EVIDENCE EVALUATIONS FOR AUSTRALIAN DRINKING WATER GUIDELINE CHEMICAL FACT SHEETS

Ammonia
Technical Report

Prepared for:

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BASIS OF REPORT

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DOCUMENT CONTROL

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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	Limit of Reporting
MRL	Minimal Risk Level (ATSDR terminology)
mTAMDI	modified Theoretical Added Maximum Daily Intake
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
RfD	Reference Dose (US EPA terminology)
Sb	Antimony
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 guidelines. For each of the 11 chemicals, SLR was asked to:

- Customise and apply the '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 Technical Report for ammonia.

2 Research Questions

Research questions for this review were drafted by SLR and peer reviewed and agreed upon by the WQAC and NHMRC prior to conducting the search. They are provided in **Table 1**.

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?)

#	Research Questions
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 Evidence Evaluation Methods

3.1 Overview

This section summarises the methods followed to undertake the evidence evaluation review for ammonia. The intention is to provide enough detail for a third party to reproduce the search.

It was evident that some flexibility was required in adapting the methodology recorded in the final Research Protocol for ammonia to maximise efficiency in sourcing relevant information. Deviations from the final Research Protocol methodology have been recorded in this report. **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).

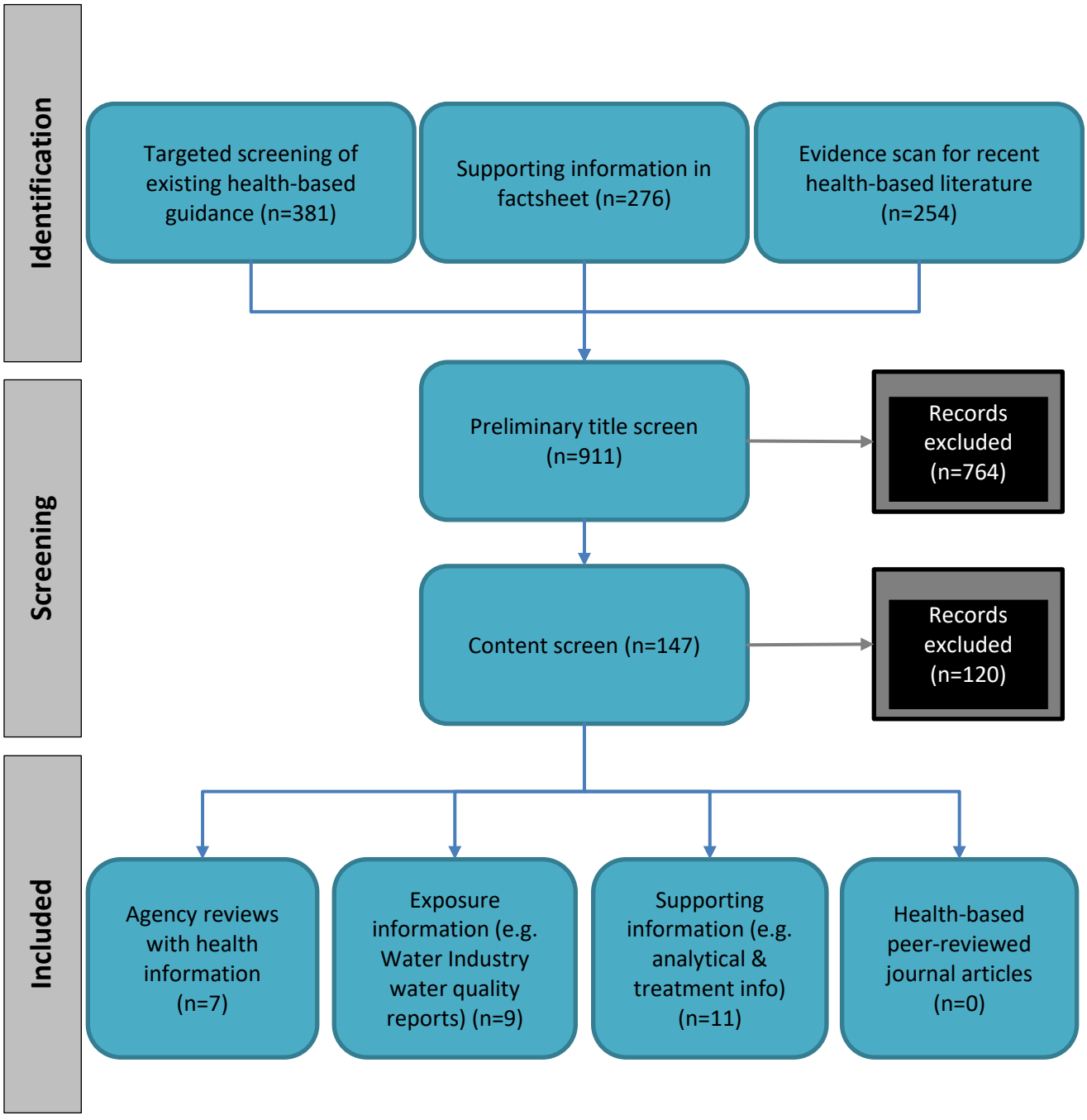

Figure 1 Overview of literature search process followed for ammonia

3.2 Targeted screening of existing health-based guidance

Literature search strategy

The literature search strategy for existing health-based guidance documentation for ammonia is summarised in **Table 2** below.

Table 2 Search strategy for Existing Guidance/Guidelines

Parameter	Comments
Search terms	After a few trial runs of various combinations of search terms, it became apparent that the search terms would need to remain relatively broad so as not to miss pivotal references/reviews. Consequently, the selected search term was: • (Ammonia)

Databases/Agency websites	The following sources were searched:
	• World Health Organization (WHO): https://www.who.int/ (in addition, 'ammonia in drinking water' was searched in Google®) [2].
	• International Programme of Chemical Safety (IPCS Inchem): http://www.inchem.org/#/search
	• Joint FAO/WHO Expert Committee on Food Additives (JECFA): (Included in IPCS Inchem search)
	• European Food Safety Authority (EFSA): https://www.efsa.europa.eu/en
	• United States Environmental Protection Agency (US EPA), specifically [1]:
	  ○ Integrated Risk Information System (IRIS): https://www.epa.gov/iris
	  ○ Provisional Peer-reviewed Toxicity Values (PPRTV): https://www.epa.gov/pprtv
	• US Agency for Toxic Substances and Disease Registry (ATSDR): https://www.atsdr.cdc.gov/
	• Californian Office of Health and Hazard Assessment (OEHHA) Public Health Goals (in Drinking Water): https://oehha.ca.gov/water/public-health-goals-phgs
	• Food Standards Australia New Zealand (FSANZ), specifically [3]:
	  ○ Publications page: https://www.foodstandards.gov.au/publications/Pages/default.aspx
	  ○ Monitoring safety of food supply page: https://www.foodstandards.gov.au/science/surveillance/Pages/default.aspx
	  ○ Chemicals in food page: https://www.foodstandards.gov.au/consumer/chemicals/Pages/default.aspx
	• Australian Pesticides and Veterinary Medicines Authority (APVMA) Health Based Guidance Values: https://apvma.gov.au/node/26596
	The following additional sources were searched to provide exposure information in Australian drinking water supplies (to inform responses to Research Questions 13 and 16):
	• Melbourne Water: https://www.melbournewater.com.au/
	• Sydney Water: https://www.sydneywater.com.au/SW/index.htm
	• TasWater: https://www.taswater.com.au/
	• SA Water: https://www.sawater.com.au/
	• Water Corporation of Western Australia: https://www.watercorporation.com.au/
	• Power and Water Corporation Northern Territory Drinking Water Quality Reports: https://www.powerwater.com.au/about/what-we-do/water-supply/drinking-water-quality/past-drinking-water-quality-reports
	• Seqwater: https://www.seqwater.com.au/
	• Icon Water: https://www.iconwater.com.au/
	• Water Research Australia: https://www.waterra.com.au/

Parameter	Comments
Publication Date	If databases/agency websites allowed for specification of date ranges, searches were constrained to the following date range to coincide with the year of the last Australian drinking water guideline fact sheet update for ammonia: • 1 January 1996 to July 2021
Language	English
Study Type	Publicly available agency/industry reports and reviews.

Inclusion and exclusion criteria	The following exclusion criteria were used to screen relevance of agency reports/reviews:
	• NR = Not Relevant. Information not directly relevant to answering research questions. Rationale for non-relevance was provided for transparency. E.g.
	  ○ Not HH related = Not human health related (e.g. criteria are for protection of aquatic life).
	  ○ Not a relevant exposure pathway = Since ammonia present in drinking water is not typically volatile unless at high pH, guidelines for non-oral and non-dermal routes of exposure are not considered relevant (e.g. inhalation of ammonia gas).
	  ○ Not relevant to chemical of interest.
	• NPA = Basis of guideline value or information underpinning review conclusions are Not Publicly Available, e.g. health-based guideline value has used unpublished proprietary information which could not be verified.
	• Language = Language other than English.

Validation methods used	Preliminary searches were undertaken with more specific search terms [(ammonia) AND (toxicity or health); (ammonia) AND (exposure) AND (Australia)]. Upon scanning preliminary search results, the reviewer found these search terms to be too specific, as a number of agency reports did not appear in the results. The search terms were consequently refined. In addition, from the preliminary search of the WHO website, it became evident that the latest background documentation for ammonia (dated 2003) did not come up in the general search results when using the search term 'ammonia'. Therefore, the WHO website search was supplemented by a Google® search to find the specific background document of interest.
Screening methods	Results were screened as follows: *Preliminary title screen* • Titles of results for each search were recorded in an Excel spreadsheet. Each website was on a separate tab of the spreadsheet. • The researcher scanned the titles. In a separate column a decision regarding relevance of the result was recorded as per the exclusion criteria. An additional column was included to provide commentary as (and if) required. • Where the researcher was uncertain as to the relevance of a particular result, the researcher discussed the matter with a subject expert prior to making a decision OR the result was considered potentially relevant and included. *Content screen* • The full text content of reports/reviews selected to be included from the preliminary title screen were reviewed by a subject expert to determine which reports/reviews to include in the data extraction step. Only reports/reviews which provided information relevant to answering the research questions were taken through to the data extraction step.

Parameter	Comments
Documentation of search	Spreadsheets with full search results and screening outcomes (i.e. reasons for exclusion) are provided in **Appendix A.** Overall results presented in **Figure 1**, adapted from the PRISMA figure presented in Moher et al. (2009) and Figure 5 in NTP (2015).
Retrieval of publications	All relevant and potentially relevant results were recorded in an Endnote library and soft copies of files saved into a designated folder on the SLR server for review. The server is backed up on a daily basis.

1. Preliminary search trials with the US EPA general search engine (https://www.epa.gov/) resulted in over 41,540 hits, regardless of search term refinement. This number of hits was considered unmanageable to screen through with the resources available for this project. Consequently, the search was targeted to specific sections of the website considered most relevant to answering the research questions.
2. From the preliminary search of the WHO website, it became evident that the latest background documentation for ammonia (dated 2003) did not come up in the general search results when using the search term 'ammonia'. Therefore, the WHO website search was supplemented by a Google® search to find the specific background document of interest.
3. From the preliminary search of the FSANZ website, it became evident that the number of search results appeared infinite (there was no set number of hits provided, and no set pages of results; every time the final page of results was clicked on, additional pages appeared), regardless of search term refinement, with the vast majority of records being not relevant to the research questions. Consequently, specific sections of the website were consulted which were considered most relevant to answering the research questions.

Data Extraction and Quality Assessment

For each relevant result for which the full text was sourced:

- The full text was skimmed by a content expert.
- Where existing health-based guidance (in the form of drinking water guidelines or toxicity reference values, i.e. TRVs) was identified, relevant data on the guidance value in relation to the research questions were extracted using the format shown in **Table 3.** The individual data extraction tables are provided in **Appendix B**.
- For each health-based guidance review, quality of existing guidance/guidelines was assessed using the Assessment Tool (Appendix C in the Research Protocol). The individual completed Assessment tool tables for each guidance/guideline document are provided in **Appendix C**.

Table 3 Example of data extraction table format for existing health-based guidance

Agency Report Reference: ***Insert full bibliographical reference for report***		
General Information	Date of data extraction	
	Authors	
	Publication date	
	Literature search timeframe	
	Publication type	
	Peer reviewed?	
	Country of origin	
	Source of funding	
	Possible conflicts of interest	
Health considerations	Guideline value type (e.g. oral TRV, drinking water guideline)	

Agency Report Reference: ***Insert full bibliographical reference for report***		
	Exposure timeframe	
	Critical human health endpoint	
	Justification provided by agency for critical endpoint	
	Critical study(ies) underpinning point of departure	
	Species for critical study(ies)	
	Point of departure type (e.g. NOAEL, LOAEL, $BMDL_{10,}$ etc)	
	Point of departure value (include units)	
	Uncertainty factor(s) & rationale	
	Guideline value (include units)	
	Mode of action for critical health endpoint	
	Genotoxic carcinogen?	
	Identified sensitive sub-populations	
	Any non-health based considerations?	
Exposure considerations	Principal routes of exposure in general population	
	Levels in drinking water supplies (include location)	
	Any special considerations to exposure levels (e.g. higher in drought?)	
	Typical exposure in general population (include units for intakes & location)	
Risk Summary	Any risks to human health from drinking water identified in agency document?	
	Any emerging risks identified?	

Data summary/synthesis

In order to effectively compare data from different sources, the data has been presented 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/interpretation differs from Australian science policy.

3.3 Evidence scan for recent studies

Literature search strategy

An evidence scan of recent literature was undertaken for research questions for which eligible guidance (for potential adoption or adaptation into the Guidelines) was identified in the targeted screening of existing health-based guidance (see **Section 3.2**). The aim of the evidence scan was to understand the availability of recent literature and to determine whether a formal systematic review to update the evidence underpinning available guidance is warranted.

The literature search strategy for undertaking the evidence scan for recent studies is summarised in **Table 4** below.

Table 4 Search strategy for evidence scan of recent health-based studies

Parameter	Comments
Search terms	The selected search terms were: • (Ammonia) AND (toxicity) AND (oral) • (Ammonia) AND (health) AND (oral) • (Ammonia) AND (toxicity) AND (drinking water) • (Ammonia) AND (health) AND (drinking water) • (Ammonia) AND (exposure) AND (Australia)
Databases	The following sources were searched: • MEDLINE/PubMed/TOXLINE
Publication Date	2012 – 2021, the bottom end of the range to coincide with the latest health-based agency review found in the targeted screening step.
Language	English
Study Type	Peer-reviewed, published, in press, unpublished and ongoing studies will be included. Study types may include existing systematic reviews or literature reviews, human epidemiological studies, animal studies, and *in vitro* studies (the latter only if they inform on the mode of action for the critical health effect of concern).
Inclusion and exclusion criteria	The following exclusion criteria were used to screen relevance of information: • NR = Not Relevant. Information not directly relevant to answering research questions. • Language = Language other than English. • UCC = Unlikely to Change Conclusions in Review.
Validation methods used	Preliminary test searches were undertaken to assist with selecting search terms. Refinements were made as considered appropriate to ensure adequate, but also specific coverage in the sources screened.

Parameter	Comments
Screening methods	Results were screened as follows: *Preliminary title and abstract screen* • Titles of results for each search were recorded in an Excel spreadsheet. The results for each combination of search terms were exported into a separate tab of the spreadsheet. To readily eliminate duplicate records, results from all search term combinations were subsequently collated into one spreadsheet. • The researcher scanned the titles (and abstracts, if required). In a separate column a decision regarding relevance of the result was recorded as per the exclusion criteria. An additional column was included to provide commentary as (and if) required. • Where the researcher was uncertain as to the relevance of a particular result, the researcher discussed the matter with a subject expert prior to making a decision OR the result was considered potentially relevant and included. *Content screen* • The full text content of literature selected to be included from the preliminary title and abstract screen were reviewed by a subject expert to determine which articles to include in the data extraction step. Only articles/reviews which provided information considered to potentially affect the overall conclusions made by other jurisdictions were taken through to the data extraction step.
Documentation of search	Spreadsheets with full search results and screening outcomes (i.e. reasons for exclusion) are provided in **Appendix A.** Overall results presented in **Figure 1**, adapted from the PRISMA figure presented in Moher et al. (2009) and Figure 5 in NTP (2015).
Retrieval of publications	All relevant and potentially relevant results were recorded in an Endnote library and soft copies of files saved into a designated folder on the SLR server for review. The server is backed up on a daily basis.

