EVIDENCE EVALUATIONS FOR AUSTRALIAN DRINKING WATER GUIDELINE CHEMICAL FACT SHEETS

Ammonia Evaluation Report

Prepared for:

National Health and Medical Research Council

SLR Ref: 640.30242-R01
Version No: -v3.0
May 2022

PREPARED BY

SLR Consulting Australia Pty Ltd
ABN 29 001 584 612
Level 11, 176 Wellington Parade
East Melbourne VIC 3002 Australia

T: +61 3 9249 9400
E: melbourne@slrconsulting.com www.slrconsulting.com

BASIS OF REPORT

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

This report is for the exclusive use of the Client. No warranties or guarantees are expressed or should be inferred by any third parties. This report may not be relied upon by other parties without written consent from SLR.

SLR disclaims any responsibility to the Client and others in respect of any matters outside the agreed scope of the work.

DOCUMENT CONTROL

Reference	Date	Prepared	Checked	Authorised
640.30242-R01-v3.0	25 May 2022	Tarah Hagen, MSc, DABT, RACTRA	Giorgio De Nola, MSc, RACTRA	Tarah Hagen
640.30242-R01-v2.1	25 May 2022	Tarah Hagen, MSc, DABT, RACTRA	Giorgio De Nola, MSc, RACTRA	Tarah Hagen
640.30242-R01-v2.0	8 April 2022	Tarah Hagen, MSc, DABT, RACTRA	Giorgio De Nola, MSc, RACTRA	Tarah Hagen
640.30242-R01-v1.3	8 April 2022	Tarah Hagen, MSc, DABT, RACTRA	Giorgio De Nola, MSc, RACTRA	Tarah Hagen
640.30242-R01-v1.2	1 March 2022	Tarah Hagen, MSc, DABT, RACTRA	Giorgio De Nola, MSc, RACTRA	Tarah Hagen

EXECUTIVE SUMMARY

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

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

The targeted screening of existing health-based guidance found seven different sources of health-related guidance on ammonia but did not identify any candidate guidance/guideline values for potential adoption/adaptation. The documents did review the available health-based information for ammonia, and the documents were found to be suitable to adopt/adapt based on an assessment against a number of administrative and technical quality requirements. There was general agreement across the included guidance documents that a health-based guideline/guidance value was not considered warranted for ammonia. This is because typical intake from water is three orders of magnitude lower than the amount of ammonia produced naturally in the body and the no effect levels observed in animal studies (ATSDR 2004; EFSA2012a, b; USEPA 2005; WHO 2003; JECFA 2010). An evidence scan of peer-reviewed literature from 2012 onwards did not identify any evidence that would change the findings from the existing guidance.

When considering a drinking water guideline (DWG) for ammonia, other considerations (e.g. aesthetic conditions, efficiency of disinfection systems, corrosion of copper pipes and staining) may be relevant to setting a guideline value. A concentration of 0.2 mg/L in water was identified as a level above which ammonia may begin to interfere with the efficiency of disinfection (WHO 2003). The current Australian DWG (0.5 mg/L) is based on corrosion of copper pipes and fittings (NHMRC 2011). The taste threshold for ammonium (1.5 mg/L) and odour threshold for ammonia (35 mg/L) occur at higher levels.

It was beyond the scope of this evaluation to determine whether the current Australian DWG of 0.5 mg/L is still considered appropriate with regards to aesthetic considerations. The concentration of the current Australian DWG of 0.5 mg/L is achievable with modern treatment technologies and readily measurable with current commercial analytical techniques.

