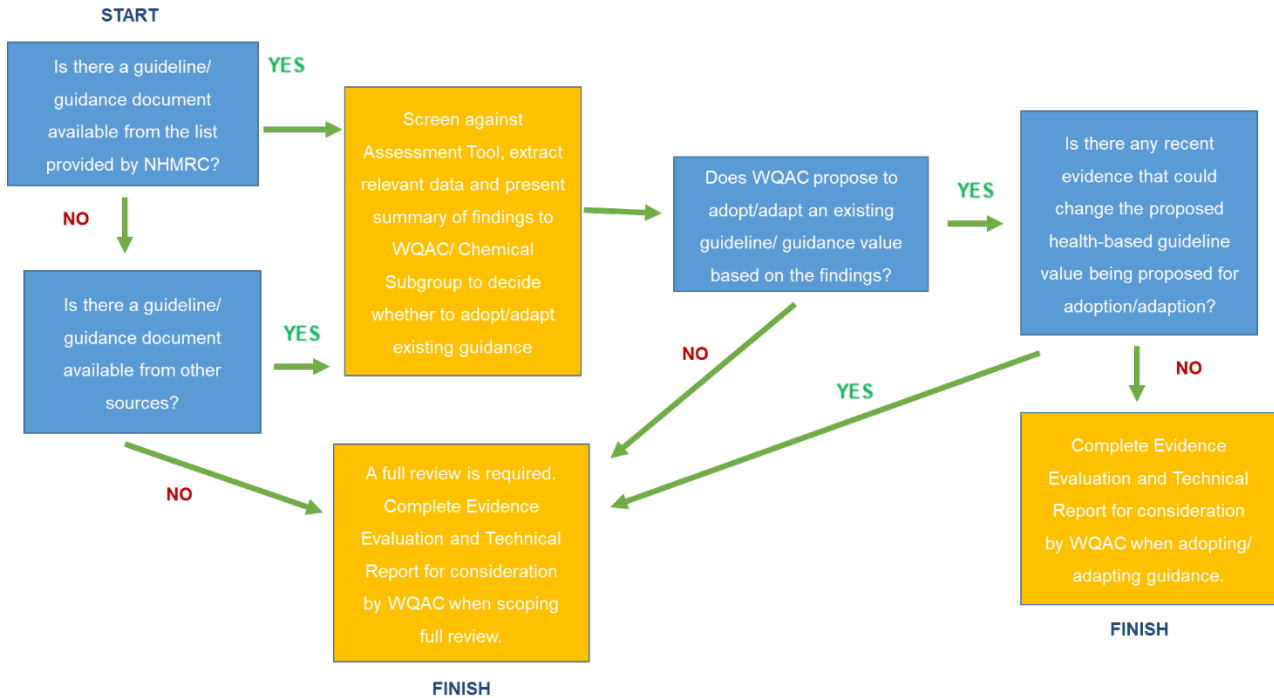
This review will be conducted using different approaches depending on the factsheet sections being updated.

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.



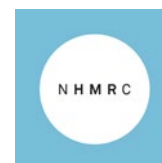
The process for reviewing health-based advice is summarised in the following flowchart:



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
<p>Health-related advice in chemical factsheet including:</p> <ul style="list-style-type: none"> • Health-based guideline value • Health considerations • Typical Australian exposure levels • Risk summary • Derivation of guideline value 	<ul style="list-style-type: none"> • 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
<p>Supporting information in chemical factsheet including:</p> <ul style="list-style-type: none"> • General description 	<ul style="list-style-type: none"> • Review information for currency • Scan evidence that could be used to update existing information



<ul style="list-style-type: none"> • Measurement (analytical methods) • Treatment options • Risk management options 	<ul style="list-style-type: none"> • Present summary of findings • Report details of literature search
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The methods outlined below will govern the searching, selecting, assessment and reporting of the evidence used to inform the update to bromate factsheet.