Data Extraction

For each relevant result for which the full text was sourced:

- Where deemed to be relevant to the research questions and potentially providing information that could alter the existing assessments (identified in the targeted screening of existing health-based guidance), relevant data were extracted using the example format shown in **Table 5.** The format was more applicable to epidemiological studies and was adapted slightly for animal studies and/or reviews. The individual data extraction tables are provided in **Appendix E**.

Table 5 Example of data extraction table format for evidence scan of recent health-based studies

Publication Reference: ***Insert full bibliographical reference for report***		
General Information	Date of data extraction	
	Authors	
	Publication date	
	Publication type	
	Peer reviewed?	

Publication Reference: ***Insert full bibliographical reference for report***		
	Country of origin	
	Source of funding	
	Possible conflicts of interest	
Study characteristics	Aim/objectives of study	
	Study type/design	
	Study duration	
	Type of water source (if applicable)	
Population characteristics	Population/s studied	
	Selection criteria for population (if applicable)	
	Subgroups reported	
	Size of study	
Exposure and setting	Exposure pathway	
	Source of chemical/contamination	
	Exposure concentrations (if applicable)	
	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 of participants (exposed/non-exposed, missing/excluded) (if applicable)	
Statistics (if any)	Statistical method used	
	Details on statistical analysis	
	Relative risk/odds ratio, confidence interval?	
Author's conclusions	Interpretation of results	
	Assessment of uncertainty (if any)	
Reviewer comments	Results included/excluded in review (if applicable)	

Publication Reference: *Insert full bibliographical reference for report*		
	Notes on study quality, e.g. gaps, methods	

Data summary/synthesis

Data summary/synthesis for the evidence scan was limited to those aspects identified which have the potential to influence the overall conclusions made by the jurisdictions who have derived existing health-based guidance/guidelines (i.e. the health-based research questions only). Relevant data were summarised in tabular format by research question.

3.4 Supporting information in factsheet

In the first instance, the existing guidance/guideline documents identified as per the methods outlined in **Section 3.2** were consulted for supporting information in the factsheet (i.e. general description, uses, measurement techniques and limits of reporting in drinking water, treatment options, etc).

The information was collated into data extraction tables such as the one in **Table 6**. The individual completed data extraction tables for supporting information are provided in **Appendix D**.

Table 6 Example of data extraction table format for supporting information in factsheet

Agency Report Reference: *Insert full bibliographical reference for report*		
General Description	Uses	
	Sources in drinking water	
	Other	
Treatment of drinking water	Treatment technology	
	Effectiveness	
	Any special conditions?	
	Other	
Measurement	Analytical method	
	Limit of determination/ Limit of Reporting (LOR)	
	Other	
Additional information	Any additional non-health related information considered important?	

In addition, an evidence scan of recent publicly available literature was undertaken as per the literature search methodology shown in **Table 7** below.

Table 7 Search strategy for evidence scan of supporting information in factsheet

Parameter	Comments
Search terms	The selected search terms for the Scopus database were: • (Ammonia) AND (treatment) AND (drinking water) [(1)] After a few trial runs of various combinations of search terms in the industry websites, it became apparent that the search capacities varied significantly between different webpages. Consequently, the selected search term (for industry websites) was kept relatively broad: • (Ammonia)
Databases/Other sources	The following source database was searched: • Scopus The following industry websites were searched: • Water Services Association of Australia: https://www.wsaa.asn.au/ • Standard Methods for the Examination of Water and Wastewater: https://www.standardmethods.org/ • US EPA Drinking Water Treatability Database: https://tdb.epa.gov/tdb/home The following Australian commercial laboratories were contacted directly via e-mail or website form for relevant information: • National Measurement Institute • SGS • ALS • Eurofins
Publication Date	Limited to last 5 years (2017-2021)
Language	English
Study Type	• Peer-reviewed, published, in press, unpublished and ongoing studies. • Australian laboratory information sheets or e-mail responses on measurement methods and limits of determination.
Inclusion and exclusion criteria	The following exclusion criteria were used to screen relevance of information: • NR = Not Relevant. Information not directly relevant to answering research questions. • Research technique (analytical or treatment) = does not appear to be commercially applied. • Language = Language other than English. • NPA = Not publicly available. • NL = Chemical not listed under specific treatment process.
Validation methods used	Preliminary test searches were undertaken to assist with selecting search terms. Refinements were made as considered appropriate to ensure adequate, but also specific coverage in the sources screened.

Parameter	Comments
Screening methods	Results were screened as follows: *Preliminary title and abstract screen* • Titles of results for each search were recorded in an Excel spreadsheet. Each source was on a separate tab of the spreadsheet. • The researcher scanned the titles (and abstracts, if required). In a separate column a decision regarding relevance of the result was recorded as per the exclusion criteria. An additional column was included to provide commentary as (and if) required. • Where the researcher was uncertain as to the relevance of a particular result, the researcher discussed the matter with a subject expert prior to making a decision OR the result was considered potentially relevant and included. *Content screen* • The full text content of literature selected to be included from the preliminary title and abstract screen were reviewed by a subject expert to determine which articles to include in the data extraction step. Only articles/reviews which provided information relevant to answering the research questions were taken through to the data extraction step.
Documentation of search	Spreadsheets with full search results and screening outcomes (i.e. reasons for exclusion) are provided in **Appendix A.** Overall results presented in **Figure 1**, adapted from the PRISMA figure presented in Moher et al. (2009) and Figure 5 in NTP (2015).
Retrieval of publications	All relevant and potentially relevant results were recorded in an Endnote library and soft copies of files saved into a designated folder on the SLR server for review. The server is backed up on a daily basis.
1. It became evident upon undertaking the initial searches using the following additional search term combinations ['(Ammonia) AND (analysis) AND (drinking water)' OR '(Ammonia) AND (testing) AND (drinking water)'] that these searches returned thousands of results that were not relevant to answering the research questions with respect to commercial analytical techniques used in Australia. Results obtained for analytical techniques in the peer-reviewed literature were research-based techniques for specific purposes and not currently commercially applied. It was considered more efficient and effective to contact Australian laboratories directly for information on their analytical techniques and commercial limits of reporting. Therefore, the search in the Scopus database was limited to information on treatment technologies.	

The following data were extracted from relevant publications and/or obtained from contacts with Australian laboratories:

- Citation information
- Name of treatment technology (as applicable)
- Name of analytical technique (as applicable)
- Associated Reporting Limit

The individual completed data extraction tables for supporting information are provided in **Appendix D**.

4 Results

A summary of the responses to the research questions for ammonia is provided the tables below. When reading the responses and information for ammonia it is important to consider that ammonia exists in two states in the environment, either as a volatile gas (ammonia gas) or as a non-volatile cation (or salt). The form of ammonia in the environment will depend on environmental conditions, particularly pH. For example, ammonia in water at neutral pH exists predominantly as a (non-volatile) cation (referred to as 'ammonium') whereas at higher (alkaline) pH, ammonia most likely exists in water 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.

4.1 Health-based research question analysis

Table 8 Synthesis of extracted data for health-based research questions

#	Research Questions	Jurisdiction	Response to Research Questions
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?	**ATSDR 2004**	No critical health end point was chosen for ammonia. No information was located for systemic effects associated with exposure to ammonia or ammonium compounds apart from metabolic acidosis following exposure in laboratory animals to ammonium chloride at doses from 500 – 1000 mg/kg/day.
		EFSA 2012a	Typically, no effects other than those related to metabolic acidosis are observed at high doses in animal experiments (with ammonium chloride).
		WHO 2003	With ammonium chloride, the acidotic effects of the chloride ion seem to be of greater importance than those of the ammonium ion. At a dose of more than 33.7 mg of ammonium ion per kg body weight per day, ammonium chloride influences metabolism by shifting the acid-base equilibrium, disturbing the glucose tolerance, and reducing the tissue sensitivity to insulin.
		EFSA 2009, EFSA 2021b, USEPA 2005, JECFA 2010 ___→____ No relevant information	
2	What are the justifications for choosing this endpoint/health hazard?	**ATSDR 2004**	No health end point was chosen considering the lack of quality and usefulness of the database for oral exposure and most available studies have been carried out using ammonium chloride studies. It was considered inappropriate to use data for ammonium chloride for ammonia or other ammonium salts.
		EFSA 2012a	Ammonia is considered to be of no concern for developmental or reproductive effects, or for carcinogenicity and it shows low acute oral toxicity. Estimated intakes in humans from drinking water at 0.5-5 mg/L (0.014 mg/kg/d – 0.14 mg/kg/d) are approximately two to three orders of magnitude lower than endogenously produced ammonia (40-60 mg/kg/d) and levels at which toxicological effects are reported (200 mg/kg/d). Ammonia is considered an important source of nitrogen for mammals.

#	Research Questions	Jurisdiction	Response to Research Questions
		USEPA 2005	No PPRTV for oral exposure has been derived for ammonia. The scientific database was considered inadequate.
		JECFA 2010	Ammonia has been evaluated by the International Programme on Chemical Safety in 1986, which concluded that ammonia does not present a direct threat to humans except as a result of accidental exposure, particularly in industry.
		WHO 2003	Ammonia is not of direct importance for health in the concentrations found in drinking-water. A health-based guideline has therefore not been derived.
		EFSA 2009, EFSA 2021b ___→____ No relevant information	
3	What is the toxicological mode of action of ammonia for the critical human health endpoint?	**EFSA 2012a**	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. Note that the anion characterises the toxicity of ammonium form with ammonium chloride the most toxic.
		ATSDR 2004, EFSA 2009, EFSA 2012b, USEPA 2005, JECFA 2010, WHO 2003___→____ No relevant information	
4	Is ammonia a genotoxic carcinogen of relevance to humans?	**ATSDR 2004**	Ammonia and the ammonium are unlikely to be a human carcinogen at the exposures encountered in the environment.
		EFSA 2009	No
		EFSA 2012a	Ammonia shows no genotoxic potential.
		USEPA 2005	US EPA concluded that data for carcinogenicity of ammonia are inadequate for an assessment of human carcinogenic potential.
		WHO 2003	No
		EFSA 2012b, JECFA 2010___→____ No relevant information	
5	What dose(s) are associated with the critical human health endpoint (if any)?	**ATSDR 2004**	Not applicable (no health-based guidance value derived).
		EFSA 2009	Not applicable (default thresholds of toxicological concern used for assessment).
		EFSA 2012a	Not applicable (no guidance value derived). However, 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	Not applicable (ADI – not specified)

#	Research Questions	Jurisdiction	Response to Research Questions
		USEPA 2005	Not applicable – no oral PPRTV derived.
		JECFA 2010	Not applicable (ADI – not specified)
		WHO 2003	Not applicable (no health-based guidance/guideline value derived).
6	Is the proposed health-based guidance value relevant to the Australian context?	**ATSDR 2004, EFSA 2009, EFSA 2012a, EFSA 2012b, USEPA 2005, JECFA 2010, WHO 2003**	No health-based guidance/guideline value was identified from any of the agencies consulted.
7	Are there groups of people in the general population who may be more sensitive to ammonia exposure?	**ATSDR 2004**	Populations with potentially high exposures (likely via inhalation rather than ingestion) include farm workers employed in inadequately-ventilated, enclosed spaces with large numbers of animals; ammonia process workers; people that use cleaning products containing concentrated ammonia in small, enclosed or un-ventilated rooms. Persons who suffer from severe liver or kidney disease, since these organs biotransform and excrete NH4+. Individuals with hereditary urea cycle disorders (i.e. levels produced endogenously are sufficient to produce toxicity).
		EFSA 2012a	People suffering from enzyme deficiencies due to genetic disorders or severe kidney or liver failure.
		EFSA 2009, EFSA 2012b, USEPA 2005, JECFA 2010, WHO 2003___→____ No relevant information	
8	Is a health-based guideline value needed for ammonia?	**ATSDR 2004, EFSA 2009, EFSA 2012a, EFSA 2012b, USEPA 2005, JECFA 2010, WHO 2003**___→____ No	
9	If not, what aesthetic characteristics of ammonia (if any) should be taken into consideration?	**ATSDR 2004**	Taste. Ammonia can be tasted in water at levels of about 35 mg/L but levels in drinking water are far less than this.
		EFSA 2012a	Ammonia in alkaline water has an odour threshold of 1.5 mg/L and the ammonium form has a taste threshold of 35 mg/L.
		USEPA 2005	Because adequate data are lacking for oral exposure to ammonia, previous determinations of toxicity reference values have used organoleptic (taste) data to estimate acceptable ammonium levels in drinking water at **34-35 mg/L.**
		WHO 2003	The threshold odour concentration of ammonia in water is approximately **1.5 mg/L**. A taste threshold of **35 mg/L** has been proposed for the ammonium cation.

#	Research Questions	Jurisdiction	Response to Research Questions
		EFSA 2009, EFSA 2012b, JECFA 2010 ___→____ No relevant information	
10	What is the guidance value (if any)?	**ATSDR 2004**	None derived.
		USEPA 2005	No PPRTV derived.
		JECFA 2010	TDI – not limited.
		WHO 2003	No health-based guideline value derived. Ammonia in drinking water at 0.2 mg /L may interfere with disinfection efficiency and may also represent taste and odour problems.
		EFSA 2009, EFSA 2012a, EFSA 2012b___→____ No relevant information	
11	Is there a knowledge gap from the time at which existing guideline values were developed?	**ATSDR 2004**	Potentially. Bibliography contained literature up to 2004.
		EFSA 2009	Potentially. Bibliography contained literature up to 2009.
		EFSA 2012a	Potentially. Literature search up to 2008, but bibliography contains literature up to 2012.
		EFSA 2012b	As per EFSA (2012a).
		USEPA 2005	Potentially. Literature search conducted up to 2002, but bibliography contained literature up to 2005.
		JECFA 2010	Potentially. Bibliography contained literature up to 2010.
		WHO 2003	Potentially. Bibliography contained literature up to 1991.
12	Does any recent literature change the guideline value? (e.g. demonstrating a new critical endpoint?)	No health-based studies which would potentially alter the conclusions of the evaluation were found in the evidence scan conducted.	

4.2 Exposure-related research question analysis

Table 9 Synthesis of extracted data for exposure-related research questions – Water Corporations

#	Research Questions	Jurisdiction	Response to Research Questions
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?	**Tas Water 2016- 2018**	Mean: 0.05 mg/L, Range: <0.005 –0.373 mg/L. No info on variability around country.
		Chapman et al. 2008	Rainwater tanks: Total detected: 37, Total tested: 44, Mean: 0.074 mg/L, Minimum: 0.002 mg/L, Maximum: 0.270 mg/L
14	Do Australian levels differ considerably from elsewhere?	Unclear from literature reviewed.	