CONTENTS

DOCUMENT REFERENCES

TABLES

FIGURES

Abbreviations/Definitions

Acronym	Definition
ADD	Acceptable Daily Dose (OEHHA terminology)
ADI	Acceptable Daily Intake (APVMA terminology)
APVMA	Australian Pesticides and Veterinary Medicines Authority
ATSDR	US Agency for Toxic Substances and Disease Registry
BW, bw	Body Weight
DW	Drinking Water
DWG	Drinking Water Guideline
EFSA	European Food Safety Authority
FSANZ	Food Standards Australia New Zealand
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LOR	Level of Reporting
MRL	Minimal Risk Level (ATSDR terminology)
NOAEL	No Observed Adverse Effect Level
OEHHA	Californian Office of Environmental Health and Hazard Assessment
NHMRC	National Health and Medical Research Council
PHG	Public Health Goal (in drinking water) (OEHHA terminology)
PPRTV	Provisional Peer-Reviewed Toxicity Value (US EPA terminology)
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PTMI	Provisional Tolerable Monthly Intake (JECFA terminology)
PTWI	Provisional Tolerable Weekly Intake (EFSA terminology)
RfD	Reference Dose (US EPA terminology)
TDI	Tolerable Daily Intake (WHO and EFSA terminology)
The Guidelines	NHMRC and NRMMC (2011). Australian Drinking Water Guidelines 6 2011; Version 3.6 updated March 2021, National Health and Medical Research Council and Natural Resource Management Ministerial Council, Commonwealth of Australia, Canberra.
US EPA	United States Environmental Protection Agency
WHO	World Health Organization
WQAC	Water Quality Advisory Committee

1 Introduction and Background

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

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

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

The report herein is the Evaluation Report for ammonia.

1.1 Objectives

The factsheet for ammonia within the Guidelines was last updated in 1996. The overarching objective of this review is to identify existing sources of guidance or guidelines on the impact of exposure to ammonia in drinking water at levels higher or lower than the current Australian drinking water guideline (DWG) of 0.5 mg/L (i.e. 500 µg/L) on human health outcomes. The intention is to identify candidate health-based guidance/guideline values for potential adoption/adaptation into the Guidelines.

Other objectives of the review are:

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

2 Research Questions

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

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

Table 1 Research Questions for Evidence Evaluation of Ammonia Factsheet Review

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

3 Methodology Overview

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

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

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

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

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

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

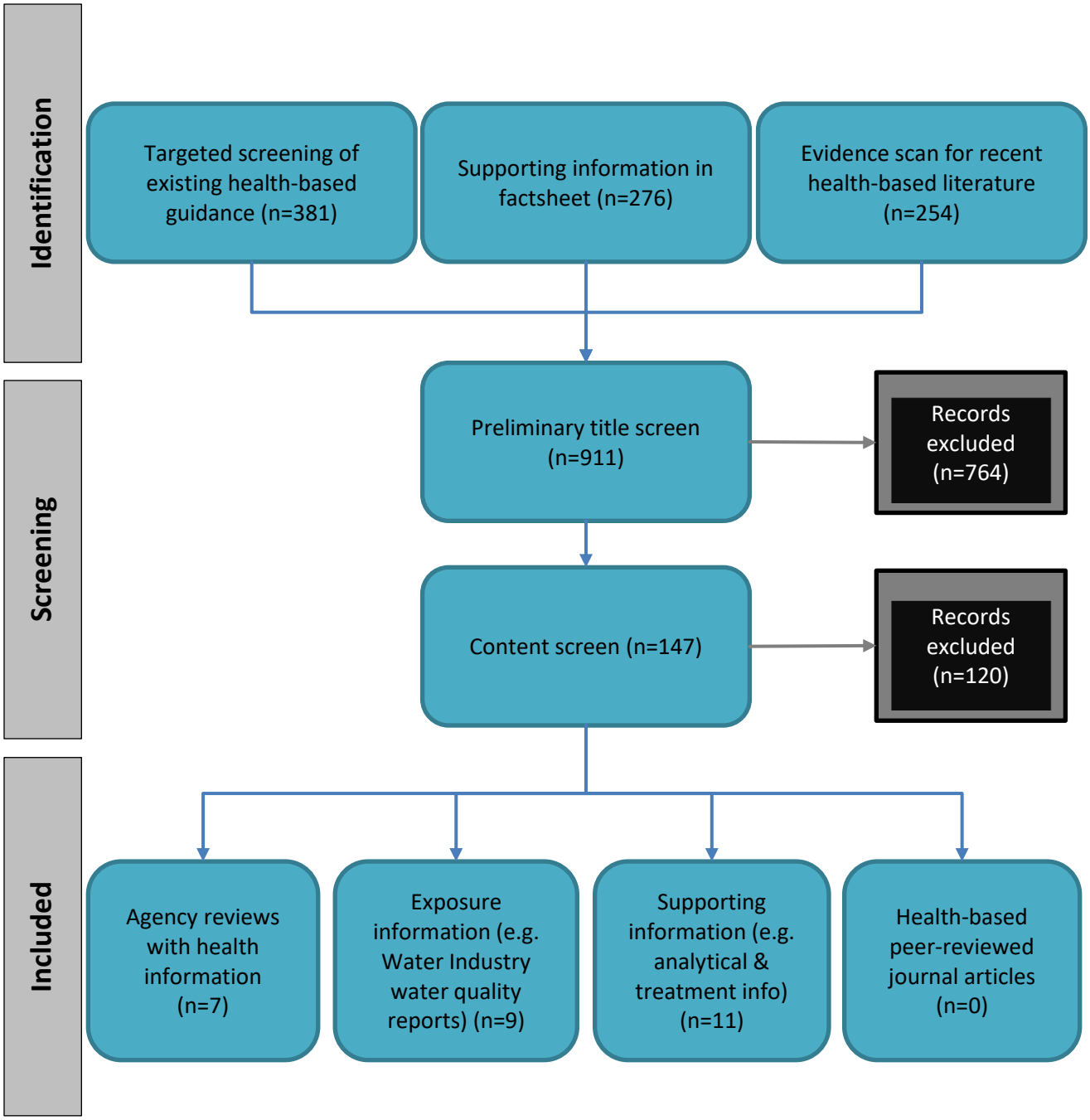

Figure 1 Overview of literature search process followed for ammonia

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

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

Guideline value (µg/L) =

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

.....**Equation 1**

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

4 Results

The targeted screening of existing health-based guidance found seven different sources of health-related guidance on ammonia, but did not identify any candidate guidance/guideline values for potential adoption/adaptation. A health-based guideline/guidance value was not considered warranted for ammonia by the various international agencies screened. This is because the typical intake from water is three orders of magnitude lower than the amount of ammonia produced naturally in the body and the no effect levels observed in animal studies. A summary of the findings from five different agencies is as follows:

- ATSDR (2004): A guidance value or Chronic MRL for oral intake has not been derived.
- EFSA (2012a): A health-based guideline for drinking water was not considered necessary. EFSA estimated intakes of ammonium at the water concentrations of 0.5-5 mg/L (0.014 mg/kg/d - 1 mg/kg/d) are ~three orders of magnitude lower than the no-effect levels reported in experimental animals, and therefore do not indicate a health concern.
- EFSA (2012b): The JECFA Scientific Committee on Food (SCF) did not specify an ADI for food additive (E527), nor for ammonium hydroxide as a food additive (acidity regulator) and established an ADI — 'not limited'.
- USEPA (2005): No Provisional Peer-Reviewed Toxicity Value (PPRTV) for oral exposure has been derived for ammonia. The database for deriving a PPTRV was considered insufficient.
- JECFA (2010): The Committee evaluated the safety of ammonium carbonate and ammonium hydrogen carbonate and allocated an ADI of 'not specified'.
- WHO (2003): No guideline value was specified.

It is important to note that ammonia exists in water at neutral pH as a (non-volatile) cation (ammonium) although at higher alkaline pH it may exist as (volatile) ammonia gas. In water, ammonium has a taste threshold of 35 mg/L whereas ammonia has an odour threshold of 1.5 mg/L.

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

4.1 Health-based aspects

Research questions 1-12 all cover health-based aspects of the review; this is considered to be the most important information in the factsheet. **Table 2** provides a synthesis of the results by showing where there is and is not agreement between different jurisdictions.

