Evaluation of the Evidence for the Recreational Water Quality Guidelines by the National Health and Medical Research Council
Section: Cyanobacteria and Algae

Technical Report

Report to the Recreational Water Quality Advisory Committee of the National Health and Medical Research Council

Australis Water Consulting

Australis Water Consulting

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Australis Water Consulting Pty Ltd
ABN: 12 621 158 487
T: +61 411 521 570
E: mike.burch@australiswater.com.au

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Contact for this report:	Mike Burch T: +61 411 521 570 E: mike.burch@australiswater.com.au	Australis Water Consulting
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Abbreviations

ACT	Australian Capital Territory
ANZECC	Australia and New Zealand Environment and Conservation Council
AWC	Australis Water Consulting
BMAA	β-methylamino-L-alanine
CASP	Critical Appraisal Skills Programme
CDC	Centers for Disease Control and Prevention
CI	confidence interval
Czech	Czech Republic
d	day
EFSA	European Food Safety Authority
ELISA	enzyme-linked immunosorbent assay
fg	femtogram
g	gram
GI	gastrointestinal infection
GIS	geographical information system
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GV	guideline value
h	hour
HABs	harmful algal blooms
HACCP	Hazard Analysis and Critical Control Points
kg	kilogram
L	litre
LC-MS	liquid chromatograph-mass spectrometry
LOAEL	lowest observed adverse effect level
LOD	limit of detection
LPS	Lipopolysaccharide
MeSH	Medical Subject Headings
m	metre
max	maximum
min	minute
minn	minimum
mg	milligram
ng	nanogram

NHMRC	National Health and Medical Research Council
NOAEL	no observed adverse effect level
NRMMC	Natural Resource Management Ministerial Council
NSW	New South Wales
OEHHA	Office of Health Hazard Assessment (California, USA)
OHAT	Office of Health Assessment and Translation
OR	odds ratio
PECO	Population Exposure Comparator Outcome
PCR	polymerase chain reaction
PFT	pulmonary function test
QMRA	quantitative microbial risk assessment
RfD	Reference Dose
RoB	Risk of Bias
RWQAC	Recreational Water Quality Advisory Committee (NHMRC) (termed 'the Committee')
SEQ	South-East Queensland
sp./spp.	species
Tas	Tasmania
tiab	title and abstract
TDI	tolerable daily intake
µg	microgram
UF	uncertainty factors
UK	United Kingdom
UNEP	United Nations Environment Programme
UNESCO	United Nations Educational, Scientific and Cultural Organization
USA	United States of America
USEPA	United States Environmental Protection Agency
Vic	Victoria
WA	Western Australia
WBDOSS	Waterborne Disease and Outbreak Surveillance System (CDC)
WHO	World Health Organization
WSAA	Water Services Association of Australia
y	year

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Foreword

This Technical Report accompanies the associated Evidence Evaluation Report which together comprise a narrative review for the topic of Cyanobacteria and Algae to inform the update to the NHMRC *Guidelines for Managing Risks in Recreational Water* (2008).

The Evidence Evaluation Report is the primary document for this narrative review and contains the Background, Purpose of the review, a summary of the Methodology and Results and the full and complete Discussion and Conclusions for the primary and secondary questions and supplementary topics for the review.

The Technical Report is a supporting document which contains identical material from the Evidence Evaluation Report related to the project background and purpose. It contains the full methodology with comprehensive detail on the development of the literature search procedures to answer the primary and secondary questions.

In addition, it provides all results for the review primary and secondary questions. This is given within the body of this report and in appendices where appropriate.

The Technical Report also includes an assessment of a selected range of international and national recreational water guidelines in relation to a suite of administrative and technical criteria for comparison to NHMRC procedures and requirements.

1 Introduction

1.1 Background Information

The National Health and Medical Research Council (NHMRC) through the Recreational Water Quality Advisory Committee (the Committee) will update the *Guidelines for Managing Risks from Recreational Water* (2008) during 2021-22.

As part of this update a series of Narrative Reviews were conducted by contractors to gather evidence to answer research questions on Microbial Risks, Chemical Hazards and Free-living Organisms, as determined by the Committee. Australis Water Consulting (AWC) was engaged to undertake the Narrative Review for the sub-topic of Cyanobacteria and Algae to inform the update to Chapters 6 and 7 of the *Guidelines for Managing Risks in Recreational Water* (2008).