Table 10 Synthesis of extracted data for other exposure-related research questions

#	Research Questions	Jurisdiction	Response to Research Questions
15	What are the principal routes of exposure to ammonia in the Australian general population?	**ATSDR 2004**	Low levels from food and drinking water intake, and possibly inhalation from ambient air. Exposure of the general population to elevated levels of ammonia (via inhalation) indoors is most commonly from the use of household cleaners that contain ammonia. Levels low compared to ammonia produced endogenously by mammals.
		EFSA 2009	EFSA reported food colours and flavouring as source of ammonia in diet.
		EFSA 2012a	Food and drinking water, inhalation and smoking. The daily exposure to ammonia from environmental sources is insignificant in comparison to endogenous synthesis of ammonia.
		EFSA 2012b	Diet.
		USEPA 2005	Not specified.
		JECFA 2010	Dietary exposure and minor exposure via drinking water.
		WHO 2003	Ammonia is a natural component of many foods. Minor amounts of ammonium compounds are also added to foods as acid regulators, stabilisers, flavouring substances, and fermentation aids. Minor amounts are taken via inhalation and through cigarette smoking. Levels low compared to endogenous ammonia.
16	What are the typical levels of Australian exposure (e.g. 'background' ammonia levels)?	**ATSDR 2004**	In USA, food & drinking-water: 18 mg. Air: 20 µg /m^3 in urban areas, up to 300 µg/m^3 on farms. Inhalation <1 mg, cigarette smoking (20/day) < 1 mg. 4000mg/d produced endogenously in human intestine.
		EFSA 2009	In Europe, estimated Daily per Capita/day Intake (based on Maximised Survey-derived Daily Intake (MSDI) approach): Ammonium chloride: 140 µg, Ammonia: 34 µg, Ammonium hydrogen sulphide: 5.6 µg. Intake based on mTAMDI approach (µg/person/day): Ammonium chloride: 110,000, Ammonia: 220,000 and Ammonium hydrogen sulphide: 220
		EFSA 2012b	In Europe, food & drinking water: 18 mg per person (0.26 mg/kg b.w. per day for a 70 kg adult). Inhalation & smoking cigarettes < 2 mg/person/d (0.029 mg/kg b.w. per day for a 70 kg adult). Daily exposure from environmental sources insignificant in comparison to endogenous synthesis of ammonia (3000-4000 mg/person (equivalent to 43-57 mg/kg b.w. per day for a 70 kg adult).
		WHO 2003	In Europe, food & drinking-water: 18 mg. Air: 20 µg /m^3 in urban areas, up to 300 µg/m^3 on farms. Inhalation <1 mg, cigarette smoking (20 cigarettes per day) <1 mg. 4000 mg of ammonia per day are produced endogenously in the human intestine.
		EFSA 2012a, USEPA 2005, JECFA 2010 __→____ No relevant information	

4.3 Risk-based research question analysis

Table 11 Synthesis of extracted data for risk-associated research questions

#	Research Questions	Jurisdiction	Response to Research Questions
17	What are the risks to human health from exposure to ammonia in Australian drinking water?	**ATSDR 2004**	None Identified
		EFSA 2009	None Identified
		EFSA 2012a	None Identified
		EFSA 2012b	None Identified
		USEPA 2005	None Identified
		JECFA 2010	None Identified
		WHO 2003	None Identified
18	Is there evidence of any emerging risks that are not mentioned in the current factsheet that require review?	**ATSDR 2004**	No
		EFSA 2009	No
		EFSA 2012a	No
		EFSA 2012b	No
		USEPA 2005	No
		JECFA 2010	No
		WHO 2003	No

4.4 Supporting factsheet information research question analysis

The supporting information in the fact sheet for Ammonia consists of the following (NHMRC and NRMMC 2011):

- **General Description:** "*Ammonia, NH3, is a colourless gas or liquid, with a sharp, intensely irritating odour. It is lighter than air and easily liquefied by pressure. Ammonia has a boiling point of –33.5°C, a freezing point of –77.7°C, and a specific gravity of 0.8 as a liquid. Ammonia gas is combustible and is very soluble in water. When hydrated, ammonia can attack copper, zinc and alloys containing these metals. Ammonia can be supplied as a compressed liquid (anhydrous ammonia), dissolved in water (aqueous ammonia) or as solutions of ammonium salts (e.g. ammonium sulfate).*

  Gaseous ammonia is compatible with some steels, stainless steel (type 316), neoprene and monel. Aqueous ammonia can be stored in iron, steel, stainless steel, fibreglass-reinforced plastic or rubber-lined vessels."
- **Typical values in Australian drinking water:** not available.
- **Treatment of drinking water:** "*In drinking-water treatment, ammonia is added with chlorine (at a fixed ratio of ammonia to chlorine) to produce chloramine disinfectants. Chloramines react with bacteria and oxidisable material more slowly than free chlorine, but last longer than free chlorine. Depending on the order and process used trihalomethanes (THMs) may form. Chloramines thus tend to be used as a secondary disinfectant to provide a disinfectant residual in the distribution system, but may also be used as a primary disinfectant if an appropriate contact time is allowed. Chloramines are particularly suited to providing disinfectant residuals in long distribution systems, where it is difficult to maintain a residual using chlorine.*

  To produce monochloramine, the pH should be between 8 and 9, and the chlorine to ammonia ratio should be between 3:1 and 4:1. A ratio above 4:1 may produce chlorinous odours. Ammonia may be added before or after chlorine. In primary disinfection, chlorine is usually added first, because it kills bacteria, viruses and spores much more efficiently than does monochloramine, provided that sufficient contact time is allowed for disinfection before the ammonia is added. Ammonia and chlorine can be added together, provided that contact time is sufficient to ensure disinfection.

  Chloramines present in water are harmful to people on kidney dialysis and to animal species in aquaria; therefore, it is important for water utilities using chloramination to inform consumers at risk.".
- **Measurement:** not part of the current Guidelines.

Table 12 Synthesis of extracted data for research questions relevant to supporting factsheet information – Agency reviews

#	Research Questions		Jurisdiction	Response to Research Questions
19	Is the general description current?	Uses	**ATSDR 2004**	In the USA, ammonia is used in smelling salts, household cleaners, and window cleaning products. 80% of all manufactured ammonia is used as fertiliser. A third of this is applied directly to soil as pure ammonia. The rest is used to make other fertilisers that contain ammonium compounds, usually ammonium salts. These fertilisers are used to provide nitrogen to plants. Ammonia is also used to manufacture synthetic fibres, plastics, and explosives. Many cleaning products also contain ammonia in the form of ammonium ions.
			EFSA 2012a	Ammonia is a widely used industrial chemical, mostly in fertilisers, but also in various other applications such as plastics, cleaning products, explosives, animal feed and food additives.
			WHO 2003	Ammonia is used in fertiliser and animal feed production and in the manufacture of fibres, plastics, explosives, paper, and rubber. It is used as a coolant, in metal processing, and as a starting product for many nitrogen-containing compounds. Ammonia and ammonium salts are used in cleansing agents and as food additives and ammonium chloride is used as a diuretic.
		Sources in DW	**ATSDR 2004**	-
			EFSA 2012a	Ammonium in water comes normally from natural, industrial, agricultural sources and from disinfection with chloramine. Elevated ammonium levels in drinking water often indicate bacterial, sewage and waste pollution. There are indications that ammonium can be released from water filters but in very low concentrations.
			WHO 2003	Ammonia in the environment originates from metabolic, agricultural and industrial processes and from disinfection with chloramine.
20	What are the indicators of the risks? How can we measure exposure? Is the information on measurement/analytical methods current?		**ATSDR 2004**	Exposure can be measured as ammonia concentration in in media (e.g. DW). Drinking water: • Sample mixed with borate buffer (Method 1689, on selective probe) (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).
			EFSA 2012a	-
			WHO 2003	Ammonia and ammonium cation at concentrations between 0.025 and 3 mg/litre can be determined by the indophenol reaction. An ammonia-selective electrode can also be used, as can titrimetry which is less sensitive. Drinking water LOD: 0.025 - 3 mg/L µg/L indophenol reaction.

Table 13 Synthesis of extracted data for research questions relevant to supporting factsheet information – Other sources

#	Research Questions	Jurisdiction	Response to Research Questions
20	What are the indicators of the risks? How can we measure exposure? Is the information on measurement/analytical methods current?	**Correspondence with Australian Commercial Laboratories**	Method: APHA 4500-NH3 Alkaline phenol and hypochlorite react with ammonia to form indophenol blue that is proportional to the ammonia concentration. The blue colour is intensified with sodium nitroprusside. This method determines ammonia in drinking, surface, and saline waters; domestic and industrial wastes.
		Water Corporations (Tas Water 2016, 2017, 2018, Chapman et al. 2008, WCWA 2014)	Water Corporation Western Australia (WCWA) compared commercially available on-line ammonia analysers and the Chemscan UV-2150/S was selected for a trial based on its claimed consistency and reliability. It uses a multiple wavelength UV absorbance detection system to measure total and free ammonia, monochloramine and also total chlorine. All four parameters are measured directly, which enables more accurate control of the chlorine dose.
		Chen 2019	Ammonia: Nessler's reagent colorimetry with spectrophotometer (U-3900H, HITACHI, Japan).
		Dos Santos & Daniel 2020	-
		Hasegawa 2017	Did not measure ammonia concentrations.
		Hu 2020	NH4+-N and NO3−-N were determined via spectrophotometric and colorimetric analyses; ammonium loading rate (SLR) was calculated based on the ammonium concentration and filtration flow rate.
		Huang et al 2019	Micro-distillation and conductance measurement instrument - Micro-DCMI a linear calibration range of 0.01–60 mg NH_3 L^{-1}
		Jantarakasem et al. 2020	Colorimetric HACH kit (TNT830, HACH, USA).
		Liu et al 2017	Colorimetric method using a spectrometer (DR 5000, HACH, USA).
		Niu et al 2018	A spectrophotometer (U2010, Hitachi, Tokyo, Japan) with the indophenol blue colorimetric method.
		Serajuddin et al 2018	HACH DR 6000 spectrophotometer (HACH LANGE, USA) & Nessler method, No. 8038.
		Wu et al 2021	Not stated.
		Xue et al 2021	HACH DR 2800 Spectrophotometer, HACH TNT 830 kits

#	Research Questions	Jurisdiction	Response to Research Questions
21	Are there commercial analytical methods available that can measure at or below guideline value?	**Correspondence with Australian Commercial Laboratories**	The standard LOR is 0.01 mg/L (i.e. 10 µg/L).
		Water Corporations (Tas Water 2016, 2017, 2018, Chapman et al.2008, WCWA 2014)	LOR 0.005 mg-N/L (i.e. 5 µg-N/L). Ammonia concentration: <0.1 mg/L (i.e. <100 µg/L).
		Chen 2019	LOR not stated.
		Dos Santos & Daniel 2020	Not stated.
		Hasegawa 2017	Not reported.
		Hu 2020	Not reported.
		Huang et al 2019	Yes, the Limit of detection (LOD): 0.014 mg L^{-1} Limit of quantification (LOQ) of 0.045 mg L^{-1}
		Jantarakasem et al. 2020	The quantification limit of the colorimetric kit was 0.015 mg NH4+-N/L.
		Liu et al 2017	Not stated.
		Niu et al 2018	Not stated.
		Serajuddin et al 2018	Not stated.
		Wu et al 2021	Not stated.
		Xue et al 2021	Yes, the approach has used LODs for the following measurements: 0.015 to 2.00 mg/L NH3-N.
22	Is the information for treatment options current in terms of current practices in Australia?	**Correspondence with Australian Commercial Laboratories**	-
		Water Corporations (Tas Water 2016, 2017, 2018, Chapman et al. 2008, WCWA 2014)	Chloramination (using monochloramine - a combination of chlorine and ammonia) is used as the preferred form of disinfection as it persists in the water much longer than chlorine. The monochloramine, however, decays over time releasing free ammonia and chlorine.
		Chen 2019	An iron–carbon micro-electrolysis (ICME) combined with up-flow biological aerated filter (UBAF) process was used to remove two types of disinfection by product (DBP) precursors in micro-polluted source water. Ammonia was 90% removed by the nitrifying bacteria in the UBAF. Pre-treatment: 1.12-1.86 mg/L. Post treatment: ~0.12-0.19 mg/L.

#	Research Questions	Jurisdiction	Response to Research Questions
		Dos Santos & Daniel 2020	Biological activated carbon (BAC) filtration is a potential treatment process for removing organic matter and ammonia through nitrification denitrification, simultaneously.
		Hasegawa 2017	BCF is a filter media onto which microorganisms are attached. When raw water such as river water flows through the BCF column, ammonia and dissolved organic matter (DOM), including those that produce foul smell, are oxidised and removed by the microorganisms attached to the filter media.
		Hu 2020	This study is not highlighting a new technique, rather it is looking at understanding ammonia-oxidising communities in rapid sand filters (RSFs) and their response to the changing conditions for their safe operation.
		Huang et al 2019	Treatment method not provided.
		Jantarakasem et al. 2020	A bench-scale column assay to determine the volumetric ammonium removal rate (VARR) of biological activated carbon (BAC).
		Liu et al 2017	A pilot lava-based biological aerated filter (BAF) was setup as a pre-treatment unit of drinking water treatment plant (DWTP). At 18.6 – 32.9 °C = NH_4^+-N: Influent 2.15 mg/L; effluent 0.15 mg/L
		Niu et al 2018	Granular activated carbon (GAC) and backwashing.
		Serajuddin et al 2018	Meteor pilot, a biological pre-treatment system.
		Wu et al 2021	A pilot-scale biological pre-treatment reactor filled with porous polyurethanes carriers (BioNET) was operated over 500 days under different hydraulic retention times (HRT) (1.3 to 0.5 h).
		Xue et al 2021	Zeolites and activated carbon were examined for ammonia and N-nitrosamine precursor removal when incorporated into drinking water treatment processes.
23	Can treatment technologies treat to the suggested level of the guideline value?	**Correspondence with Australian Commercial Laboratories**	-
		Water Corporations (Tas Water 2016, 2017, 2018, Chapman et al. 2008, WCWA 2014)	Yes, this treatment technology reduced ammonia concentration to: Tas Water [(1)]: <0.005-0.373 mg/L WCWA 2014 [(1)]: <0.1 mg/L (i.e. 100 µg/L) (WCWA 2014).
		Chen 2019	ICME had no significant contribution to ammonia removal. However, ammonia was 90% removed by the nitrifying bacteria in the UBAF.

#	Research Questions	Jurisdiction	Response to Research Questions
		Dos Santos & Daniel 2020	Ammonia conversion across different studies as part of this literature review: 30-100%. Concentration of ammonia in influent mg N-NH_4 L^{-1} 0.02-4.9 mg N-NH4 L^{-1}
		Hasegawa 2017	Effectiveness on ammonia concentrations *per se* not discussed.
		Hu 2020	Effectiveness on reducing ammonia concentrations *per se* not discussed.
		Huang et al 2019	No treatment information provided.
		Jantarakasem et al. 2020	The water matrix factor reduced the VARR in ozonated water at 25 °C by 33% on average. Volumetric ammonia loading rate: 4-6 g NH_4^+- N/m^3 Ammonia in the effluent: 0.4 g NH_4^+- N/m^3
		Liu et al 2017	BAF performance concentrations for maximum 92.6% NH^{4+}-N and 97.88% (NO2-N) efficiency: $NH4^+$-N: Influent 2.15 mg/L; effluent 0.15 mg/L
		Niu et al 2018	Without pre-chlorination, the ammonium removal potential was 0.040 mg N/L/h/g-dry. It increased by 12% after backwashing in the first sampling. The removal potential decreased by 12% after backwashing (from 0.048 to 0.042 mg N/L/h/g-dry) when prechlorination was implemented.
		Serajuddin et al 2018	Ammonia reduction 73%. Raw water ammonia concentration: < 15 mg NH3-N/L. Ammonia in pre-treatment effluent < 4.0 mg/L.
		Wu et al 2021	Under 0.5 h hydraulic retention times (HRT) 84 % nitrification efficiency and 0.42 kg-N/m^3/day ammonia removal rate could be achieved with influent ammonia concentration of 10.4 mg N/L. Influent ammonia range (mg-N/L): 3.5-12.0, effluent ammonia range (mg-N/L): 0.2-5.7
		Xue et al 2021	The results showed that Mordenite zeolite can remove ammonia and five of seven N-nitrosamine precursors efficiently by single step adsorption test. Alum coagulation more than 67% ammonia and 70-100% N-nitrosamine precursors were removed by Mordenite zeolite.
24	Is there any new information which should be added? Should anything be removed?		Update LOR in measurement section, treatment section can be expanded.

1. It is noted that it is not always clear from the various Water Corporation performance reports whether the data presented are for treated or untreated supplies. Thus the data presented may be for reticulated treated or raw water.

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Tas Water (2018a). Annual Drinking Water Quality Report: Adventure Bay Drinking water supply system results. Tasmanian Water and Sewerage Corporation.

Tas Water (2018c). Annual Drinking Water Quality Report 2017-18 Section B – Drinking Water Systems. Tasmanian Water and Sewerage Corporation.

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

APPENDIX A

Literature search screening outcome spreadsheets

Appendix A contents here

APPENDIX B

Data extraction tables – Health-based guidance/guidelines

Existing Health-Based Guidance for Ammonia

ATSDR 2004

Agency Report Reference: *ATSDR (2004). Toxicological Profile for Ammonia. US Department of Health and Human Services, Agency for Toxic Substances and Disease Registry. September 2004.*		
General Information	Date of data extraction	30/08/2021
	Authors	Roney N, Llados F, Little S, Knaebel D.
	Publication date	September 2004
	Literature search timeframe	Not stated, but bibliography contained literature up to 2004.
	Publication type	Agency review
	Peer reviewed?	Yes, profile underwent numerous internal ATSDR reviews, was peer reviewed by a non-governmental panel and was released for public comment prior to finalisation.
	Country of origin	United States
	Source of funding	Not stated, but assumed to be United States government
	Possible conflicts of interest	Not indicated
Health considerations	Guideline value type (e.g. oral TRV, drinking water guideline)	Normally oral Minimal Risk Level (MRL), but no health-based MRLs were derived.
	Exposure timeframe	Not applicable – no oral MRLs derived.