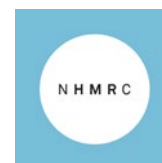
Any changes to the Research Protocol once finalised on the advice of the Water Quality Advisory Committee will be recorded and documented in the Technical Report.

Health-related advice in factsheet

Research questions

Explicit research questions should be identified for each health-based recommendation or guidance in the factsheet for which updated evidence is sought, for example using a population, exposure, comparator, outcome (PECO) framework².

Health-related advice	Research questions to consider
Health-based guideline value	<p>What level of chlorate in drinking water causes adverse health effects? What is the endpoint that determines this value?</p> <p>Is the proposed guideline value relevant to the Australian context?</p> <p>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?)</p>
Health considerations	<p>What are the key adverse health hazards from exposure to chlorate in Australian drinking water?</p> <p>What is the critical human health endpoint for chlorate?</p> <p>What are the justifications for choosing this endpoint?</p>
Typical Australian water levels or exposure profile	<p>What are the typical levels in Australian drinking water? Do they vary around the country or under certain conditions?</p>
Risk summary	<p>What are the risks to human health from exposure to chlorate in Australian drinking water?</p> <p>Is there evidence of any emerging risks that are not mentioned in the current factsheet that require review?</p>

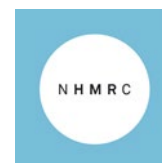


Other research questions?	Are there studies quantifying health burden (reduced or increased) due to chlorate?
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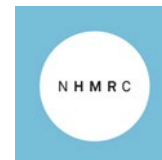
Targeted screening of existing health-based guidance

Criteria for considering existing guidelines/guidance

Study designs for adopt/adapt approach	<p>In the first instance, guidelines/guidance on chlorate developed by the following agencies will be considered:</p> <ul style="list-style-type: none"> • World Health Organization (WHO) (including the Joint FAO/WHO Expert Committee on Food Additives [JECFA]) • European Food Safety Authority (EFSA) • Health Canada • 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 Standards Australia New Zealand (FSANZ) • Australian Pesticides and Veterinary Medicine Authority (APVMA) <p>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.</p>
Population	<p>Humans, including the general population as well as specific populations who may be at higher risk of adverse health outcomes such as:</p> <ul style="list-style-type: none"> • Infants and children • People who are pregnant • Aboriginal and Torres Strait Islander peoples • People with pre-existing health conditions identified in peer reviewed competent authority reviews [for example thyroid glands, neurodevelopmental disorders] • People who ingest higher than average amounts of water (e.g. tropical locations, outdoor workers)]
Exposure	<p>Exposure parameters that will be considered for chlorate include:</p> <ul style="list-style-type: none"> • Exposure over a lifetime

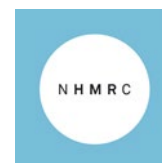


	<ul style="list-style-type: none"> • Short-term exposure (e.g. over days or weeks during a water contamination event) • Exposure through drinking, cooking, washing, skin contact • Combination or reaction with other substances • Exposure models that allow more accurate characterisation of exposure between animal studies and humans or between humans subpopulations (for example pharmacologically based physiological kinetic models)
<p>Comparator(s)</p>	<p>The review will be used to determine whether the existing health-based guideline value(s) in the factsheet should be changed, so comparisons between the current value and higher/lower values are of interest.</p> <p>Comparisons between different water treatment approaches may be required to assess incremental exposure levels and observational study results (incidence or relative incidence).</p> <p>Comparison to no exposure may be of interest to demonstrate that a particular level is below the 'no observed adverse effect level'.</p>
<p>Outcome(s)</p>	<p>The human health and aesthetic outcomes of concern from exposure to chlorate include:</p> <ul style="list-style-type: none"> • Mortality • Severe human health outcomes, including incidence of life-threatening illness, disability or chronic disease with ongoing impact on quality of life. • Less severe or short-term human health outcomes, e.g. irritation. • Aesthetic outcomes, including taste, smell, colour, clarity, etc. • Other (bioanalytical assays that support health outcomes, for example results from Tox21 screening assays) <p>Consideration regarding these outcomes will be given to:</p> <ul style="list-style-type: none"> • The level of chlorate in drinking water considered to be safe or acceptable to human health over a lifetime • The level of chlorate in drinking water considered to be safe or acceptable to human health during a short-term event • The level of chlorate in drinking water considered to be acceptable in relation to aesthetic factors, including taste, smell, colour, clarity, etc.