1.2 Purpose of this Review

The update of the *Guidelines for Managing Risks in Recreational Water* (2008) includes a Risk Management Framework (referred to as the "Framework"). The proposed Framework for the updated Australian Recreational Water Quality Guidelines (the "Guidelines") is a new feature developed by the NHMRC that provides a structured process for identifying, planning for, and managing risks related to recreational water quality.

As such, the Framework is intended as an overarching risk assessment and management framework for recreational water quality. To support this Framework, the Guidelines will provide comprehensive elements including guideline values, technical fact sheets and specific technical guidance along with citing of associated evidence.

The Narrative Reviews, comprising of Evidence Evaluation and Technical Reports, as part of this project are designed to gather, assess and contribute to the detailed and up-to-date evidence. They will provide the rigour to support the above comprehensive information components contained within the Framework and the Guidelines.

1.3 Approach

Unlike the *Guidelines for Managing Risks in Recreational Water* (2008), the updated Guidelines will cover the public health risks associated with recreational water quality only. This includes human health risks from biological and chemical hazards that affect the quality of recreational water that people might be exposed to. Other risks associated with recreational water use such as physical risks should be considered as part of the risk management planning process while applying the Framework; however, specific guidance on how to manage these risks will not be provided in the updated Guidelines. In addition, the Guidelines will not cover details on rescue, resuscitation or treatment associated with risks from recreational water quality.

The Guidelines should be applied within the broader context of protecting public health and as such are not intended to be prescriptive given the variety of recreational water settings and climates across Australia. The inclusion of the Framework is intended to allow for structured risk assessment and risk management planning across the wide variety of existing and emerging recreational water environments that Australian risk managers might encounter. This also includes any unique sites that are currently unregulated and may present risks to public health. The risks to be addressed in Framework are as follows:

Included:

- Risks from microorganisms, cyanobacteria and algae, free-living microorganisms, chemical hazards.

Excluded:

- Risks from sun, heat and cold and other physical hazards associated with recreational water (e.g. drowning, animal attacks)
- Risks associated with exposure to foodstuffs collected from recreational water or its surroundings
- Risks associated with ancillary facilities that are not part of the recreational water environment other than risks that may affect water quality (e.g. toilet facilities in adjacent areas are not considered unless these need to be managed to minimise contamination of the recreational water body)
- Adverse health effects that are not caused by recreational water quality (e.g. seasickness, the 'bends')
- Risks from sand/soil around recreational water bodies (unless disturbances of sand/soil affect water quality); however, the risk management framework should include assessment of these risks.

The definitions of recreational water, recreational water use and recreational water users to be applied are:

Recreational water:
Included: Any natural or artificial water bodies without a chlorine disinfectant residual that might be used for recreating including coastal, estuarine, and freshwater environments. Includes public, private, commercial, and non-commercial recreational water sites. Includes unique unregulated sites such as wave pools, ocean- or river-fed swimming pools, artificial lagoons, and water ski parks.
Excluded: Aquatic facilities using chemical disinfection including swimming pools, spas, splash parks, ornamental water sites.

Recreational water use:
Included: Any designated or undesignated activity relating to sport, pleasure and relaxation that involves whole body contact or incidental exposure (through any exposure route) to recreational water (e.g. swimming, diving, boating, fishing).
Excluded: Consuming the catch from fishing or foodstuffs collected from recreational water or its surroundings. Therapeutic uses of waters (e.g. hydrotherapy pools). Occupational exposure.

Recreational water users:
Recreators or users of recreational water bodies including:

- the general public including all relevant life stages, ages and states of health other than persons that are explicitly advised to avoid such activities (e.g. for specific medical conditions)
- tourists
- specialist sporting users (e.g. athletes, anglers, kayakers, divers, surfers)
- any groups that may have high exposures to recreational water.

Target audience for the Guidelines

The Guidelines are intended for end users that will implement the Guidelines (government agencies, local councils, private recreational water managers); however, it is anticipated that there will also be significant public interest. It is anticipated that tailored guidance (e.g. plain English fact sheets or summaries) will be developed for specific groups where necessary.

2 Methodology

This section provides full details of all methods used for this review. It reproduces and provides further comprehensive information from the summary of methods given in the Evidence Evaluation Report

2.1 Literature Review Protocol

This review was comprised of answering a series of questions to inform the update of the NHMRC *Guidelines for Managing Risks in Recreational Water* in relation to the sub-topic of Cyanobacteria and Algae. The research questions to be addressed consisted of one primary question and five secondary questions (Table 1).