Agency Report Reference: *ATSDR (2004). Toxicological Profile for Ammonia. US Department of Health and Human Services, Agency for Toxic Substances and Disease Registry. September 2004.*		
	Critical health endpoint(s) – oral exposure	No critical health end points were specified for ammonia following oral exposure for the following reasons: 1) Quality and/or usefulness of the oral database is limited. The only human acute oral studies available were case reports with no exposure levels. Animal studies were limited to a food intake study, single-exposure studies with no effect, serious effects, or unsupported effects, a gavage study that lacked study details, and a 6-day DW study with effects at high levels. 2) Majority of animal studies have been carried out using ammonium chloride. Ammonium chloride is commonly used to induce metabolic acidosis in experimental animals due to the formation of hydrogen chloride. Although it will occur with any ammonium salt, the degree of acidosis (and associated consequences) will be determined by the ability of the kidneys to excrete the specific anion. It would therefore be inappropriate to extrapolate findings obtained with ammonium chloride (or any ammonium salt) to equivalent amounts of ammonium, but derived from a different salt. 3) The amount of excess ammonia (over and above the amount normally produced by the body) that can be safely ingested and assimilated is difficult to define. However, data from humans and animals suggest that the amount may be substantial based on the existence of various efficient ways in which the body can dispose of ammonia. However, the following effects have been observed in experimental animals: • Decreased binding of somatostatin to receptors in frontoparietal cortex and hippocampus in 15-day oral rat study with ammonium acetate (NOAEL 22 mg/kg/d); • Decreased body weight in 90-day rat study with $NH_4NH_2SO_3$ and ammonium acetate (NOAELs 22 or 39.5 mg/kg/d).
	Justification provided by agency for critical endpoint	No information was located for systemic effects associated with exposure to ammonia or ammonium compounds with the exception of metabolic acidosis ammonium chloride.
	Critical study(ies) underpinning point of departure	Not applicable (no critical endpoint selected).
	Species for critical study(ies)	Not applicable (no critical endpoint selected).
	Point of departure type (e.g. NOAEL, LOAEL, BMDL10, etc)	Not applicable (no critical endpoint selected).
	Point of departure value (include units)	Not applicable (no critical endpoint selected).
	Uncertainty factor(s) & rationale	Not applicable (no critical endpoint selected).
	The derivation:	Not applicable (no critical endpoint selected).
	Guideline value (include units)	Not applicable (no critical endpoint selected).

Agency Report Reference: *ATSDR (2004). Toxicological Profile for Ammonia. US Department of Health and Human Services, Agency for Toxic Substances and Disease Registry. September 2004.*		
	Mode of action for critical health endpoint	Not applicable (no critical endpoint selected).
	Genotoxic oral carcinogen?	Although data indicate ammonia and the ammonium ion may have clastogenic and mutagenic properties, ammonia is unlikely to be a human carcinogen at the exposures encountered in the environment.
	Identified sensitive sub-populations	• Populations with potentially high exposures include farm workers employed in inadequately-ventilated, enclosed spaces with large numbers of animals; ammonia process workers; people that use cleaning products containing concentrated ammonia is small, enclosed or un-ventilated rooms. • Persons who suffer from severe liver or kidney disease, since these organs biotransform and excrete $NH4^+$. • Individuals with hereditary urea cycle disorders (i.e. levels produced endogenously are sufficient to produce toxicity).
	Any non-health-based considerations?	Not in MRL development. But ATSDR notes that ammonia (but not the ammonium form) has a strong odour that is irritating and that you can smell when at levels >5ppm; in water the odour threshold is given as 1.5 mg/L. Therefore, ammonia is likely to be smelt before exposure to a concentration that can harm people is experienced however it is noted that ammonium ions are not volatile and have no odour. Ammonia can be tasted in water at levels of about 35 mg/L.
Exposure considerations	Principal routes of exposure in general population	Exposure to ammonia is the environment is most likely to occur by breathing in ammonia released to air. Ammonia is found in air, water and soil. There are relatively low levels of exposure from food and drinking water intake, and inhalation from ambient air compared to the amount of ammonia produced endogenously. Ammonia occurs naturally in the environment and is naturally produced in the body of all mammals during normal metabolism. Indoors, inhalation exposure of the general population to elevated levels of ammonia is most commonly from the use of household cleaners that contain ammonia.
	Levels in drinking water supplies (include location)	Low (not stated). Ammonia can be tasted in water at levels of about 35 mg/L but levels in drinking water are far less than this. Concentrations in rivers and bay waters are less than 6 mg/L as the ammonium form.
	Any special considerations to exposure levels (e.g. higher in drought?)	People who live near farms or who visit farms during the application of fertiliser that contain or release ammonia may also be exposed. People living near cattle feedlots, poultry confinement buildings, or other areas where animal populations are concentrated can also be exposed to ammonia, in addition to other gases generated by putrefaction.

Agency Report Reference: *ATSDR (2004). Toxicological Profile for Ammonia. US Department of Health and Human Services, Agency for Toxic Substances and Disease Registry. September 2004.*		
	Typical exposure in general population (include units for intakes & location)	The estimated daily ammonia intake: • food and drinking-water is 18 mg due to the use of ammonium salts in food stabilisers, • 0.36 mg from untreated water noting that ammonia levels in drinking water is negligible following treatment. • inhalation less than 1 mg, and through cigarette smoking (20 cigarettes per day) also less than 1 mg. • 4000 mg of ammonia per day are produced endogenously in the human intestine
Risk Summary	Any risks to human health from drinking water identified in agency document?	No
	Any emerging risks identified?	No

EFSA 2009

Agency Report Reference: *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.*		
General Information	Date of data extraction	02/09/2021
	Authors	Not listed.
	Publication date	2012
	Publication type	Agency review
	Description	No guidance value derived in this document *per se* but contains relevant information on ammonia exposure levels in European diets (may or may not be relevant for context). Evaluations for the flavouring substances ammonia, ammonium chloride and ammonium hydrogen sulphide were undertaken using the default Threshold of Toxicological Concern (TTC) approach.

Agency Report Reference: *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.*		
	Findings	Estimated Daily per Capita/day Intake (based on Maximised Survey-derived Daily Intake (MSDI) [(1)] approach): Ammonium chloride: 140 µg Ammonia: 34 µg Ammonium hydrogen sulphide: 5.6 µg Intake based on mTAMDI [(1)] approach (µg/person/day): Ammonium chloride: 110 000 Ammonia: 220 000 Ammonium hydrogen sulphide: 220 Threshold of toxicological concern (µg/person/day): Ammonium chloride: 1800 (Cramer Class I) Ammonia: 1800 (Cramer Class I) Ammonium hydrogen sulphide: 90 (Cramer Class III) Although the genotoxicity data for the flavouring substances in this group are limited, the available data on genotoxicity do not preclude an evaluation of the flavouring substances through the Procedure. For ammonium chloride there is a well-performed carcinogenicity study available, which indicates that the substance does not induce tumours. Ammonia is a substance that is readily absorbed in the gut. It is produced endogenously in amounts that far exceed those that are to be ingested as flavourings. The two ammonium salts are expected to give rise to ammonium ion and chloride or hydrogen sulphide. Ammonia is expected to be transported by the portal circulation to the liver and metabolised to urea by the Krebs urea cycle and subsequently excreted by the kidneys. Hydrogen sulphide is a substance that is produced endogenously. The major pathway for sulphide metabolism is oxidation to sulphate and excretion by the kidney. The major oxidation product of sulphide is thiosulphate, which is then converted to sulphate. The primary location for these reactions is the liver. All three substances are accordingly expected to be metabolised to innocuous substances at the anticipated levels of intake as flavouring substances.

1. The MSDI approach estimates *per capita* intakes of flavouring substances in Europe based on survey data. However, when EFSA (2009) examined the information provided by the European Flavour Industry on the use levels in various foods, it appeared obvious that the MSDI approach in a number of cases would grossly underestimate the intake by regular consumers of products flavoured at the use level reported by the Industry, especially in those cases where the annual production values were reported to be small. As a result, EFSA (2009) had reservations about the data on use and use levels provided and the intake estimates obtained by the MSDI approach. In the absence of more precise information that would enable a more realistic estimate, EFSA (2009) also decided to perform an estimate of the daily intakes per person using a modified Theoretical Added Maximum Daily Intake (mTAMDI) approach based on the normal use levels reported by Industry. In those cases where the mTAMDI approach indicated that the intake of a flavouring substance might exceed its corresponding threshold of concern, EFSA (2009) decided not to carry out a formal safety assessment using the Procedure. In these cases, EFSA (2009) requires more precise data on use and use levels.

EFSA 2012a

Agency Report Reference: ***EFSA (2012a). Scientific Opinion: Health risk of ammonium released from water filters. Adopted 15 October 2012. European Food Safety Authority (EFSA). The EFSA Journal (2012) 10 (10): 2918***		
General Information	Date of data extraction	30/08/2021
	Authors	Panel members: Benford D, Barthelemy E, Binaglia M, Cioacata G, Eskola M, Gustavsson N, Thatcher N and Thessalonikeos E.
	Publication date	15 October 2012
	Literature search timeframe	1972 – October 2008
	Publication type	Agency review
	Peer reviewed?	Yes, stated in document.
	Country of origin	Europe (not further specified)
	Source of funding	Not specified; likely European governments.
	Possible conflicts of interest	At least once every year, and in any case within 45 calendar days following any change in his/her interests, experts (and other staff of EFSA) submit a declaration of interest (DoI) to EFSA (EFSA 2018b). DoI's are made publicly available on the EFSA website (EFSA 2006). The detailed approach to managing potential conflicts of interest is described in EFSA (2017b, 2018b).
Health considerations	Guideline value type (e.g. oral TRV, drinking water guideline)	No guideline value derived. EFSA (2012) was asked to assess the human health risks following exposure from ammonium in water at concentrations of 0.5-5 mg/L, since ammonium had been found in drinking water at levels above 0.5 mg/L after filtering tap water with water filter cartridges.
	Exposure timeframe	Not applicable (no guidance value was derived).

	Critical health endpoint(s) – oral exposure	EFSA (2012) provided a summary of available toxicological information for ammonia: • Ammonium chloride is more toxic than other ammonium salts, since its toxicity is driven by the release of hydrochloric acid during metabolism of ammonium to urea, leading to hypercholeremic metabolic acidosis. • Rats exposed for 70 days to ammonium chloride at 684 mg/kg b.w. per day (equivalent to 230 mg ammonium/kg b.w. per day) showed decreased urinary pH and increased calcium levels in urine, but no histopathological changes in the bladder. • In another series of studies, ammonium chloride was administered to rats in the diet for period of 4 weeks, 13 weeks, 18 months or 30 months. No effects other than those related to metabolic acidosis were observed up to doses of approximately 3500-4000 mg/kg b.w. per day (1200-1400 mg ammonium/kg b.w. per day) in the 4 and 13-week studies, or up to approximately 1200-1300 mg/kg b.w. per day (400-440 mg ammonium/kg b.w. per day) in the 18 and 30-month studies. • In contrast, ammonium sulphate did not induce metabolic acidosis in rats exposed via the diet to up to 1527 mg/kg b.w. per day (415 mg ammonium/kg b.w. per day) for 52 weeks or up to 1371 mg/kg b.w. per day (373 mg ammonium/kg b.w. per day) for 104 weeks. Increased absolute and relative liver and kidney weights were only observed at the highest dose tested in male and female rats in the 52-week study. These organ weight increases were without related histopathological changes and within 10% in both sexes, and are likely indicative of an adaptive response to ammonium metabolism and urea excretion. In the 104-week study, an increased incidence of chronic nephropathy was observed only in male rats exposed at all the tested doses (564 and 1288 mg/kg b.w. per day, equivalent to 153 and 350 mg ammonium/kg b.w. per day, respectively). Chronic nephropathy is a common finding in aging rats, particularly in males, and its incidence and severity are exacerbated by many chemicals, therefore this effect is thus considered of low relevance for humans. • EFSA (2012) estimated intakes of ammonium at the water concentrations of 0.5-5 mg/L by adults would be 0.014 mg/kg/d – 0.14 mg/kg/d. For infants and children the exposures are higher (0.1-1 mg/kg/d for infants, 0.054-0.54mg/kg/d for children). • These estimated intakes are approximately three orders of magnitude lower than the no-effect levels reported in experimental animals, and therefore do not indicate a health concern. • Considering the large contribution of endogenously produced ammonium to the overall exposure, and the efficient detoxification of ammonium in humans, the additional exposure to ammonium from water at concentrations ranges of 0.5-5 mg/L is negligible and does not pose a risk to human health.

Agency Report Reference: *EFSA (2012a). Scientific Opinion: Health risk of ammonium released from water filters. Adopted 15 October 2012. European Food Safety Authority (EFSA). The EFSA Journal (2012) 10 (10): 2918*		
	Justification provided by agency for critical endpoint	See above.
	Critical study(ies) underpinning point of departure	Not applicable (no guidance value was derived).
	Species for critical study(ies)	Not applicable (no guidance value was derived).
	Point of departure type (e.g. NOAEL, LOAEL, BMDL10, etc)	Not applicable (no guidance value was derived).
	Point of departure value (include units)	Not applicable (no guidance value was derived).
	Uncertainty factor(s) & rationale	Not applicable (no guidance value was derived).
	The derivation:	Not applicable (no guidance value was derived).
	Guideline value (include units)	Not applicable (no guidance value was derived).
	Mode of action for critical health endpoint	Not stated.
	Genotoxic oral carcinogen?	Ammonium shows no genotoxic potential and is not considered to be a carcinogenic concern.
	Identified sensitive sub-populations	Subjects with reduced ammonia metabolism or urea excretion (caused by e.g. enzyme deficiencies due to genetic disorders, or severely impaired hepatic or renal functions) are exposed to higher concentrations of ammonia in the body and represent thus the vulnerable groups of the population to ammonium exposure. However, even for these vulnerable groups of the population the contribution of ammonium in water is marginal, the endogenous ammonium production being by far the most relevant sources.
	Any non-health-based considerations?	No.
Exposure considerations	Principal routes of exposure in general population	Not specified. Exposure to ammonium form in the diet is much lower than the amount of ammonium form produced endogenously.
	Levels in drinking water supplies (include location)	In ground and surface waters natural ammonium levels are usually below 0.2 mg/L.
	Any special considerations to exposure levels (e.g. higher in drought?)	Not stated.
	Typical exposure in general population (include units for intakes & location)	• Estimated daily dietary exposure to ammonium from food and drinking water is 18 mg per person (0.26 mg/kg b.w. per day for a 70 kg adult). • Estimated exposure to ammonia from inhalation and smoking cigarettes is less than 2 mg/person per day (equivalent to 0.029 mg/kg b.w. per day for a 70 kg adult). • The daily exposure to ammonia from environmental sources is insignificant in comparison to endogenous synthesis of ammonia (3000-4000 mg/person (equivalent to 43-57 mg/kg b.w. per day for a 70 kg adult)).

Agency Report Reference: *EFSA (2012a). Scientific Opinion: Health risk of ammonium released from water filters. Adopted 15 October 2012. European Food Safety Authority (EFSA). The EFSA Journal (2012) 10 (10): 2918*		
Risk Summary	Any risks to human health from drinking water identified in agency document?	No.
	Any emerging risks identified?	No. Based on the available information from one of the water filter manufacturers, ammonium is formed in the water filter cartridges during a steam sterilisation step at the end of their manufacturing process. This ammonium is released during the filtration of tap water. However, the assessment showed this does not pose a risk to human health.

References:

EFSA (2006). Transparency in risk assessment carried out by EFSA: guidance document on procedural aspects. Prepared by a working group consisting of members of the Scientific Committee and various EFSA Departments, European Food Safety Authority. EFSA Journal 2006; 353: 1-16.

EFSA (2007). Scientific advice by the Scientific Committee (Question No EFSA-Q-2007-060) adopted by written procedure on 3 August 2007. Proposal for a review system for EFSA's scientific activities. European Food Safety Authority. The EFSA Journal 2007. 526: 1-15.

EFSA (2017b). EFSA's policy on independence. European Food Safety Authority. http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf.

EFSA (2018b). EFSA rules on competing interest management. European Food Safety Authority. http://www.efsa.europa.eu/sites/default/files/corporate_publications/files/competing_interest_management_17.pdf.