Search methods

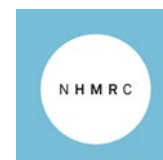
Expertise	<p>The searches will be:</p> <p><input checked="" type="checkbox"/> conducted by content experts, Paolin Rocio Caceres Velez</p> <p><input type="checkbox"/> conducted by an information specialist [initials]</p> <p><input type="checkbox"/> independently peer reviewed.</p>
Sources initially screened	<p>The following sources will be screened initially:</p> <p><input checked="" type="checkbox"/> World Health Organization (WHO) (including the Joint FAO/WHO Expert Committee on Food Additives [JECFA])</p> <p><input checked="" type="checkbox"/> European Food Safety Authority (EFSA)</p> <p><input checked="" type="checkbox"/> United States Environmental Protection Agency (US EPA)</p> <p><input checked="" type="checkbox"/> US Agency for Toxic Substances and Disease Registry (ATSDR)</p> <p><input checked="" type="checkbox"/> Californian Office of Health and Hazard Assessment (OEHHA)</p> <p><input checked="" type="checkbox"/> Health Canada</p> <p><input checked="" type="checkbox"/> Food Standards Australia New Zealand (FSANZ)</p> <p><input checked="" type="checkbox"/> Australian Pesticides and Veterinary Medicine Authority (APVMA)</p>
Other sources	<p>If no suitable guidance is found from initial screening above the following sources will be screened for existing guidance:</p> <p><input checked="" type="checkbox"/> Australian agencies [water research Australia (waterRA), CSIRO]</p> <p><input checked="" type="checkbox"/> International agencies [IARC, UNECE, RIVM, German]</p> <p><input type="checkbox"/> Other [please specify]</p>
Limits:	<p>Guidance/guidelines that will be included:</p> <p><input checked="" type="checkbox"/> Publicly available documents (near publication drafts will be accepted if available).</p> <p><input checked="" type="checkbox"/> Guidance/guidelines in languages other than English [German]</p> <p><input type="checkbox"/> Other [please specify]</p>
Dates:	<p>The search for existing guidance/guidelines will be conducted 2004 (WHO, 2004) to the present date.</p> <p>The literature search will be restricted to studies post the implementation of the latest drinking water guidelines identified in guideline review.</p>
Key search terms to be used:	<p>Chlorate, chlorate AND drinking water, chlorate AND disinfect, chlorate AND adverse health effect, chlorate AND toxicity</p>



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.

Data collection and analysis

Expertise	Data extraction will be performed by Paolin Rocio Caceres Velez
Data to be extracted from existing guidance/guidelines	<ul style="list-style-type: none"> ☒ 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 chlorate (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 (either drawn from the guideline or assessed 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, 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 ADWG³]. ☒ 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