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

#	Research Questions	Is there agreement between different jurisdictions?	Any disagreement or things to note?
1	What is the critical human health endpoint for ammonia (if any)? Therefore, what are the key adverse health hazards from exposure to ammonia in Australian drinking water?	The jurisdictions agree that the available database is limited and do not define a critical endpoint. ATSDR (2004), WHO (2003) and EFSA (2012a) agreed on metabolic acidosis resulting from exposure to ammonium chloride.	No disagreements to note.
2	What are the justifications for choosing this endpoint/health hazard?	No health endpoint is chosen. Critical endpoints, if observed, occur following much higher intakes than observed from exposure to water. Also, the critical health endpoint associated with exposure to ammonium chloride is not relevant as toxicity is by the anion and not ammonia.	Ammonia is produced naturally in the body at levels that are much higher than intakes from water and metabolised rapidly and excreted to urea and other compounds.
3	What is the toxicological mode of action of ammonia for the critical human health endpoint (if applicable)?	EFSA (2012a) noted that the toxicity of ammonium chloride is mainly driven by the release of hydrochloric acid during the metabolism of ammonium into urea, leading to hyperchloremic metabolic acidosis.	-
4	Is ammonia an oral genotoxic carcinogen of relevance to humans? Is ammonia an oral genotoxic carcinogen of relevance to humans?	There is agreement between jurisdictions that ammonia is not an oral genotoxic carcinogen at levels found in the environment.	Ammonia and ammonium may display clastogenic and mutagenic properties at much higher intakes than from the environment.
5	What dose(s) are associated with the critical human health endpoint (if any)?	Not applicable (as no critical endpoint was selected).	EFSA estimated intakes of ammonium at the water concentrations of 0.5-5 mg/L (0.014 mg/kg/d – 1 mg/kg/d) are ~three orders of magnitude lower than the no-effect levels reported in experimental animals, and therefore do not indicate a health concern.
6	Is the proposed health-based guideline value relevant to the Australian context?	No health-based guideline value is proposed.	-

#	Research Questions	Is there agreement between different jurisdictions?	Any disagreement or things to note?
7	Are there groups of people in the general population who may be more sensitive to ammonia exposure?	Yes. ATSDR (2004) suggests farm workers are more exposed to ammonia than general population, but this is likely from inhalation exposure (not relevant to drinking water). There is agreement between jurisdictions that persons who suffer from severe liver or kidney disease may be more susceptible, since these organs biotransform and excrete $NH4^+$. Individuals with hereditary urea cycle disorders are also more susceptible, since levels produced endogenously are sufficient to produce toxicity in these individuals.	
8	Is a health-based guideline value needed for ammonia?	It is agreed between jurisdictions that a health-based guideline value is not necessary for ammonia. See discussion in **Section 5**.	
9	If not, what aesthetic characteristics of ammonia (if any) should be taken into consideration?	There is an agreement between agencies that the threshold odour concentration of ammonia in water and taste are lower than concentrations at which no adverse effects are seen. Ammonia may also interfere with disinfection efficiency.	Agencies agree that the taste threshold for ammonium is 35 mg/L and odour threshold for ammonia is 1.5mg/L.
10	What is the guidance value (if any)?	There is no guidance value derived for ammonia from the agencies consulted.	
11	Is there a knowledge gap from the time at which existing guideline values were developed?	Unlikely although bibliography of latest review contained literature up to 2012.	As intake of ammonia from water is much lower than produced endogenously it is unlikely that any new information will have become available that could alter the conclusions.
12	Does any recent literature change the guideline value? (e.g. demonstrating a new critical endpoint?)	Evidence scan for recent studies did not reveal any new pivotal studies which may impact the findings of the five jurisdictions summarised above.	

NOAEL = No Observed Adverse Effect Level. BW = Body weight. ADD = Acceptable Daily Dose. UF = Uncertainty Factor.

4.2 Exposure-related aspects

Another important aspect of the factsheet covers the exposure-related considerations. This is important for consideration of whether exposures to the chemicals evaluated by Australians are approaching the health-based guidance value used for deriving a DWG (it is noted that for ammonia, no such health-based guidance value was identified). It is also important for considerations of whether typical levels of the chemicals in Australian drinking water supplies would currently adhere to any new or revised DWG. Research questions 13-16 cover exposure-related aspects of the review. For these aspects, drinking water quality reports from various water corporations around Australia were consulted in addition to the agency reviews identified in the targeted search.