EFSA 2012b

Agency Report Reference: *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. EFSA Panel on Contaminants in the Food Chain (CONTAM). European Food Safety Authority (EFSA). The EFSA Journal (2012) 10(5): 2703.**		
General Information	Date of data extraction	30/08/2021
	Authors	Panel members: Alexander J, Benford D, Boobis A R, Ceccatelli S, Cottrill B, Cravedi J-P, Di Domenico A, Doerge D, Dogliotti E, Edler L, Farmer P, Filipič M, Fink-Gremmels J, Fürst J, Guérin T, Knutsen H K, Machala M, Mutti A, Rose M, Schlatter J R, and van Leeuwen R.
	Publication date	6 June 2013
	Publication type	Agency review

Agency Report Reference: *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. EFSA Panel on Contaminants in the Food Chain (CONTAM). European Food Safety Authority (EFSA). The EFSA Journal (2012) 10(5): 2703.**]		
	Description	No guidance value derived in this document *per se* but contains relevant information potentially important to decision making by WQAC. The Scientific Committee on Food (SCF) evaluated ammonium hydroxide as a previous cargo in 1996 and considered it acceptable. This conclusion was since ammonium hydroxide is an authorised food additive (E527) with an ADI —'not specified'. In the 2003 SCF evaluation of acceptable previous cargoes, ammonium hydroxide was not further evaluated as it was already considered acceptable materials and occur naturally in foodstuffs. The SCF therefore considered that —no safety problems are likely to arise from their use in food, provided the contributions from food intake do not disturb the homeostatic mechanisms controlling the electrolyte balance of the body and based their ADI —'not specified'. JECFA has also evaluated ammonia solution (ammonium hydroxide) as a food additive (acidity regulator) and established an ADI —'not limited'.
	Genotoxic carcinogen?	The CONTAM Panel concluded that ammonium hydroxide is unlikely to be genotoxic. Forty male and forty female Swiss mice administered ammonium hydroxide as a 0.1 % solution in drinking water over their entire life span did not show any evidence of a carcinogenic effect (Toth 1972). The CONTAM Panel noted the limited validity of this study.
	Findings	JECFA has established an ADI —not limited and the SCF has established an ADI —not specified for ammonium hydroxide, which the CONTAM Panel considers appropriate. Ammonium hydroxide is not genotoxic or allergenic. It is only toxic when it is present at sufficient concentration that it changes the local OH- concentration. It will be diluted and buffered by the contents of the GI tract so that the levels that would occur following oral ingestion of fats or oils transported subsequent to ammonium hydroxide as a previous cargo do not give rise to any toxicological concern. Exposure to small amounts of ammonium hydroxide locally may cause irritation to the skin or eyes. However, the maximum potential levels of ammonium hydroxide arising in fats or oils following its transport as a previous cargo would be of no concern. There are no reactions of concern with edible fats and oils, nor are any anticipated impurities likely to be present at levels of toxicological relevance. Therefore, the CONTAM Panel concludes that ammonium hydroxide meets the criteria for acceptability as a previous cargo for edible fats and oils.

US EPA 2005

Agency Report Reference: *US EPA (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.*		
General Information	Date of data extraction	31/08/2021
	Authors	Not stated.
	Publication date	2005
	Literature search timeframe	Literature searches to identify studies relevant to the derivation of provisional toxicity values for ammonia were conducted for the period 1988 through September 18, 2002. Databases searched included: TOXLINE, MEDLINE, TSCATS, RTECS, CCRIS, DART, EMIC/EMICBACK, HSDB, GENETOX and CANCERLIT. Additional literature searches were conducted through May 2004 by NCEA-Cincinnati using TOXLINE, MEDLINE, Chemical and Biological Abstract databases and no relevant information was found.
	Publication type	Agency review
	Peer reviewed?	Not stated but according to title most likely the document has gone through a peer review process.
	Country of origin	USA
	Source of funding	US Government.
	Possible conflicts of interest	Not stated.
Health considerations	Guideline value type (e.g. oral TRV, drinking water guideline)	Normally Provisional Peer-Reviewed Toxicity Value (PPRTV), but no health-based guidance value was derived.
	Exposure timeframe	Not applicable – no oral PPRTV derived.
	Critical human health endpoint – oral exposure	The animal database includes one study (Gupta et al. 1979) that was reasonably well-documented, evaluated appropriate endpoints, and included a histopathological evaluation of potential target tissues. This study was not used to derive p-RfD values for two reasons. • First, the test article was ammonium sulfamate, which is hydrolysed under certain conditions to bisulfate ion and ammonia. It is not known whether hydrolysis occurred when the compound was administered to rats; thus, the actual dose of ammonia/ammonium ion administered to the test animals is uncertain. • Second, comparison of the data from this study to results from human studies suggests that health effects may occur in humans at lower concentrations of ammonium salts. Route-to-route extrapolation is not feasible for derivation of oral reference values because the toxicokinetic properties of ammonia differ significantly for the oral and inhalation pathways.
	Justification provided by agency for critical endpoint	No PPRTV for oral exposure has been derived for ammonia. Therefore, no justification has been used for derivation of PPRTV.

Agency Report Reference: *US EPA (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.*		
	Critical study(ies) underpinning point of departure	Not applicable (no guidance value derived).
	Species for critical study(ies)	Not applicable (no guidance value derived).
	Point of departure type (e.g. NOAEL, LOAEL, $BMDL_{10}$, etc)	Not applicable (no guidance value derived).
	Point of departure value (include units)	Not applicable (no guidance value derived).
	Uncertainty factor(s) & rationale	Not applicable (no guidance value derived).
	Guideline value (include units)	Because adequate data are lacking for oral exposure to ammonia, previous determinations of toxicity reference values have used organoleptic (taste) data to estimate acceptable ammonium levels in drinking water at **34-35 mg/L.** No health-based PPRTV was derived.
	Mode of action for critical health endpoint	Not applicable.
	Genotoxic carcinogen?	There is some indication that ammonia contributes to the development of cancer when co-administered with DEPC (via formation of urethane) or MNNG (via stimulation of cell proliferation in the gastric mucosa). Limited genotoxicity testing of ammonia has produced mixed results. Therefore, US EPA concluded that data for carcinogenicity of ammonia are inadequate for an assessment of human carcinogenic potential.
	Identified sensitive sub-populations	Not stated.
	Any non-health based considerations?	Not applicable.
Exposure considerations	Principal routes of exposure in general population	No statements about exposure to general population.
	Levels in drinking water supplies (include location)	Not stated.
	Any special considerations to exposure levels (e.g. higher in drought?)	No indication on contribution to drinking-water concentrations from this source.
	Typical exposure in general population (include units for intakes & location)	Not stated.
Risk Summary	Any risks to human health from drinking water identified in agency document?	No.
	Any emerging risks identified?	Not stated.

References:

Gupta, B.N., R.N. Kanna and K.K. Data. 1979. Toxicological studies of ammonium sulfamate in rat after repeated oral administration. Toxicology. 13: 45-49.

JECFA 2010

Agency Report Reference: ***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.***		
General Information	Date of data extraction	02/09/2021
	Authors	Harrison R A, Benford D J, Larsen J C, DiNovi M.
	Publication date	2010
	Publication type	Agency evaluation
	Description	No guidance value was derived in this document, however it contains relevant information on previous evaluations of ammonium salts.
	Findings	The Committee previously evaluated ammonium salts. At its twenty-sixth meeting, the Committee evaluated the safety of ammonium carbonate and ammonium hydrogen carbonate and allocated an ADI "**not specified",** while noting that although toxicological data for these ammonium salts were limited, extrapolation of results from studies with ammonium compounds (primarily ammonium chloride) and with sodium or potassium carbonate provided a basis for evaluation. At its twenty-ninth meeting, the Committee prepared a table giving the ADIs for a large number of combinations of cations and anions, including ammonium salts. No restriction was placed on the intake of ammonium from ammonium salts, provided that the contribution made to food is assessed and considered acceptable. Ammonia has also previously been evaluated by the International Programme on Chemical Safety (1986), which concluded that ammonia does not present a direct threat to humans except as a result of accidental exposure, particularly in industry. The World Health Organization (2006) has also previously assessed the safety of ammonia in its Guidelines for Drinking-water Quality and concluded that ammonia is not of direct importance for health in the concentrations expected in drinking-water; therefore, a health-based guideline was not derived.

WHO 2003

Agency Report Reference: ***WHO (2003). Ammonia in Drinking Water. Background document for development of WHO Guidelines for Drinking-water Quality. World Health Organisation.***		
General Information	Date of data extraction	30/08/2021
	Authors	2003 revision of background document published in 1996 undertaken by Fawell J. Lund U, Mintz B.
	Publication date	2003
	Literature search timeframe	Not stated.
	Publication type	Agency review

Agency Report Reference: *WHO (2003). Ammonia in Drinking Water. Background document for development of WHO Guidelines for Drinking-water Quality. World Health Organisation.*		
	Peer reviewed?	Not stated in the document.
	Country of origin	Not specified (World Health Organization - concerted effort).
	Source of funding	Not specified; likely WHO
	Possible conflicts of interest	Individual experts are invited to serve as members of the Drinking Water Quality Committee (DWQC). Members are selected primarily on the basis of excellence, independence, relevance of their expertise and willingness to support the work of the DWQC (WHO 2009). All members sign a Declaration of Interest as a pre-requisite to participation. Members refrain from participating in decision-making processes related to their particular area of conflicting interest (if applicable) (WHO 2009, JECFA 2017a).
Health considerations	Guideline value type (e.g. oral TRV, drinking water guideline)	Normally Drinking water guideline, but no health-based guideline was derived.
	Exposure timeframe	Not applicable.
	Critical human health endpoint	-
	Justification provided by agency for critical endpoint	If ammonia is administered in the form of its ammonium salts, the effects of the anion must also be taken into account. With ammonium chloride, the acidotic effects of the chloride ion seem to be of greater importance than those of the ammonium ion. At a dose of more than 33.7 mg of ammonium ion per kg body weight per day, ammonium chloride influences metabolism by shifting the acid-base equilibrium, disturbing the glucose tolerance, and reducing the tissue sensitivity to insulin. Ammonia is not of direct importance for health in the concentrations found in drinking-water. A health-based guideline has therefore not been derived.
	Guideline value (include units)	No health-based guideline value derived. Ammonia in drinking water at 0.2 mg/L may interfere with disinfection efficiency and may also represent taste and odour problems at higher concentrations.
	Mode of action for critical health endpoint	Ammonia has an essential role in acid–base regulation and the biosynthesis of purines, pyrimidines, and non-essential amino acids. It is formed in the body by the deamination of amino acids in the liver, as a metabolite in nerve excitation and muscular activity, and in the gastrointestinal tract by the enzymatic breakdown of food components with the assistance of bacterial flora.
	Genotoxic carcinogen?	No
	Identified sensitive sub-populations	-
	Any non-health based considerations?	Yes, odour and taste. The threshold odour concentration of ammonia in water is approximately **1.5 mg/L**. A taste threshold of **35 mg/L** has been proposed for the ammonium cation. Ammonia can compromise disinfection efficiency, result in nitrite formation in distribution systems, cause the failure of filters for the removal of manganese and cause taste and odour problems.

Agency Report Reference: *WHO (2003). Ammonia in Drinking Water. Background document for development of WHO Guidelines for Drinking-water Quality. World Health Organisation.*		
Exposure considerations	Principal routes of exposure in general population	Ammonium is a natural component of many foods. Minor amounts of ammonium compounds (<0.001–3.2%) are also added to foods as acid regulators, stabilizers, flavouring substances, and fermentation aids. The estimated daily ammonia intake through food and drinking-water is 18 mg, by inhalation less than 1 mg, and through cigarette smoking (20 cigarettes per day) also less than 1 mg. In contrast, 4000 mg of ammonia per day are produced endogenously in the human intestine.
	Levels in drinking water supplies (include location)	Natural levels in groundwaters are usually below 0.2 mg /L.
	Any special considerations to exposure levels (e.g. higher in drought?)	Intensive rearing of farm animals can give rise to much higher levels in surface water. Ammonia contamination can also arise from cement mortar pipe linings. Ammonia in water is an indicator of possible bacterial, sewage and animal waste pollution.
	Typical exposure in general population (include units for intakes & location)	The estimated daily ammonia intake: • Food and drinking-water: 18 mg • Air: 20 µg /m^3 in urban areas, up to 300 µg/m^3 on farms. Inhalation less than 1 mg, and through cigarette smoking (20 cigarettes per day) also less than 1 mg. • 4000 mg of ammonia per day are produced endogenously in the human intestine.
Risk Summary	Any risks to human health from drinking water identified in agency document?	No.
	Any emerging risks identified?	-

References:

JECFA (2017a). Joint FAO/WHO Expert Committee on Food Additives (JECFA) - Working Procedures. Joint FAO/WHO Expert Committee on Food Additives. Geneva, February 2017. https://www.who.int/foodsafety/chem/jecfa/JECFA-WP-REV2017.pdf?ua=1.

WHO (2009). WHO Guidelines for Drinking-water quality: Policies and procedures used in updating the WHO Guidelines for Drinking-water Quality. World Health Organization.

Exposure-Related Information for Ammonia

Tas Water 2016a, 2016b, 2016c, 2017a, 2017b, 2017c, 2018a, 2018c

Agency Report Reference: *See bibliography*		
General Information	Date of data extraction	03/09/2021
	Authors	Jes Temby, Luc Richard, Frances Smith, Ailsa Sypkes, Michael Brewster
	Publication date	2016-2018

Agency Report Reference: *See bibliography*		
	Publication type	Drinking Water Corporation report.
	Description	No guidance value derived in this document *per se* but contains relevant information on ammonia exposure levels in Australian drinking water supply system (may or may not be relevant for context).
	Findings[1]	Australian Drinking Water Guideline (aesthetic): 0.5 mg/L Mean: 0.05 mg/L Range: <0.005 – 0.373 mg/L
[1]Summary data for all drinking water quality zones in the supply system		

Chapman et al. 2008

Agency Report Reference: WRA *(2008). Chapman H, Cartwright T, Huston R, and O'Toole (2008). Water quality and health risks from urban rainwater tanks. Research Report 42. Cooperative Research Centre for Water Quality and Treatment. CRC for Water Quality and Treatment 2008.*		
General Information	Date of data extraction	02/09/2021
	Authors	Heather Chapman, Tony Cartwright, 2, Rob Huston, and Joanne O'Toole
	Publication date	2008
	Publication type	Research report No 42.
	Description	No guidance value derived in this document *per se* but contains relevant information on ammonia exposure levels in Australian drinking water supply system (may or may not be relevant for context).
	Findings	Total detected: 37 Total tested: 44 Mean: 0.074 mg/L Minimum: 0.002 mg/L Maximum: 0.270 mg/L ADWG Limit: 0.5 mg/L

APPENDIX C

Existing guideline/guidance assessment tables

Criteria for assessing existing guidance or guidelines

No health-based guidelines for ammonia were found in the literature consulted. Nevertheless, there was agreement between the various jurisdictions that a health-based guidance/guideline value for ammonia is not applicable. Thus, these reviews have still been assessed against the administrative and technical criteria for assessing existing guidance.