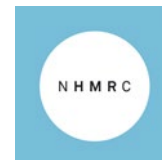


	<p>https://www.nhmrc.gov.au/guidelinesforguidelines/plan/adopt-adapt-or-start-scratch.</p> <p><input checked="" type="checkbox"/> Any considerations or health outcomes noted in the guideline that appear not to be addressed in the current version of the ADWG</p>
Data extraction methods	<p><input checked="" type="checkbox"/> Single, no second reviewer</p> <p><input type="checkbox"/> Dual; second reviewer checks all data</p> <p><input type="checkbox"/> Dual; second reviewer checks [add proportion]</p> <p><input type="checkbox"/> Dual; independent screen and cross check</p>
Analysis	<p>Results will be tabulated for each eligible guideline. The following tables will be presented:</p> <p><input checked="" type="checkbox"/> Table to compare guideline characteristics e.g. developing organisation, setting, context, study design features.</p> <p><input checked="" type="checkbox"/> Table of health-based guideline values (or equivalent) for each guideline, and associated additional considerations.</p> <p><input checked="" type="checkbox"/> Table summarising findings of Assessment Tool against all included guidelines [heat map comparing performance of each guidance document against the assessment criteria to demonstrate areas of uncertainty]</p>
Reporting	<p>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.</p> <p>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 <i>Evidence scan for recent studies</i>).</p>

Evidence scan for recent studies

An evidence scan should proceed for each research question for which eligible guidance has been identified in the previous stage to ensure there is no recent data that would change the recommendation. The aim of this scoping search is not to present a systematic review or evidence synthesis, nor to present recommendations to the Water Quality Advisory Committee, but to understand the availability of recent literature, and to determine whether a formal systematic review to update the evidence underpinning available guidance is warranted. This decision will be made by the Water Quality Advisory Committee, based on the certainty and applicability of the evidence underpinning the identified guidance, and the probability that new evidence would be sufficient to affect the existing recommendations.⁴ Any further evidence reviews arising from this decision are out of scope for this project.

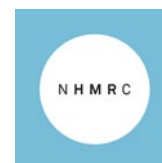
Preliminary aspects of the Research Protocol for the evidence scans may be agreed with the Water Quality Advisory Committee in advance, but the specific details of each evidence scan will need to be confirmed upon completion of the first stage of this review. This will include confirming



which research questions to be covered and publication dates. All changes to the Research Protocol will be agreed with the Water Quality Advisory Committee or bromate Subgroup at that point before proceeding.

Criteria for considering recent evidence

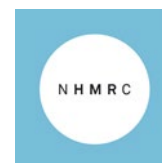
Study designs	<input checked="" type="checkbox"/> Existing systematic reviews or literature reviews <input checked="" type="checkbox"/> Human epidemiological studies <input checked="" type="checkbox"/> Animal studies <input type="checkbox"/> In vitro studies <input type="checkbox"/> Other [please specify]
Population	<input checked="" type="checkbox"/> Humans, including the general population as well as specific populations who may be at higher risk of adverse health outcomes such as:] <ul style="list-style-type: none"> • Infants and children • People who are pregnant • Aboriginal and Torres Strait Islander peoples • People with pre-existing health conditions [thyroid effects, neurodevelopmental disorders] • People who ingest higher than average amounts of water (e.g. tropical locations, outdoor workers)
Exposure	Exposure parameters that will be considered for chlorate include: <ul style="list-style-type: none"> • Exposure over a lifetime • Short-term exposure (e.g. over days or weeks during a water contamination event) • Exposure through drinking, cooking, washing, skin contact • Combination or reaction with other substances • Other (PBPK models)
Comparator(s)	In most cases, for the purposes of the Guidelines, the review will be used to determine whether the existing health-based guideline value(s) in the factsheet should be changed, so comparisons between the current value and higher/lower values would be of interest. Alternatively, comparisons between any higher and lower doses at different incremental levels would be of interest.



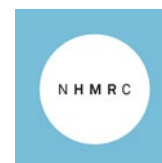
	Comparison to no exposure may be of interest to demonstrate that a particular level is below the 'no observed adverse effect level'.
Outcome(s)	<p>The human health and aesthetic outcomes of concern from exposure to chlorate include:</p> <ul style="list-style-type: none"> • Mortality • Severe human health outcomes, including incidence of life-threatening illness, disability or chronic disease with ongoing impact on quality of life. • Less severe or short-term human health outcomes, e.g. irritation. • Aesthetic outcomes, including taste, smell, colour, clarity, etc. <p>Consideration regarding these outcomes will be given to:</p> <ul style="list-style-type: none"> • The level of chlorate in drinking water considered to be safe or acceptable to human health over a lifetime • The level of chlorate in drinking water considered to be safe or acceptable to human health during a short-term event • The level of chlorate in drinking water considered to be acceptable in relation to aesthetic factors, including taste, smell, colour, clarity, etc.