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

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

#	Research Questions	Findings
13	What are the typical ammonia levels in Australian drinking water? Do they vary around the country or under certain conditions e.g. source of water, drought?	Mean concentrations of ammonia in drinking water: • Range: <0.005-0.373 mg/L • Rainwater tanks around Australia: Mean 0.074 mg/L, Range: 0.002 mg/L-0.270 mg/L Other states just report that the current DWG (0.5 mg/L) was met in their latest sampling. Chloramination is a common water treatment process used in Australia to treat water for drinking. Monochloramine, however, decays over time releasing free ammonia and chlorine.
14	Do Australian levels differ considerably from elsewhere?	Unclear from the information reviewed.
15	What are the principal routes of exposure to ammonia in the Australian general population?	The principal route of exposure to ammonium is consumption (from the diet) whereas for ammonia it is from air based on reviews by overseas jurisdictions. It is expected that the same routes of exposure occur in Australia.
16	What are the typical levels of Australian exposure? (e.g. 'background' ammonia levels)?	No information available for Australia. According to ATSDR (2004) and WHO (2003) intakes from food and drinking water are 18 mg/person/day, <1 mg from inhalation and, <1mg/day from cigarette smoking (20 cigarettes per day). In contrast, approximately 4000 mg of ammonia per day is produced endogenously in the human intestine.

4.3 Risk-based aspects

Research questions 17 and 18 are risk-based considerations. The five jurisdiction reviews subjected to detailed data extraction mentioned at the start of **Section 4** were also consulted to answer these questions. **Table 4** presents a summary of the findings.

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

#	Research Questions	Findings
17	What are the risks to human health from exposure to ammonia in Australian drinking water?	No review found for Australia. In USA and Europe, risk of harm from ammonia in drinking water is considered low due to low levels in DW and the fact that intake from the diet and drinking water is well below the amount of ammonia produced endogenously (ATSDR 2004, EFSA 2012a).
18	Is there evidence of any emerging risks that are not mentioned in the current factsheet that require review?	None identified by the agencies and none identified from the evidence scan of recent information.

DW = Drinking Water.

4.4 Supporting information

The ammonia factsheet contains a range of supporting information, including a brief general description (i.e. uses of ammonia, sources in drinking water), typical values in Australian drinking water, treatment of drinking water, and measurement (i.e. analytical) considerations. The remaining research questions 19-24 cover the supporting information of the review. For these aspects, in addition to consulting the previously mentioned sources (e.g. the drinking water quality reports from various water corporations around Australia, the agency reviews identified in the targeted search), additional targeted searches were undertaken (for details, refer to Technical Report). **Table 5** provides a summary of the results.

Table 5 Summary of findings from data extraction for supporting information

#	Research Questions	Findings
19	Is the general description current?	Yes, however WQAC advised it would be useful to note that ammonia may be used for hydrogen storage in coming years.
20	What are the indicators of the risks? How can we measure exposure? Is the information on measurement/analytical methods current?	Exposure can be measured as ammonia concentration in water. There are various analytical methods which can be used to measure ammonia: • Sample mixed with borate buffer (Method 1689, on selective probe) (Level of Reporting, LOR: 0.1 mg/L). • Method 1690, colorimetric determination of indophenol blue (LOR: 0.2 mg/L). • Method 350.1, colorimetric, automated phenate (LOR: 0.1 mg/L). • Method 350.2 Nessier reagent, colorimetric, titrimetric (LOR: 0.05mg/L). • Method 350.3 ion selective electrode (LOR: 0.03 mgN/L). (ATSDR 2004).
21	Are there commercial analytical methods available that can measure at or below the guideline value?	Commercial analytical methods can measure at or below the current Australian DWG value of 0.5 mg/L (with standard limits of determination of 0.01 mg/L.
22	Is the information for treatment options current in terms of current practices in Australia?	Additional treatment methods have been identified in the literature search. Commercial methods include chloramination as a form of more stable disinfectant in long distribution system. Other methods identified include iron–carbon micro-electrolysis (ICME) combined with up-flow biological aerated filter (UBAF), Biological activated carbon (BAC) filtration, ammonia oxidising bacteria, micro distillation, granular activated carbon etc.
23	Can treatment technologies treat to the suggested level of the guideline value?	Yes. Current technologies can treat water down to below the current drinking water guideline.
24	Is there any new information which should be added? Should anything be removed?	General description, LOR in measurement section, treatment section can be expanded.