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'

ATSDR 2004

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

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?	Y	
	Are the administrative processes documented and publicly available?	Y	
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?	Y	Yes, proposed minimal risk levels (MRLs) are reviewed by the Health Effects/MRL Workgroup within the Division of Toxicology and Human Health Sciences; an expert panel of external peer reviewers; the agency wide MRL Workgroup, with participation from other federal agencies, including EPA; and are submitted for public comment. Regarding potential conflicts of interest, peer reviewers are screened for potential conflicts of interest.
	Are funding sources declared?	Y	Although funding sources are not declared in the tox profile, the profiles are produced by congressional mandate, indicating they are likely government-funded.
	Was there public consultation on this work? If so, provide details.	Y	Yes, a draft for public comment was released in September 2002.
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?	Y	Independent peer review panel provided comments. Scientists from the ATSDR have reviewed the peer reviewers' comments and determined which comments to include in the profile, with a brief explanation of the rationale for their exclusion; this exists as part of the administrative record.
	Was the guidance/advice developed or updated recently? Provide details.	NA	
	Evidence review parameters		

Criteria		Y/N/?/NA	Notes
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?	Y	A list of databases reviewed and a list of unpublished documents cited are included in the administrative record.
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?	?	Not stated
	Does the organisation use or undertake systematic literature review methods to identify and select data underpinning the advice? Are the methods used documented clearly?	Y (1/2)	Literature review methods are not provided in the tox profile but do exist as part of the administrative record for the compound. It is unclear if systematic review methods were used, however. Thus half a mark is allocated.
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?	Y	Unpublished documents cited are included in the administrative record.
	Are inclusion/exclusion criteria used to select or exclude certain studies from the review? If so, is justification provided?	N	Not stated in the profile.
	Does the organisation use or adopt review findings or risk assessments from other organisations? What process was used to critically assess these external findings?	NA	Review undertaken was done *de novo* by ATSDR; the agency does not appear to have adopted findings from another agency.
	Can grey literature such as government reports and policy documents be included?	Y	
	Is there documentation and justification on the selection of a toxicological endpoint for use as point of departure for health-based guideline derivation?	Y	Yes, rationale is provided for not selecting a critical health endpoint for ammonia.
	Evidence search		
	Are databases and other sources of evidence specified?	Y	A list of databases reviewed and a list of unpublished documents cited are included in the administrative record.
	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)?	?	Unknown, as the administrative record could not be found to check this.
	Is it specified what date range the literature search covers? Is there a justification?	N	Literature search methods are included as part of the administrative record, however the administrative record could not be found to check this.
	Are search terms and/or search strings specified?	N	Literature search methods are included as part of the administrative record, however the administrative record could not be found to check this.
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?	NA	Literature search methods are included as part of the administrative record, however the administrative record could not be found to check this.
	Critical appraisal methods and tools		

Criteria		Y/N/?/NA	Notes
	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?	N	Risk of bias does not appear to have been taken into consideration in a formal manner in this profile.
	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.	Y	ATSDR summarises health endpoint information in the form of figures and tables organised by route of exposure. This allows the reader to quickly assimilate the most sensitive health effects associated with exposure to the substance.
	Does the organisation assess the overall certainty of the evidence and reach recommendations? If so, provide details.	Y (1/2)	Although this has not been done in a formal manner as would be expected in a systematic literature review, ATSDR does comment on certainty of information which has an influence on the overall uncertainty factors applied for MRL derivation.
	Derivation of health-based guideline values		
	Is there justification for the choice of uncertainty and safety factors?	Y	No oral MRL derived as it was not considered necessary, but justification is provided.
	Are the parameter value assumptions documented and explained?	Y	
	Are the mathematical workings/algorithms clearly documented and explained?	NA	No oral MRL derived as it was not considered necessary, but justification is provided.
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?	NA	No, non-health related matters do not appear to be considered in guideline development. Recorded as 'not applicable'.
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?	N	Guidance documentation is not cited.
	What processes are used when expert judgement is required and applied? Is the process documented and published?	Y	ATSDR only derives MRLs if quantitative or qualitative information is available for all potential systemic, neurological and developmental effects. If insufficient data are judged to be available, an MRL is not derived (ATSDR 2018).
	Is dose response modelling (e.g. BMDL) routinely used?	Y	Although routinely used by ATSDR where data allow, this was not used for ammonia since no oral MRL was derived.
	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?	Y	ATSDR only derives MRLs for non-cancer health endpoints.
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	NA	

Criteria	Y/N/?/NA	Notes
Summary: Total # of 'Must-Have' criteria met (or not applicable): 14.5/20 = 73 % Total # of 'Should-Have' criteria met (or not applicable): 7.5/10 = 75% Total # of 'May-Have' criteria met (or not applicable): 2/2 = 100%		
References: ATSDR (2018). DRAFT guidance on the preparation of toxicological profiles. Agency for Toxic Substances and Disease Registry. April 2018. https://www.atsdr.cdc.gov/toxprofiles/guidance/profile_development_guidance.pdf		

EFSA 2012a, b

Agency Report Reference: ***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. EFSA Panel on Contaminants in the Food Chain (CONTAM). European Food Safety Authority (EFSA). The EFSA Journal (2012) 10(5): 2703.

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?	Y	
	Are the administrative processes documented and publicly available?	Y	
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?	?	Not stated.
	Are funding sources declared?	Y	Although funding sources are not declared in the report, EFSA is funded by the European Union that operates independently of the European legislative and executive institutions and EU Member states.
	Was there public consultation on this work? If so, provide details.	N	Done on a case-by-case basis; does not appear to have been done for this piece of work.

Criteria		Y/N/?/NA	Notes
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?	Y	Yes, stated in EFSA (2012a) document. Not stated in EFSA (2012b) document, but the latter only provides supporting information and was not used as a primary source of making conclusions.
	Was the guidance/advice developed or updated recently? Provide details.	NA	
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?	Y (1/2)	Yes, for specific aspects of the work. In EFSA (2012b), the evaluation of substances as acceptable previous cargoes was based on available studies/ information from literature searches carried out up to the time of the evaluation on public databases, e.g. PubMed, IUCLID, ECHA, evaluations made by national and international bodies (WHO and OECD) and on information requested from FOSFA.
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?	?	Not stated.
	Does the organisation use or undertake systematic literature review methods to identify and select data underpinning the advice? Are the methods used documented clearly?	?	Yes, the organisation conducts these for specific purposes. In the case of ammonia, it is unclear whether systematic processes have been followed.
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?	Y	Yes, all unpublished studies appear to be described appropriately.
	Are inclusion/exclusion criteria used to select or exclude certain studies from the review? If so, is justification provided?	N	
	Does the organisation use or adopt review findings or risk assessments from other organisations? What process was used to critically assess these external findings?	Y	Yes, the organisation does adopt review findings from other related national and international bodies (WHO and OECD) but does not critically assess the information.
	Can grey literature such as government reports and policy documents be included?	Y	
	Is there documentation and justification on the selection of a toxicological endpoint for use as point of departure for health-based guideline derivation?	NA	No health-based guideline values was derived in these documents, however justification for this is provided.
	Evidence search		
	Are databases and other sources of evidence specified?	Y (1/2)	Yes, for specific aspects of the work. In EFSA (2012b), the evaluation of substances as acceptable previous cargoes was based on available studies/ information from literature searches carried out up to the time of the evaluation on public databases, e.g. PubMed, IUCLID, ECHA, evaluations made by national and international bodies (WHO and OECD) and on information requested from FOSFA.

Criteria		Y/N/?/NA	Notes
	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)?	Y (1/2)	See above comment.
	Is it specified what date range the literature search covers? Is there a justification?	N	
	Are search terms and/or search strings specified?	N	
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?	NA	Exclusion criteria are not provided as details of literature searches are lacking in these documents.
	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?	N	No information given regarding whether risk of bias assessment was undertaken for individual studies. However, the shortcomings of some studies (where identified by the authors) have been provided in the text.
	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.	?	Not clear from the information in these documents.
	Does the organisation assess the overall certainty of the evidence and reach recommendations? If so, provide details.	N	Yes, typically done in newer tox profiles where a systematic review was undertaken. However, this has not been done for the Cd tox profile.
	Derivation of health-based guideline values		
	Is there justification for the choice of uncertainty and safety factors?	Y	No health-based guideline value was derived as it was not considered necessary, but justification is provided.
	Are the parameter value assumptions documented and explained?	Y	
	Are the mathematical workings/algorithms clearly documented and explained?	NA	No health-based guideline value was derived as it was not considered necessary, but justification is provided.
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?	NA	No, non-health related matters do not appear to be considered in guideline development. Recorded as 'not applicable'.
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?	N	Guidance documentation is not cited.
	What processes are used when expert judgement is required and applied? Is the process documented and published?	Y	According to EFSA (2012b), the CONTAM Panel of experts are in charge of expert judgement. Detailed processes followed are not necessarily specified.
	Is dose response modelling (e.g. BMDL) routinely used?	NA	Unclear from the documents reviewed

Criteria		Y/N/?/NA	Notes
	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?	NA	Processes are likely similar to JECFA processes. Where a contaminant is found to be a genotoxic carcinogen, for which JECFA considers it inappropriate to establish a health-based guidance value, JECFA will usually calculate a margin of exposure (MOE) between the critical point of departure and the dietary exposure for a high or average consumer to provide guidance for risk managers. Alternatively a quantitative assessment of the risk (e.g. additional cancer risk) at defined levels of exposure is undertaken (JECFA 2017a). However, these processes were not applied for ammonia because it was not considered a genotoxic carcinogen.
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	NA	

Summary:

Total # of 'Must-Have' criteria met (or not applicable): 12.5/20 = 63 %
Total # of 'Should-Have' criteria met (or not applicable): 5/10 = 50%
Total # of 'May-Have' criteria met (or not applicable): 2/2 = 100%

References:

EFSA (2007). Scientific advice by the Scientific Committee (Question No EFSA-Q-2007-060) adopted by written procedure on 3 August 2007. Proposal for a review system for EFSA's scientific activities. European Food Safety Authority. The EFSA Journal 2007. 526: 1-15.

JECFA (2017a). Guidance document for WHO monographers and reviewers evaluating contaminants in food and feed. Joint FAO/WHO Expert Committee on Food Additives (JECFA). January 2017. Version 1.0. http://apps.who.int/iris/bitstream/handle/10665/254630/9789241512008-eng.pdf;jsessionid=8AB23D3A0003A624A67704756BB3A938?sequence=1

US EPA 2005

Agency Report Reference: Agency Report Reference: ***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.***

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?	Y	Yes (US EPA 2021). PPRTVs follow similar guidance documentation to that used to develop RfDs and RfCs in the IRIS programme.
	Are the administrative processes documented and publicly available?	Y	US EPA (2021).
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?	Y (1/2)	All PPRTV assessments receive internal review by EPA scientists and external peer review by independent scientific experts. However, it is not clear from the documentation consulted how potential conflicts of interest are managed.
	Are funding sources declared?	Y	Although funding sources are not declared, the documents are likely US government-funded.
	Was there public consultation on this work? If so, provide details.	N	
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?	Y	All PPRTV assessments receive internal review by EPA scientists and external peer review by three independently selected scientific experts. It is unclear from documents whether outcomes of peer review are published.
	Was the guidance/advice developed or updated recently? Provide details.	NA	
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?	N	Not specifically provided in the ammonia review.
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?	?	Unclear from documentation consulted.
	Does the organisation use or undertake systematic literature review methods to identify and select data underpinning the advice? Are the methods used documented clearly?	N	Systematic literature reviews have been a relatively recent introduction after the National Research Council (NRC) offered suggestions for improvements to the IRIS development process in 2011. However the process does not appear to be followed for PPRTV derivation.
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?	NA	Unclear from documentation consulted.

Criteria		Y/N/?/NA	Notes
	Are inclusion/exclusion criteria used to select or exclude certain studies from the review? If so, is justification provided?	N	
	Does the organisation use or adopt review findings or risk assessments from other organisations? What process was used to critically assess these external findings?	Y	If an IRIS assessment is available, PPRTV documentation adopts the results of that assessment, as it is the same broader agency that produces these assessments but they undergo a higher degree of review and scrutiny by interrelated agencies.
	Can grey literature such as government reports and policy documents be included?	Y	
	Is there documentation and justification on the selection of a toxicological endpoint for use as point of departure for health-based guideline derivation?	Y	
	Evidence search		
	Are databases and other sources of evidence specified?	Y	Literature searches to identify studies relevant to the derivation of provisional toxicity values for ammonia were conducted for the period 1988 through September 18, 2002. Databases searched included: TOXLINE, MEDLINE, TSCATS, RTECS, CCRIS, DART, EMIC/EMICBACK, HSDB, GENETOX and CANCERLIT. Additional literature searches were conducted through May 2004 by NCEA-Cincinnati using TOXLINE, MEDLINE, Chemical and Biological Abstract databases and no relevant information was found.
	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)?	Y	Yes.
	Is it specified what date range the literature search covers? Is there a justification?	Y	See above comments.
	Are search terms and/or search strings specified?	N	Search strings not specified.
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?	NA	Not stated.
	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?	?	Unclear from documentation whether risk of bias was taken into consideration for the ammonia PPRTV review.
	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.	?	Unclear whether such a process was followed for the 2005 ammonia PPRTV review.

Criteria		Y/N/?/NA	Notes
	Does the organisation assess the overall certainty of the evidence and reach recommendations? If so, provide details.	Y (1/2)	Does not appear to have been done formally for the 2005 ammonia PPRTV reviews. However the agency considers the uncertainty in the available information when deciding whether it is appropriate to recommend a PPRTV value and deciding which uncertainty factors to use.
	Derivation of health-based guideline values		
	Is there justification for the choice of uncertainty and safety factors?	Y	Typically yes, however no guidance/guideline value was recommended. Justification for this was provided.
	Are the parameter value assumptions documented and explained?	Y	See above comment.
	Are the mathematical workings/algorithms clearly documented and explained?	NA	Not applicable since no guidance/guideline value was recommended for ammonia.
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?	NA	No, non-health related matters do not appear to be considered in guideline development. Recorded as 'not applicable'.
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?	Y (1/2)	It is noted the guidance documentation is generic health risk assessment guidance and post-dates the date of the ammonia reviews.
	What processes are used when expert judgement is required and applied? Is the process documented and published?	N	Unclear from documentation consulted.
	Is dose response modelling (e.g. BMDL) routinely used?	Y	Yes, typically used by US EPA. But not used for ammonia since no guidance/ guideline value was derived.
	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?	NA	In the absence of sufficiently, scientifically justifiable mode of action information, US EPA generally takes the default position that animal tumour findings are judged to be relevant to humans and cancer risks are assumed to conform with low dose linearity. It is noted this is a divergence from other agencies, and Australia, where a genotoxic MOA drives use of linear dose response modelling. Nevertheless, this does not affect the assessment for ammonia, as data were insufficient for quantitative assessment via low-dose linearity assumptions.
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	NA	

Summary:
Total # of 'Must-Have' criteria met (or not applicable): 14.5/20 = 73%
Total # of 'Should-Have' criteria met (or not applicable): 5/10 = 50%
Total # of 'May-Have' criteria met (or not applicable): 2/2 = 100%

Criteria	Y/N/?/NA	Notes
References: US EPA (2021). Basic information about provisional peer-reviewed toxicity values (PPRTVs). Last updated August 19, 2021. [Accessed 12/09/2021]. https://www.epa.gov/pprtv/basic-information-about-provisional-peer-reviewed-toxicity-values-pprtvs#tools		

WHO 2003

Agency Report Reference:

Agency Report Reference: ***WHO (2003). Ammonia in Drinking Water. Background document for development of WHO Guidelines for Drinking-water Quality. World Health Organisation.***

	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?	Y	
	Are the administrative processes documented and publicly available?	Y	
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?	Y	
	Are funding sources declared?	Y	Although funding sources are not declared in the document, it is likely funded by the WHO.
	Was there public consultation on this work? If so, provide details.	Y	The front matter of the text indicates the draft documents were released to the public domain for comment and submitted for final evaluation by expert meetings.
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?	Y	
	Was the guidance/advice developed or updated recently? Provide details.	NA	
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?	Y	

Criteria		Y/N/?/NA	Notes
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?	?	Not specified.
	Does the organisation use or undertake systematic literature review methods to identify and select data underpinning the advice? Are the methods used documented clearly?	N	Unclear in this document.
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?	Y	Unpublished proprietary data are referenced as such in reference lists, and where they form pivotal information they are described in detail.
	Are inclusion/exclusion criteria used to select or exclude certain studies from the review? If so, is justification provided?	N	
	Does the organisation use or adopt review findings or risk assessments from other organisations? What process was used to critically assess these external findings?	Y	WHO use JECFA evaluations in a number of instances as the basis of the guidance values used to derive the drinking water guideline. JECFA is a sub-committee of the WHO (and FAO) and follows similar procedures for their reviews.
	Can grey literature such as government reports and policy documents be included?	Y	
	Is there documentation and justification on the selection of a toxicological endpoint for use as point of departure for health-based guideline derivation?	Y	
	Evidence search		
	Are databases and other sources of evidence specified?	N	Although the bibliography provides references for all literature consulted, the databases consulted for the literature review are not listed in the agency review.
	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)?	NA	Unable to be ascertained from the information in the document.
	Is it specified what date range the literature search covers? Is there a justification?	N	Literature search details are not specified.
	Are search terms and/or search strings specified?	N	Literature search details are not specified.
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?	NA	Literature search details are not specified.
	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?	N	No information given regarding whether risk of bias assessment was undertaken for individual studies. However, the shortcomings of some studies (where identified by the authors) have been provided in the text.