Search methods

Expertise	<p>The searches will be:</p> <ul style="list-style-type: none"> <input checked="" type="checkbox"/> conducted by a content expert Paolin Rocio Caceres Velez <input type="checkbox"/> conducted by an information specialist [initials] <input type="checkbox"/> independently peer reviewed.
Electronic databases	<ul style="list-style-type: none"> <input checked="" type="checkbox"/> MEDLINE/PubMed/TOXLINE <input type="checkbox"/> Scopus <input checked="" type="checkbox"/> SciFinder <input type="checkbox"/> Trials registers [please specify] <input type="checkbox"/> Other [Wiley, Science Direct]



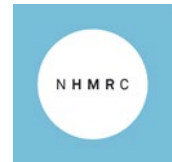
Other sources	<input checked="" type="checkbox"/> Citation tracking of primary studies identified in existing reviews <input type="checkbox"/> Systematic review references <input checked="" type="checkbox"/> Data from government/ intergovernmental agencies [water research Australia (waterRA), CSIRO] <input type="checkbox"/> Data from industry [please specify] <input type="checkbox"/> Contact experts for references <input type="checkbox"/> Other [please specify]
Limits:	<p>We will include:</p> <input checked="" type="checkbox"/> Peer reviewed, published, in press, unpublished and ongoing studies will be included. <input type="checkbox"/> Abstracts and conferences proceedings <input type="checkbox"/> Studies in languages other than English [please specify]
Dates:	The search will be conducted from 2004 (since WHO 2004 guideline set) to the present date.
Key search terms to be used:	Chlorate, chlorate AND drinking water, chlorate AND disinfect, chlorate AND adverse health effect, chlorate AND toxicity
Search strategy:	<input type="checkbox"/> The complete search strategy for [at least one database] is provided in [Appendix X]. <input checked="" type="checkbox"/> 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. <input type="checkbox"/> If available, the search strategies used to underpin an eligible guideline will be replicated.
Screening search results:	<input checked="" type="checkbox"/> Screening will be performed by Paolin Rocio Caceres Velez in excel or like tool
Abstracts	<input checked="" type="checkbox"/> Single reviewer screens all records. <input type="checkbox"/> Dual; second reviewer checks all excluded records <input type="checkbox"/> Dual; second reviewer checks [X%] of excluded records <input type="checkbox"/> Dual; independent screen and cross check
Full text	<input checked="" type="checkbox"/> Single reviewer screens all records



	<input type="checkbox"/> Dual; second reviewer checks all excluded records <input type="checkbox"/> Dual; second reviewer checks [X%] of excluded records <input type="checkbox"/> Dual; independent screen and cross check
Discrepancy resolution	<input type="checkbox"/> Consensus and/or third reviewer <input type="checkbox"/> Other (please specify)
Excluded studies	<input checked="" type="checkbox"/> All decisions taken during screening will be documented and outlined in the final report with a list of excluded studies and justification of exclusion. <input checked="" type="checkbox"/> 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 Paolin Rocio Caceres Velez.
Data to be extracted from recent literature	<input checked="" type="checkbox"/> Details on the review/study [including citation information, publication status, type of study, sample size, and summary of methods] <input checked="" type="checkbox"/> Population, setting, exposure, comparison and outcome characteristics (PECO) of the study <input checked="" type="checkbox"/> 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.
Data extraction methods	<input checked="" type="checkbox"/> Single, no second reviewer <input type="checkbox"/> Dual; second reviewer checks all data <input type="checkbox"/> Dual; second reviewer checks [add proportion] <input type="checkbox"/> Dual; independent screen and cross check
Analysis	<input checked="" type="checkbox"/> Results will be tabulated across studies, grouping together studies of relevance to each research question, and by study design. <input checked="" type="checkbox"/> Synthesis will not be conducted. The following tables will be presented: <input checked="" type="checkbox"/> Table to compare PECO characteristics/ study design features