5 Discussion

5.1 Suitability of health-based guidance for adoption / adaptation

No candidate health-based guidance/guideline values for ammonia were identified for possible adoption/adaptation in Australia. Nevertheless, a number of international jurisdictions have reviewed the available health information for ammonia and have concluded that no health-based guideline value is required (ATSDR 2004, EFSA 2012a, b; JECFA 2010, US EPA 2005, WHO 2003). These agency documents have been evaluated using the Assessment Tool provided in Appendix C in the Technical Report. This tool evaluates each document against administrative and technical criteria that demonstrate transparent and robust guideline development and evidence review processes that meet NHMRC standards for guidelines. The overall suitability of the guidance/guideline values for adoption/adaption can be gauged at least partially by examining the percentage of 'must-have', 'should-have', and 'may-have' criteria met by each jurisdiction.

Figure 2 presents the percentage of criteria (combined technical and administrative criteria) met by each jurisdiction. It is evident from the figure that most agencies met similar percentages of 'must-have' criteria, ranging from 63 to 73%. Most of the instances where these criteria were not met were related to lack of reporting of literature search and review details. Whilst all jurisdictions provided comprehensive bibliographies of the information relied upon, none reported detail of the literature searches conducted. The percentage of other criteria met ranged from 50-75% for 'should-have' criteria depending on the jurisdiction and was 100% for 'may-have' criteria.

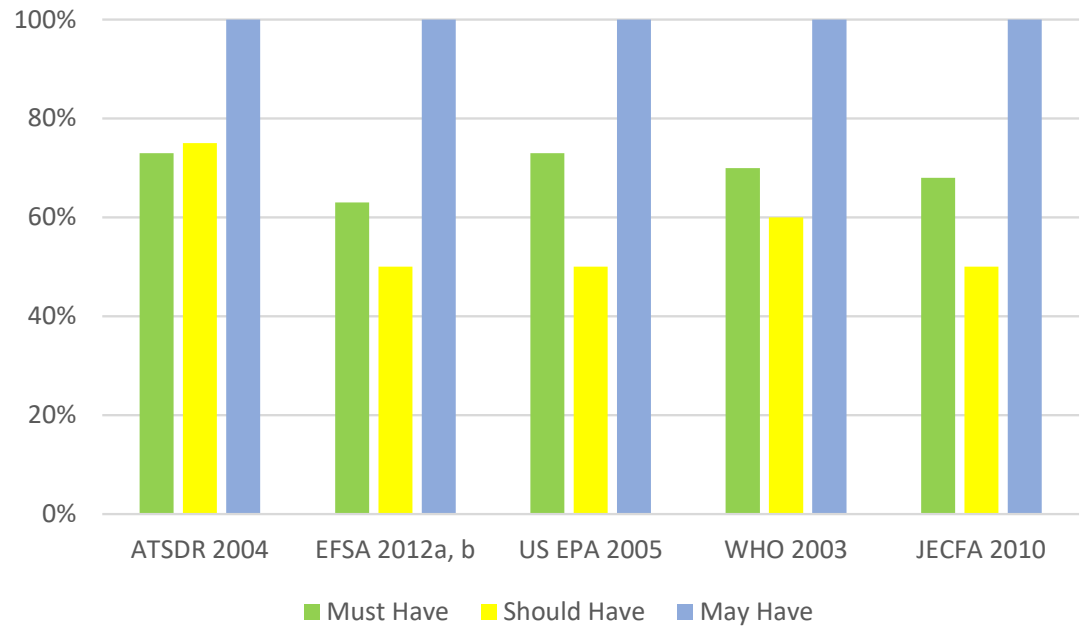

Figure 2 Overall proportion of 'must-have', 'should-have' and 'may-have' technical/administrative criteria met by jurisdictions who have reviewed health-based information for ammonia for possible adoption/adaptation in Australia

This analysis indicates that the highest proportion of criteria have been met by ATSDR (2004).