Criteria		Y/N/?/NA	Notes
	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.	N	Unclear if this was done for ammonia.
	Does the organisation assess the overall certainty of the evidence and reach recommendations? If so, provide details.	N	Uncertainties/certainties in the available information are not specifically discussed in this document.
	Derivation of health-based guideline values		
	Is there justification for the choice of uncertainty and safety factors?	Y	Typically yes, but no guidance/guideline value was derived. Justification for this decision was provided.
	Are the parameter value assumptions documented and explained?	Y	
	Are the mathematical workings/algorithms clearly documented and explained?	NA	Typically yes, but no guidance/guideline value was derived. Justification for this decision was provided.
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?	Y	Yes, for ammonia, non-health related matters (taste and odour threshold) have been considered in guideline development.
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?	Y	Guidance documentation is not cited. However, guidance document does exist (FAO/WHO 2009, WHO 2005, 2007).
	What processes are used when expert judgement is required and applied? Is the process documented and published?	N	Unclear from documentation consulted.
	Is dose response modelling (e.g. BMDL) routinely used?	Y	Yes, where data permit and where a BMDL would provide greater confidence in the point of departure (WHO 2009). Not done for ammonia.
	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?	NA	For genotoxic carcinogens, the DWG represents an excess lifetime cancer risk of $1x10^{-5}$ for people drinking water containing the chemical at the DWG for 70 yrs (WHO 2009). Compounds shown to be a carcinogen are evaluated on a case-by-case basis, where evidence of genotoxicity & human relevance is considered to determine correct approach for risk assessment (WHO 2009). Not done for ammonia as not identified to be an oral genotoxic carcinogen.
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	NA	

Summary:
Total # of 'Must-Have' criteria met (or not applicable): 14/20 = 70%
Total # of 'Should-Have' criteria met (or not applicable): 6/10 = 60%
Total # of 'May-Have' criteria met (or not applicable): 2/2 = 100%

Criteria	Y/N/?/NA	Notes
References: FAO/WHO (2009). Environmental Health Criteria 240: Principles and methods for the risk assessment of chemicals in food. Chapter 5: Dose-response assessment and derivation of health-based guidance values. Geneva: A joint publication of the Food and Agriculture Organization of the United Nations and the World Health Organization. http://www.inchem.org/documents/ehc/ehc/ehc240_chapter5.pdf. JECFA (2017a). Guidance document for WHO monographers and reviewers evaluating contaminants in food and feed. Joint FAO/WHO Expert Committee on Food Additives (JECFA). January 2017. Version 1.0. http://apps.who.int/iris/bitstream/handle/10665/254630/9789241512008-eng.pdf;jsessionid=8AB23D3A0003A624A67704756BB3A938?sequence=1 JECFA (2017b). Guidance to JECFA Experts on Systematic Literature Searches. Prepared by WHO JECFA (Joint FAO/WHO Expert Committee on Food Additives) Secretariat. January 2017. https://www.who.int/foodsafety/chem/jecfa/Litertature_Search.pdf?ua=1. WHO (2005). Harmonization Project Document No. 2: Chemical-specific adjustment factors for interspecies differences and human variability: guidance document for use of data in dose/concentration response assessment. World Health Organization (IPCS). http://www.inchem.org/documents/harmproj/harmproj/harmproj2.pdf. WHO (2007). Harmonization Project Document No. 4. Part 1: IPCS framework for analysing the relevance of a cancer mode of action for humans and case-studies Part 2: IPCS framework for analysing the relevance of a non-cancer mode of action for humans." World Health Organization (IPCS). http://www.who.int/ipcs/methods/harmonization/areas/cancer_mode.pdf?ua=1.		

JECFA 2010

Agency Report Reference: ***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.***

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?	Y	
	Are the administrative processes documented and publicly available?	Y	

Criteria		Y/N/?/NA	Notes
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?	Y	Yes, Provisional tolerable Weekly Intake levels (PTWIs) are reviewed by the Health Effects/PTWI Workgroup within the JECFA Committee; an expert panel of external peer reviewers; the agency wide PTWI Workgroup, with participation from JECFA/FAO agencies. Potential conflicts of interest were disclosed and managed appropriately.
	Are funding sources declared?	Y	Although funding sources are not declared in the document, it is likely funded by the WHO/FAO.
	Was there public consultation on this work? If so, provide details.	N	There is no evidence that the document was released for public comment.
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?	Y	Yes, document is prepared by 1-2 panel members, other members act as peer reviewers.
	Was the guidance/advice developed or updated recently? Provide details.	NA	
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?	Y (1/2)	Not all of these are specifically provided, however the scope of the review is stated.
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?	N	Not specified.
	Does the organisation use or undertake systematic literature review methods to identify and select data underpinning the advice? Are the methods used documented clearly?	N	JECFA (2017b) provides written, publicly-available guidance to its experts on how to conduct systematic literature searches. However, it is unclear if this methodology was followed for the 2010 document.
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?	Y	Unpublished proprietary data are referenced as such in reference lists, and where they form pivotal information they are described in detail.
	Are inclusion/exclusion criteria used to select or exclude certain studies from the review? If so, is justification provided?	N	Literature search details not 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?	NA	
	Can grey literature such as government reports and policy documents be included?	Y	
	Is there documentation and justification on the selection of a toxicological endpoint for use as point of departure for health-based guideline derivation?	Y	
	Evidence search		

Criteria		Y/N/?/NA	Notes
	Are databases and other sources of evidence specified?	N	Although the bibliography provides references for all literature consulted, the databases consulted for the literature review are not listed in the agency review.
	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)?	NA	Unable to be ascertained from the information in the document.
	Is it specified what date range the literature search covers? Is there a justification?	N	Literature search details are not specified, however the dates of publications in the bibliography suggest a literature search cutoff date of 2008.
	Are search terms and/or search strings specified?	N	Literature search details are not specified.
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?	NA	Literature search details are not specified.
	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?	N	No information given regarding whether risk of bias assessment was undertaken for individual studies. However, the shortcomings of some studies (where identified by the authors) have been provided in the text.
	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.	N	Unclear from document reviewed.
	Does the organisation assess the overall certainty of the evidence and reach recommendations? If so, provide details.	N	
	Derivation of health-based guideline values		
	Is there justification for the choice of uncertainty and safety factors?	Y	Typically yes, however no guidance/guideline value was derived for ammonia. Justification for this is provided.
	Are the parameter value assumptions documented and explained?	Y	
	Are the mathematical workings/algorithms clearly documented and explained?	NA	Typically yes, however no guidance/guideline value was derived for ammonia. Justification for this is provided.
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?	NA	No, non-health related matters do not appear to be considered in guideline development. Recorded as 'not applicable'.
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?	Y	Guidance documentation is not cited. However, guidance document does exist (FAO/WHO 2009, WHO 2005, 2007).
	What processes are used when expert judgement is required and applied? Is the process documented and published?	N	Unclear from documentation consulted.

Criteria		Y/N/?/NA	Notes
	Is dose response modelling (e.g. BMDL) routinely used?	Y	Yes, where data permit and where a BMDL would provide greater confidence in the point of departure (WHO 2009).
	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?	NA	Where a contaminant is found to be a genotoxic carcinogen, for which JECFA considers it inappropriate to establish a health-based guidance value, JECFA will usually calculate a margin of exposure (MOE) between the critical point of departure and the dietary exposure for a high or average consumer to provide guidance for risk managers. Alternatively a quantitative assessment of the risk (e.g. additional cancer risk) at defined levels of exposure is undertaken (JECFA 2017a). However, these processes were not applied for Cd because it was not considered a genotoxic carcinogen.
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	NA	

Summary:

Total # of 'Must-Have' criteria met (or not applicable): 13.5/20 = 68%
Total # of 'Should-Have' criteria met (or not applicable): 5/10 = 50%
Total # of 'May-Have' criteria met (or not applicable): 2/2 = 100%

References:

FAO/WHO (2009). Environmental Health Criteria 240: Principles and methods for the risk assessment of chemicals in food. Chapter 5: Dose-response assessment and derivation of health-based guidance values. Geneva: A joint publication of the Food and Agriculture Organization of the United Nations and the World Health Organization. http://www.inchem.org/documents/ehc/ehc/ehc240_chapter5.pdf.

JECFA (2017a). Guidance document for WHO monographers and reviewers evaluating contaminants in food and feed. Joint FAO/WHO Expert Committee on Food Additives (JECFA). January 2017. Version 1.0. http://apps.who.int/iris/bitstream/handle/10665/254630/9789241512008-eng.pdf;jsessionid=8AB23D3A0003A624A67704756BB3A938?sequence=1

JECFA (2017b). Guidance to JECFA Experts on Systematic Literature Searches. Prepared by WHO JECFA (Joint FAO/WHO Expert Committee on Food Additives) Secretariat. January 2017. https://www.who.int/foodsafety/chem/jecfa/Litertature_Search.pdf?ua=1.

WHO (2005). Harmonization Project Document No. 2: Chemical-specific adjustment factors for interspecies differences and human variability: guidance document for use of data in dose/concentration response assessment. World Health Organization (IPCS). http://www.inchem.org/documents/harmproj/harmproj/harmproj2.pdf.

WHO (2007). Harmonization Project Document No. 4. Part 1: IPCS framework for analysing the relevance of a cancer mode of action for humans and case-studies Part 2: IPCS framework for analysing the relevance of a non-cancer mode of action for humans." World Health Organization (IPCS). http://www.who.int/ipcs/methods/harmonization/areas/cancer_mode.pdf?ua=1.

APPENDIX D

Data extraction tables – Supporting Information in Factsheet

Supporting Information in Ammonia Factsheet

ATSDR 2004a

Agency Report Reference: *ATSDR (2004a). Toxicological Profile for Ammonia. US Department of Health and Human Services, Agency for Toxic Substances and Disease Registry. September 2004.*		
General Description	Uses	Ammonia is used in smelling salts, household cleaners, and window cleaning products. 80% of all manufactured ammonia is used as fertiliser. A third of this is applied directly to soil as pure ammonia. The rest is used to make other fertilisers that contain ammonium compounds, usually ammonium salts. These fertilisers are used to provide nitrogen to plants. Ammonia is also used to manufacture synthetic fibres, plastics, and explosives. Many cleaning products also contain ammonia in the form of ammonium ions.
	Sources in drinking water	No specified.
	Other	-
Treatment of drinking water	Treatment technology	-
	Effectiveness	-
	Any special conditions?	-
	Other	-
Measurement	Analytical method	Drinking water: • Sample mixed with borate buffer (Method 1689, on selective probe) (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).
	Limit of determination/ Limit of Reporting (LOR)	See above
	Other	-
Additional information	Any additional non-health related information considered important?	-

EFSA 2012a

Agency Report Reference: 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.*		
General Description	Uses	Ammonia is a widely used industrial chemical, mostly in fertilisers, but also in various other applications such as plastics, cleaning products, explosives, animal feed and food additives.
	Sources in drinking water	Ammonium in water comes normally from natural, industrial, agricultural sources and from disinfection with chloramine. Elevated ammonium levels in drinking water often indicate bacterial, sewage and waste pollution. There are indications that ammonium can be released from water filters but in very low concentrations.
	Other	Ammonium is known to be formed in the water filter cartridges during a steam sterilisation step at the end of the manufacturing process of the cartridges. The sterilisation step is needed to prevent bacterial growth in the water filter. During the sterilisation at high temperatures, nitrogen compounds in the filter packing material react to form ammonium, which is then bound to the ion exchange resin. This ammonium is released when the ion exchange process with the anions present in the influent water takes place during the filtration of tap water.
Treatment of drinking water	Treatment technology	-
	Effectiveness	-
	Any special conditions?	-
	Other	-
Measurement	Analytical method	Not stated.
	Limit of determination/ Limit of Reporting (LOR)	Not stated.
	Other	-
Additional information	Any additional non-health related information considered important?	-

WHO 2003

Agency Report Reference: WHO (2003). Ammonia in Drinking Water. Background document for development of WHO Guidelines for Drinking-water Quality. World Health Organisation.		
General Description	Uses	Ammonia is used in fertilisers and animal feed production and in the manufacture of fibres, plastics, explosives, paper, and rubber. It is used as a coolant, in metal processing, and as a starting product for many nitrogen-containing compounds. Ammonia and ammonium salts are used in cleansing agents and as food additives and ammonium chloride is used as a diuretic.
	Sources in drinking water	Ammonia in the environment originates from metabolic, agricultural and industrial processes and from disinfection with chloramine.

Agency Report Reference: WHO (2003). Ammonia in Drinking Water. Background document for development of WHO Guidelines for Drinking-water Quality. World Health Organisation.		
	Other	-
Treatment of drinking water	Treatment technology	-
	Effectiveness	-
	Any special conditions?	-
	Other	-
Measurement	Analytical method	Ammonia and ammonium cation at concentrations between 0.025 and 3 mg/litre can be determined by the indophenol reaction. An ammonia-selective electrode can also be used, as can titrimetry which is less sensitive.
	Limit of determination/ Limit of Reporting (LOR)	Drinking water LOD: 0.025 - 3 mg/L indophenol reaction
	Other	-
Additional information	Any additional non-health related information considered important?	The presence of ammonia at higher than geogenic levels is an important indicator of faecal pollution. Taste and odour problems as well as decreased disinfection efficiency are to be expected if drinking-water containing more than 0.2 mg of ammonia per litre is chlorinated as up to 68% of the chlorine may react with the ammonia and become unavailable for disinfection. Cement mortar used for coating the insides of water pipes may release considerable amounts of ammonia into drinking-water and compromise disinfection with chlorine.

Tas Water 2016a, 2016b, 2016c, 2017a, 2017b, 2017c, 2018a, 2018c

Agency Report Reference: ***See bibliography***		
General Description	Sources in drinking water	-
	Other	-
Treatment of drinking water	Treatment technology	Not stated.
	Effectiveness	-
	Any special conditions?	-
	Other	-
Measurement	Analytical method	Not stated.
	Limit of determination/ Limit of Reporting (LOR)	LOR: <0.005 mg-N/L
	Other	-
Additional information	Any additional non-health related information considered important?	-

Chapman et al. 2008

Agency Report Reference: ***Chapman H, Cartwright T, Huston R, and O'Toole (2008). Water quality and health risks from urban rainwater tanks. Research Report 42. Cooperative Research Centre for Water Quality and Treatment. CRC for Water Quality and Treatment 2008.***		
General Description	Sources in drinking water	Ammonia present in rainwater tanks is possibly from degradation of organic matter in the tank.
	Other	-
Treatment of drinking water	Treatment technology	-
	Effectiveness	-
	Any special conditions?	-
	Other	-
Measurement	Analytical method	Not stated.
	Limit of determination/ Limit of Reporting (LOR)	Not stated.
	Other	-
Additional information	Any additional non-health related information considered important?	-

WCWA 2014

WCWA (2014). Drinking Water Quality. Annual Report 2013/14. Water Corporation Western Australia.		
General Description	Sources in drinking water	-
	Other	The Goldfields and Agricultural Water Supply (GAWS) is one of the most extensive water supply systems in the world. For this reason, chloramination (using monochloramine - a combination of chlorine and ammonia) is used as the preferred form of disinfection as it persists in the water much longer than chlorine. The monochloramine, however, decays over time releasing free ammonia and chlorine.
Treatment of drinking water	Treatment technology	-
	Effectiveness	-
	Any special conditions?	-
	Other	-
Measurement	Analytical method	A comparison of commercially available on-line ammonia analysers was carried out and the Chemscan UV-2150/S was selected for a trial based on its claimed consistency and reliability. It uses a multiple wavelength UV absorbance detection system to measure total and free ammonia, monochloramine and also total chlorine. All four parameters are measured directly, which enables more accurate control of the chlorine dose.

WCWA (2014). Drinking Water Quality. Annual Report 2013/14. Water Corporation Western Australia.		
	Limit of determination/ Limit of Reporting (LOR)	Not stated. Ammonia concentration reported as <0.1 mg/L.
	Other	-
Additional information	Any additional non-health related information considered important?	Chloramination involves the use of chlorine and ammonia to produce a longer lasting disinfectant compared to chlorine alone. Chloramination is used in the Goldfields and Agricultural Water Supply Scheme to maintain a disinfectant residual along the length of the extensive pipe network. Ultraviolet (UV) light is used at some water treatment plants across the state for additional disinfection where there are increased microbiological risks from activities in the catchment. UV does not provide a residual disinfection barrier, so it is used in combination with chlorination.