	<input checked="" type="checkbox"/> Table of extracted numerical data for compilation of meta-analyses. Where multiple eligible numerical results are reported from a single study, all will be reported.
Reporting	A summary of relevant studies will be tabulated for consideration by the Water Quality Advisory Committee.

Supporting information in factsheet

Research questions

Explicit research questions should be identified for each recommendation in the ADWG for which updated evidence is sought, for example using the PECO framework.² This may require different eligibility criteria and search strategies for each question.



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? current LODs achieved, with respect to various GVs?
Treatment options	Is this information current?
Risk management options	Is this information current? What are the current practices to minimise or manage the risks identified?
Are there any new sections that should be added? Should anything be removed?	At this point no new sections are anticipated.
Other research questions?	No additional research questions are anticipated, this maybe informed by the literature search results.

Evidence scan to assess currency of information

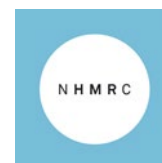
The supporting information provided in the factsheet will be reviewed for currency. This information focuses on implementation advice (monitoring, treatment etc.) and is generally a summary of best practice options for end users with difference resources.

Criteria for considering evidence

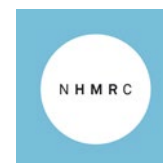
All study types that are relevant to answering the research questions will be considered.

Search methods

Expertise	The searches will be: <input checked="" type="checkbox"/> conducted by content expert Paolin Rocio Caceres Velez <input type="checkbox"/> conducted by an information specialist [initials] <input type="checkbox"/> independently peer reviewed.
Electronic databases	<input checked="" type="checkbox"/> MEDLINE/PubMed/TOXLINE <input type="checkbox"/> Scopus <input checked="" type="checkbox"/> SciFinder



Other sources	<input type="checkbox"/> Citation tracking of primary studies identified in existing reviews <input type="checkbox"/> Systematic review references <input type="checkbox"/> Data from government/ intergovernmental agencies [please specify] <input type="checkbox"/> Data from industry [please specify] <input type="checkbox"/> Contact experts for references <input type="checkbox"/> Other [please specify]
Limits:	Evidence to be considered will include: <input checked="" type="checkbox"/> Peer reviewed, published, in press, unpublished and ongoing studies. <input type="checkbox"/> Abstracts and conferences proceedings <input type="checkbox"/> Studies in languages other than English [please specify] <input type="checkbox"/> Other [please specify]
Dates:	The search will be conducted from 2004 to the present date.
Key search terms to be used:	Chlorate, chlorate AND drinking water, chlorate AND disinfect, chlorate AND adverse health effect, chlorate AND toxicity
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:	<input checked="" type="checkbox"/> Screening will be performed by Paolin Rocio Caceres Velez in excel or like tool
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 Paolin Rocio Caceres Velez
Data to be extracted	<input checked="" type="checkbox"/> Study design details (including citation information, publication status, sample size, summary of methods). [see Appendix B for example] <input checked="" type="checkbox"/> 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. <input checked="" type="checkbox"/> Other relevant citations in bibliography.
Data extraction methods	<input checked="" type="checkbox"/> Single, no second reviewer <input type="checkbox"/> Dual; second reviewer checks all data <input type="checkbox"/> Dual; second reviewer checks [add proportion] <input type="checkbox"/> Dual; independent screen and cross check
Analysis	<input checked="" type="checkbox"/> Results will be tabulated across studies, grouping together studies of relevance to each research question, and by study design. <input checked="" type="checkbox"/> Synthesis will not be conducted. The following tables will be presented: <input checked="" type="checkbox"/> Table of relevant extracted data to answer research questions. Where multiple eligible numerical results are reported from a single study, all will be reported.