5.2 Overall Evaluation

There was no information identified in the reviews from five different jurisdictions nor in the evidence scan of peer-reviewed literature which indicated a reason to derive a health-based DWG. An evaluation of the available reviews on ammonia from these jurisdictions identified there is clear agreement between different jurisdictions that a health-based guideline is not necessary for ammonia in water.

- Estimated intakes in humans from drinking water at 0.5-5 mg/L are approximately three orders of magnitude lower than the no-effect levels reported in experimental animals, and therefore do not indicate a health concern (EFSA 2012a).
- Ammonia produced endogenously in the body (~4000 mg/day) far exceeds the typical daily intake for ammonia from both food and drinking water (18 mg/day) (ATSDR 2004, WHO 2003).
- Ammonia may be present in drinking water as a result of adding ammonia (and chlorine) to drinking water supply systems (chloramination).
- The evidence scan undertaken for this report did not reveal any recently published studies which could potentially impact the conclusions made in this report.
- There is no information provided on the ammonia dietary intakes in the Australian general population, but intake is likely about 18 mg/day in line with Europe and the USA (ATSDR 2004, WHO 2003, EFSA 2012a).

When considering a DWG for ammonia, other considerations (e.g. aesthetic conditions, efficiency of disinfection systems, corrosion of copper pipes and staining) are relevant to setting a guideline value. A concentration of 0.2 mg/L in water was identified as a level above which ammonia may begin to interfere with the efficiency of disinfection (WHO 2003). The current Australian DWG (0.5 mg/L) is based on corrosion of copper pipes and fittings (NHMRC and NRMMC 2011). The taste threshold for ammonium (1.5 mg/L) and odour threshold for ammonia (35 mg/L) occur at higher levels.

6 Conclusions

Overall, there was general agreement across six existing guidance documents included in the review that there is no need for a health-based DWG for ammonia. The evidence underpinning the guidance documents indicated that there are no health effects of concern from ammonia at levels typically observed in drinking water supplies. The guidance/guideline documents assessed were found to be suitable to adopt/adapt based on an assessment of the administrative and technical criteria described in Appendix C of the Technical Report. An evidence scan of peer-reviewed literature from 2012 onwards did not identify any evidence that would change the findings from the existing guidance. Instead, a DWG based on other (i.e. aesthetic) considerations may be appropriate. It was beyond the scope of this evaluation to determine whether the current Australia DWG of 0.5 mg/L is still considered appropriate with regards to aesthetic considerations.

The concentration of the current Australian DWG of 0.5 mg/L is achievable with existing treatment technologies and readily measurable with current commercial analytical techniques.

7 Review Team

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

Name	Position	Responsibilities
Mr Giorgio De Nola, MSc, RACTRA	Principal Consultant – Toxicology & Risk Assessment, SLR	Internal peer review

8 Declared Interests

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

9 Acknowledgements

The authors acknowledge NHMRC and the members of WQAC for their insightful review comments.

10 References

ATSDR (2004). Toxicological Profile for Ammonia. US Department of Health and Human Services, Agency for Toxic Substances and Disease Registry. September 2004.

EFSA (2004). Scientific opinion on the re-evaluation of caramel colours (E 150 a,b,c,d) as food additives1 EFSA Panel on Food Additives and Nutrient Sources added to Food. European Food Safety Authority (EFSA). EFSA Journal 2011; 9(3):2004 FSA Journal 2011; 9(3):2004.

EFSA (2009). Opinion Flavouring Group Evaluation 46 (FGE.46)1: Ammonia and two ammonium salts from chemical group 30 Scientific Opinion of the Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC) (EFSA-Q-2008-050). European Food Safety Authority (EFSA). The EFSA Journal (2009) ON-955, 1-34.