Chen et al. 2019

Chen Y., Lin T. and Chen W. (2019). Enhanced removal of organic matter and typical disinfection byproduct precursors in combined iron–carbon micro electrolysis-UBAF process for drinking water pre-treatment. Journal of Environmental Sciences 78: 315-327.		
General Description	Sources in drinking water	-
	Other	Conventional drinking water treatment has a poor removal efficiency for organic matter and ammonia nitrogen. Ammonia may be a threat to the bio-stability of drinking water by providing nutrients for nitrifying bacteria. Ammonia may react with organics and chlorine to form nitrogenous disinfection by-products (N-DBPs).
Treatment of drinking water	Treatment technology	An iron–carbon micro-electrolysis (ICME) combined with up-flow biological aerated filter (UBAF) process was used to remove two types of disinfection by product (DBP) precursors in micro-polluted source water.
	Effectiveness	ICME had no significant contribution to ammonia removal. However, ammonia was 90% removed by the nitrifying bacteria in the UBAF. Ammonia concentration pre-treatment: 1.12-1.86 mg/L. Supplementary Information (SI) (Table S1). Calculated concentration post treatment based on pre-treatment data from Table S1 (SI): 0.12-0.19 mg/L.
	Any special conditions?	-
	Other	
Measurement	Analytical method	Ammonia: Nessler's reagent colorimetry with spectrophotometer (U-3900H, HITACHI, Japan)
	Limit of determination/ Limit of Reporting (LOR)	Not stated.

Chen Y., Lin T. and Chen W. (2019). Enhanced removal of organic matter and typical disinfection byproduct precursors in combined iron–carbon micro electrolysis-UBAF process for drinking water pre-treatment. Journal of Environmental Sciences 78: 315-327.		
	Other	-
Additional information	Any additional non-health related information considered important?	-

Dos Santos & Daniel 2020

Dos Santos P. and Daniel L. (2020). A review: organic matter and ammonia removal by biological activated carbon filtration for water and wastewater treatment. International Journal of Environmental Science and Technology 17(1): 591-606.		
General Description	Sources in drinking water	The nutrient nitrogen is commonly present in contaminated water resources and municipal wastewater, especially under the form of ammonia which is very harmful when discharged into the environment and toxic to living organisms.
	Other	-
Treatment of drinking water	Treatment technology	Biological activated carbon (BAC) filtration is a potential treatment process for removing organic matter and ammonia through nitrification–denitrification, simultaneously.
	Effectiveness	Ammonia conversion across different studies as part of this literature review: 30-100%
	Any special conditions?	Temperature, dissolved oxygen concentrations, feed water characteristics, empty bed contact time (EBCT), relative carbon/nitrogen, influent ammonia concentration, and backwashing regime are some of the operating parameters that effectively affect nitrification–denitrification processes in BAC filters.
	Other	-
Measurement	Analytical method	-
	Limit of determination/ Limit of Reporting (LOR)	Not stated. Influent ammonia (mg $N\text{-}NH_4$ L^{-1}): 0.02-4.9 mg/L
	Other	-
Additional information	Any additional non-health related information considered important?	-

Hasegawa et al. 2017

Hasegawa S., Iwamoto T., Miyoshi T., Onoda S., Morita K., Takagi R. and Matsuyama H. (2017). Effect of biological contact filters (BCFs) on membrane fouling in drinking water treatment systems. Water 9(12): 981.		
General Description	Sources in drinking water	-
	Other	-
Treatment of drinking water	Treatment technology	The study investigated the effect of Biological Contact Filter (BCF) pre-treatment on membrane fouling in a drinking water treatment system. The main foulants were confirmed to be biopolymers. BCF is a filter media onto which microorganisms are attached. When raw water such as river water flows through the BCF column, ammonia and dissolved organic matter (DOM), including those that produce foul smell, are oxidised and removed by the microorganisms attached to the filter media.
	Effectiveness	The humic substances were not removed by the BCF pretreatment; the concentrations were essentially identical regardless of the contact time. By comparison, the biopolymer was removed ~30% by the BCF pretreatment, even at the very low temperature of 5°C. Effectiveness on ammonia *per se* not discussed.
	Any special conditions?	-
	Other	-
Measurement	Analytical method	Did not measure ammonia concentrations.
	Limit of determination/ Limit of Reporting (LOR)	-
	Other	-
Additional information	Any additional non-health related information considered important?	-

Hu et al. 2020

Hu J., Zhao Y., Yang W., Wang J., Liu H., Zheng P. and Hu B. (2020). Surface ammonium loading rate shifts ammonia-oxidizing communities in surface water-fed rapid sand filters. FEMS Microbiology Ecology 96(10): fiaa179.		
General Description	General	Nitrification is important in drinking water treatment plants (DWTPs) for ammonia removal and is widely considered as a stepwise process mediated by ammonia- and nitrite-oxidising microorganisms. The recent discovery of complete ammonia oxidisers (comammox) has challenged the long-held assumption that the division of metabolic labour in nitrification is obligate.
	Sources in drinking water	-
	Other	

Hu J., Zhao Y., Yang W., Wang J., Liu H., Zheng P. and Hu B. (2020). Surface ammonium loading rate shifts ammonia-oxidizing communities in surface water-fed rapid sand filters. FEMS Microbiology Ecology 96(10): fiaa179.		
Treatment of drinking water	Treatment technology	Study explored relative importance of comammox Nitrospira, canonical ammonia-oxidising archaea (AOA) and bacteria (AOB) in 12 surface water-fed rapid sand filters (RSFs).
	Effectiveness	All three ammonia-oxidising guilds had the potential to dominate nitrification in DWTPs. Spearman's correlation and redundancy analysis revealed that the surface ammonium loading rate (SLR) was the key environmental factor influencing ammonia-oxidising communities. Comammox Nitrospira were likely to dominate the nitrification under a higher SLR. Effectiveness on reducing ammonia concentrations *per se* not discussed.
	Any special conditions?	-
	Other	This study is not highlighting a new technique, rather it is looking at understanding ammonia-oxidising communities in RSFs and their response to the changing conditions for their safe operation.
Measurement	Analytical method	NH4+-N and NO_3–-N were determined via spectrophotometric and colorimetric analyses; ammonium loading rate (SLR) was calculated based on the ammonium concentration and filtration flow rate.
	Limit of determination/ Limit of Reporting (LOR)	Not stated.
	Other	-
Additional information	Any additional non-health related information considered important?	-

Huang et al 2019

Huang J., Chow C. W., Kuntke P., Cruveiller L., Gnos G., Davey D. E. and Teasdale P. T. (2019). The development and evaluation of a microstill with conductance detection for low level ammonia monitoring in chloraminated water. Talanta 200: 256-262.		
General Description	Sources in drinking water	Elevated concentrations of ammonia in drinking water supplies are mainly caused by anthropogenic factors, such as human wastes, widespread fertiliser use, agricultural runoff and municipal discharges.
	Other	Low level ammonia is crucial for managing drinking water disinfection using chloramination. Chloramine, a persistent disinfectant, is added after primary disinfection with chlorine, UV or ozone. Chloramine is usually formed *in situ* by mixing chlorine and ammonia in a precise ratio.
Treatment of drinking water	Treatment technology	-
	Effectiveness	-
	Any special conditions?	-

Huang J., Chow C. W., Kuntke P., Cruveiller L., Gnos G., Davey D. E. and Teasdale P. T. (2019). The development and evaluation of a microstill with conductance detection for low level ammonia monitoring in chloraminated water. Talanta 200: 256-262.		
	Other/Comments	-
Measurement	Analytical method	Micro-distillation and conductance measurement instrument - Micro-DCMI a linear calibration range of 0.01–60 mg NH_3 L^{-1}
	Limit of determination/ Limit of Reporting (LOR)	Limit of detection (LOD): 0.014 mg L^{-1} Limit of quantification (LOQ) of 0.045 mg L^{-1}
	Other	The free ammonia concentration in the water, measured by the Micro-DCMI were comparable to the free ammonia concentration determined by the plant ammonia ion selective electrode analyser. Most of the free ammonia concentrations measured by the Micro-DCMI were between 0.05 and 0.15 mg L^{-1}. Micro-DCMI could provide a good performance of monitoring low level of ammonia in chloraminated water.
Additional information	Any additional non-health related information considered important?	A custom-built automated analytical system was evaluated at a water treatment plant in Australia and the results compared favourably with the in plant online ammonia ion selective analyser. The Micro-DCMI method was a simple, robust and low cost online monitoring system suitable for determining low concentration ammonia to manage chloramination.

Jantarakasem et al. 2020

Jantarakasem C., Kasuga I., Kurisu F. and Furumai H. (2020). Temperature-dependent ammonium removal capacity of biological activated carbon used in a full-scale drinking water treatment plant. Environmental Science & Technology 54(20): 13257-13263.		
General Description	General information	-
	Sources in drinking water	-
	Other	Nitrification is a key function of biological activated carbon (BAC) filters for drinking water treatment. It is empirically known that the nitrification activity of BAC filters depends on water temperature, potentially resulting in the leakage of ammonium from BAC filters when the water temperature decreases.
Treatment of drinking water	Treatment technology	A bench-scale column assay to determine the volumetric ammonium removal rate (VARR) of biological activated carbon (BAC).
	Effectiveness	The water matrix factor reduced the volumetric ammonium removal rate VARR in ozonated water at 25°C by 33% on average. The VARR of ammonium for the bench-scale column assay was 5.0 g NH_4^+- N/m^3 packed BAC/h, and full scale BAC filter<0.3 g NH_4^+- N/m^3 packed BAC/h (Table 1). From Supplementary Information: Volumetric ammonia loading rate: 4-6 g NH_4^+- N/m^3 Ammonia in the effluent: 0.4 g NH_4^+- N/m^3

Jantarakasem C., Kasuga I., Kurisu F. and Furumai H. (2020). Temperature-dependent ammonium removal capacity of biological activated carbon used in a full-scale drinking water treatment plant. Environmental Science & Technology 54(20): 13257-13263.		
	Any special conditions?	The VARR in ozonated water was dependent on water temperature, indicating that the microbial activity of BAC did not adapt to low water temperature.
	Other	-
Measurement	Analytical method	Ammonium was measured by a colorimetric HACH kit (TNT830, HACH, USA).
	Limit of determination/ Limit of Reporting (LOR)	The quantification limit of the colorimetric kit was 0.015 mg NH4+-N/L.
	Other	-
Additional information	Any additional non-health related information considered important?	VARR is useful for water engineers to re-examine the loading and filter depth of BAC filters.

Liu et al 2017

Liu H., Zhu L., Tian X. and Yin Y. (2017). Seasonal variation of bacterial community in biological aerated filter for ammonia removal in drinking water treatment. Water Research 123: 668-677.		
General Description	Uses	-
	Sources in drinking water	-
	Other	Biological aerated filter (BAF) is widely used in wastewater treatment plants (WWTPs) and shows potential application to micropolluted drinking water sources with a higher ammonia removal efficiency during short warm seasons.
Treatment of drinking water	Treatment technology	A pilot lava-based biological aerated filter (BAF) was setup as a pre-treatment unit of drinking water treatment plant (DWTP).
	Effectiveness	92.62% of NH_4^+-N removal efficiency, 97.88% of NO^2 -N removal efficiency in summer, and 77.52% NH_4^+-N removal efficiency in winter down to 5°C. At 18.6 – 32.9 °C = NH_4^+-N: Influent 2.15 mg/L; effluent 0.15 mg/L
	Any special conditions?	-
	Other	-
Measurement	Analytical method	Colorimetric method using a spectrometer (DR 5000, HACH, USA).
	Limit of determination/ Limit of Reporting (LOR)	Not stated.
	Other	-
Additional information	Any additional non-health related information considered important?	-

Niu et al 2018

Niu J., Kasuga I., Kurisu F. and Furumai H. (2018). Effects of backwashing on granular activated carbon with ammonium removal potential in a full-scale drinking water purification plant. Water 10(12): 1830.		
General Description	Uses	-
	Sources in drinking water	-
	Other	-
Treatment of drinking water	Treatment technology	Granular activated carbon (GAC) and backwashing.
	Effectiveness	Ammonia removal potential of the GAC: Without prechlorination, the ammonium removal potential was 0.040 mg N/L/h/g-dry. It increased by 12% after backwashing in the first sampling. The removal potential decreased by 12% after backwashing (from 0.048 to 0.042 mg N/L/h/g-dry) when prechlorination was implemented.
	Any special conditions?	-
	Other	-
Measurement	Analytical method	A spectrophotometer (U2010, Hitachi, Tokyo, Japan) with the indophenol blue colorimetric method.
	Limit of determination/ Limit of Reporting (LOR)	Not stated.
	Other	-
Additional information	Any additional non-health related information considered important?	-

Serajuddin et al 2018

Serajuddin M. and Chowdhury M. A. I. (2018). Towards a novel approach to improve drinking water quality at Dhaka, Bangladesh. Environmental Engineering Research 23(2): 136-142.		
General Description	Uses	-
	Sources in drinking water	-
	Other	-
Treatment of drinking water	Treatment technology	Meteor pilot, a biological pre-treatment system
	Effectiveness	Ammonia reduction 73% Raw water ammonia concentration: < 15 mg NH_3-N/L. Ammonia in pretreatment effluent < 4.0 mg/L.
	Any special conditions?	-
	Other	-

Serajuddin M. and Chowdhury M. A. I. (2018). Towards a novel approach to improve drinking water quality at Dhaka, Bangladesh. Environmental Engineering Research 23(2): 136-142.		
Measurement	Analytical method	Ammonia : HACH DR 6000 spectrophotometer (HACH LANGE, USA) & Nessler method, No. 8038
	Limit of determination/ Limit of Reporting (LOR)	Not stated.
	Other	-
Additional information	Any additional non-health related information considered important?	-

Wu et al 2021

Wu Y.-J., Liu Y.-W., Cheng H.-H., Ke C.-W., Lin T.-F. and Whang L.-M. (2021). Biological pre-treatment system for ammonia removal from slightly contaminated river used as a drinking water source. Process Safety and Environmental Protection 147: 385-391.		
General Description	Uses	-
	Sources in drinking water	-
	Other	-
Treatment of drinking water	Treatment technology	Feasibility and efficiency of ammonia removal evaluated using a pilot-scale biological pre-treatment reactor filled with porous polyurethanes carriers (BioNET) operated over 500 days under different hydraulic retention times (HRT) (1.3 to 0.5 h).
	Effectiveness	Under 0.5 h hydraulic retention times (HRT) 84 % nitrification efficiency and 0.42 kg-N/m^3/day ammonia removal rate could be achieved with influent ammonia concentration of 10.4 mg N/L. Influent ammonia (mg-N/L): 3.5-12.0 Effluent ammonia (mg-N/L): 0.2-5.7
	Any special conditions?	Results of batch tests indicated that the effect of aeration on nitrification of BioNET was more significant than temperature and components in raw water.
	Other	-
Measurement	Analytical method	Not stated.
	Limit of determination/ Limit of Reporting (LOR)	Not stated.
	Other	-
Additional information	Any additional non-health related information considered important?	-

Xue et al 2021

Xue R., Donovan A., Zhang H., Ma Y., Adams C., Yang J., Hua B., Inniss E., Eichholz T. and Shi H. (2018). Simultaneous removal of ammonia and N-nitrosamine precursors from high ammonia water by zeolite and powdered activated carbon. Journal of Environmental Sciences 64: 82-91.		
General Description	Sources in drinking water	When adding sufficient chlorine to achieve breakpoint chlorination to source water containing high concentration of ammonia during drinking water treatment, high concentrations of disinfection by-products (DBPs) may form. If N-nitrosamine precursors are present, highly toxic N-nitrosamines, primarily N-nitrosodimethylamine (NDMA), may also form. Removing their precursors before disinfection should be a more effective way to minimize these DBPs formation.
	Other	-
Treatment of drinking water	Treatment technology	Zeolites and activated carbon were examined for ammonia and N-nitrosamine precursor removal when incorporated into drinking water treatment processes. The test results indicate that Mordenite zeolite can remove ammonia and five of seven N-nitrosamine precursors efficiently by single step adsorption test.
	Effectiveness	Alum coagulation more than 67% ammonia and 70-100% N-nitrosamine precursors were removed by Mordenite zeolite.
	Any special conditions?	-
	Other	-
Measurement	Analytical method	Ammonia: HACH DR 2800 Spectrophotometer, HACH TNT 830 kits Dissolved organic carbon (DOC): TOC-L analyzer with ASI-L liquid autosampler N-nitrosamine precursors: UFLC-MS/MS method
	Limit of determination/ Limit of Reporting (LOR)	Ammonia LOD: 0.015 to 2.00 mg/L NH_3-N
	Other	-
Additional information	Any additional non-health related information considered important?	The combination of two types of adsorbents is an efficient method for removal of ammonia and N-nitrosamine precursors from drinking water system.

APPENDIX E

Data extraction tables – Evidence Scan for Recent (Health-based) Studies

Recent Health-Based Studies for Ammonia

No health-based studies which would potentially alter the conclusions of the evaluation were found in the evidence scan conducted. Since no studies passed the content screening stage, there were no studies deemed relevant to include in this data extraction step.

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