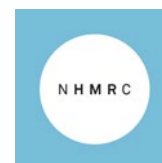
Reporting

Evidence Evaluation and Technical Reports

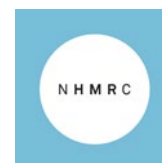
The Evidence Evaluation Report will interpret, synthesise and summarise the findings of the evidence review and address the research questions. This Report will contain high-level information only.

The Technical Report will contain technical information about the review methodology and any other details relating to the Evidence Evaluation Report. The Technical Reports will describe all details of the methodology used that would be too exhaustive for the Evidence Evaluation Report.]

An example of similar reports and the information required (although please note that these were done for systematic reviews and not an adopt/adapt/scoping approach) is available at <https://www.nhmrc.gov.au/about-us/publications/water-fluoridation-dental-and-other-human-health-outcomes>]



Section	Description of content	Evaluation Report	Technical Report
Executive summary	Overarching statement about review and findings	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Introduction and Background	Definitions (key terms, outcome measures, abbreviations), rationale for review and objectives.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Research question/s	Questions underpinning the review and factsheet update	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Evidence Evaluation Methods	Brief overview of the approach taken for evidence search and evaluation (reference complete details in Technical Report)	<input checked="" type="checkbox"/>	<input type="checkbox"/>
	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]	<input type="checkbox"/>	<input checked="" type="checkbox"/>
	Process for selecting studies (i.e. application of inclusion/exclusion criteria) and list of included studies (and excluded if available).	<input type="checkbox"/>	<input checked="" type="checkbox"/>
	Methods for data extraction and completed table of extracted data for each piece of evidence	<input type="checkbox"/>	<input checked="" type="checkbox"/>
	Methods of assessing quality of existing guidance/ guidelines (i.e. use of Assessment Tool). Completed copy of Assessment tool for each guidance/guideline document.	<input type="checkbox"/>	<input checked="" type="checkbox"/>
	Methods used to analyse/synthesise/summarise or compare data from different sources. Summary of findings tables directly comparing data from different sources and uncertainty.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
	Methods used for any calculations and explanatory text for any assumptions if used (can have different levels of information about this in each Report)	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
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	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>



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	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Other	[delete if not required]	<input type="checkbox"/>	<input type="checkbox"/>
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	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Review team	List members of Review Team	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Declared interests	Documentation of the declared interest(s) of reviewers	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Acknowledgements	Documentation of any inputs from individuals not on the Team	<input checked="" type="checkbox"/>	<input type="checkbox"/>
References	Included references	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Appendices	Additional technical detail or examples of templates used in methods to be provided as required	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Declaration of interests

None to declare.

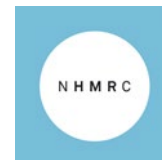
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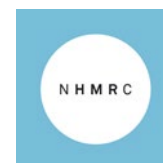
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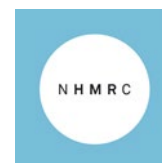


Appendix A – Search strategy and selection of evidence

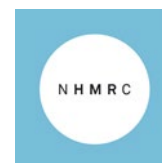
Example template of documenting a search strategy and how evidence is selected (if required).

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

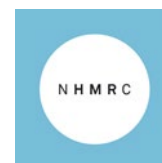


	abstracts for key words? What will you do with publications that you aren't sure about?]
Quality check	[Methods for checking that key publications have been picked up the search – are there any omissions or missed papers from the database searches?]
Grey literature	[Detail how you will search and retrieve 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	
Population characteristics	Population/s studied	
	Selection criteria for population	
	Subgroups reported	
	Size of study	
Exposure and setting	Type of water source	
	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?		