EFSA (2012a). Scientific Opinion: Health risk of ammonium released from water filters. European Food Safety Authority (EFSA). Adopted 15 October 2012. The EFSA Journal (2012) 10 (10): 2918.

EFSA (2012b). Scientific Opinion on the evaluation of the substances currently on the list in the annex to Commission Directive 96/3/EC as acceptable previous cargoes for edible fats and oils – Part II of III. European Food Safety Authority (EFSA). EFSA Panel on Contaminants in the Food Chain (CONTAM). The EFSA Journal (2012) 10(5): 2703.

JECFA (2010). Safety evaluation of certain food additives. Series 62. Seventy-first meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA) Joint FAO/WHO Expert Committee of Food Additives

Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Medicine 2009; 6(7):e1000097.

NHMRC and NRMMC (2011). Australian Drinking Water Guidelines 6 2011; Version 3.6 updated March 2021, National Health and Medical Research Council and Natural Resource Management Ministerial Council, Commonwealth of Australia, Canberra.

ToxConsult (2019). Assessment of International and National Agency processes for deriving HBGVs and DWGs. Prepared for National Health and Medical Research Council. ToxConsult document: ToxCR070519-TF, dated 24th December 2019.

USEPA (2005). Provisional Peer Reviewed Toxicity Values for Ammonia (Various CASRNs). Superfund Health Risk Technical Support Center. National Center for Environmental Assessment Office of Research and Development U.S. Environmental Protection Agency Cincinnati, OH.

WCWA (2014). Drinking Water Quality. Annual Report 2013/14. Water Corporation Western Australia.

WHO (2003). Ammonia in Drinking Water. Background document for development of WHO Guidelines for Drinking-water Quality. World Health Organization.

ASIA PACIFIC OFFICES

ADELAIDE
60 Halifax Street
Adelaide SA 5000
Australia
T: +61 431 516 449

BRISBANE
Level 2, 15 Astor Terrace
Spring Hill QLD 4000
Australia
T: +61 7 3858 4800
F: +61 7 3858 4801

CANBERRA
GPO 410
Canberra ACT 2600
Australia
T: +61 2 6287 0800
F: +61 2 9427 8200

DARWIN
Unit 5, 21 Parap Road
Parap NT 0820
Australia
T: +61 8 8998 0100
F: +61 8 9370 0101

GOLD COAST
Level 2, 194 Varsity Parade
Varsity Lakes QLD 4227
Australia
M: +61 438 763 516

MACKAY
21 River Street
Mackay QLD 4740
Australia
T: +61 7 3181 3300

MELBOURNE
Level 11, 176 Wellington Parade
East Melbourne VIC 3002
Australia
T: +61 3 9249 9400
F: +61 3 9249 9499

NEWCASTLE CBD
Suite 2B, 125 Bull Street
Newcastle West NSW 2302
Australia
T: +61 2 4940 0442

NEWCASTLE
10 Kings Road
New Lambton NSW 2305
Australia
T: +61 2 4037 3200
F: +61 2 4037 3201

PERTH
Grd Floor, 503 Murray Street
Perth WA 6000
Australia
T: +61 8 9422 5900
F: +61 8 9422 5901

SYDNEY
Tenancy 202 Submarine School
Sub Base Platypus
120 High Street
North Sydney NSW 2060
Australia
T: +61 2 9427 8100
F: +61 2 9427 8200

TOWNSVILLE
12 Cannan Street
South Townsville QLD 4810
Australia
T: +61 7 4722 8000
F: +61 7 4722 8001

WOLLONGONG
Level 1, The Central Building
UoW Innovation Campus
North Wollongong NSW 2500
Australia
T: +61 2 4249 1000

AUCKLAND
Level 4, 12 O'Connell Street
Auckland 1010
New Zealand
T: 0800 757 695

NELSON
6/A Cambridge Street
Richmond, Nelson 7020
New Zealand
T: +64 274 898 628

WELLINGTON
12A Waterloo Quay
Wellington 6011
New Zealand
T: +64 2181 7186

SINGAPORE
39b Craig Road
Singapore 089677
T: +65 6822 2203