Table 1: Research Questions for the Narrative Review: Cyanobacteria and Algae (provided by the Committee)

Research Questions
Primary Question: What is the risk of any adverse health outcome for water users from exposure to cyanobacteria or algae in recreational water? **Secondary Questions:** 1. What are the indicators/surrogates of this/these hazard/s? What are the advantages and disadvantages of using surrogates versus monitoring specific toxins? 2. What guidelines, guidance and implementation practices are in place in comparable countries to minimise or manage this/these hazards and risks/s? 3. What are the specific exposure scenarios that might increase risk for sub-populations (e.g. infants playing in shallow waters in presence of benthic mats, water skiers/beach goers inhaling aerosolised cells/toxins) and how are these managed by other organisations? 4. What is the extent of evidence of adverse effects due to recreational exposure to marine cyanobacteria or algae (e.g. skin irritation due to *Lyngbya majuscula* or inhalation-related symptoms due to cells/toxins aerosolised by wave action, boats, jet-skis, etc.)? Are there any existing guidelines that address these exposure risks? 5. Much of the evidence for freshwater benthic cyanotoxin production in Australia is anecdotal and often linked to dog deaths following swimming in water bodies (e.g. at least 4 dog deaths in Lake Burley Griffin). It would be useful to try to collate the grey literature evidence to provide a clearer picture of the extent of any risk.

The review process to answer the research questions included four components. Each component had a different methodological approach selected to optimise information collection and evidence evaluation to answer the specific question. These components were:

1. A conventional systematic literature search and review of primary studies to address the Primary Question about the risk of adverse health outcomes from exposure to cyanobacteria and algae in recreational water.

2. A review of selected reviews to address Secondary Question 1 related to the indicators/surrogates of hazards posed by cyanobacterial toxins.
3. A review of guidelines, guidance, and implementation practices in place in comparable countries from grey literature obtained from organisational or jurisdictional agency websites to address Secondary Question 2.
4. A systematic review of selected primary studies and other reports derived from the search to answer the Primary Question, and additional supplementary searches and other sources specifically related to Secondary Questions 3, 4 and 5.

The justification for this differential approach related to the different questions is provided in the next section.

2.1.1 Methodological Approach Related to Research Questions

Primary Question

The approach taken to answer the Primary Question was a conventional systematic search and review of primary evidence studies and reports. This followed the procedures outlined in subsequent sections of this protocol and involved constructing a structured literature search based around the PECO criteria (see 4.1.2 Population, Exposure, Comparator, Outcome Table); searching for and selecting publications in multiple literature databases; screening these publications for suitability for full review based upon inclusion and exclusion criteria and critical assessment and appraisal of studies for risk of bias and where appropriate the evaluation of evidence quality and certainty assessment.

Secondary Questions

The secondary questions (Table 1) sought to identify a range of supplementary information required to provide context to assist in the development and application of sound revised guidelines. These related to the use of surrogates/indicators for monitoring hazards (Q 1); examples of other guidelines and guidance practices (Q 2); exposure scenarios for sub-populations, such as Aboriginal and Torres Strait Islander indigenous peoples (Q 3); evidence related to exposure to marine cyanobacteria and algae (e.g. *Lyngbya majuscula*) (Q 4); and sourcing of additional evidence for hazards and risks posed by benthic cyanobacteria (Q 5).

Secondary Questions 3, 4 and 5 were assessed by minor variations on the comprehensive search described for the Primary Question. This involved incorporating additional search terms to cover, for example, marine cyanobacteria and algal types (Q4) and specific toxins and benthic cyanobacteria (Q5). In addition, evidence of potential adverse health outcomes for sensitive sub-groups specifically included reference to Aboriginal and Torres Strait Islander indigenous peoples in Australia to address (Q3).

Secondary Questions 1 and 2 were addressed by different methodological approaches which were selected to optimise information collection and evidence evaluation to specifically answer the question type. These approaches were:

Question 1) A review of selected reviews was conducted to address Secondary Question 1.

The justification for undertaking a review of selected reviews was that it was agreed with the Committee that it was not time-effective to structure a specific additional search to review monitoring of cyanobacteria and algae to investigate the use of surrogates for monitoring specific cyanotoxins more widely. This was because monitoring of cyanobacteria in natural waters is a very extensive research and management topic for lake, reservoir and river management and is not restricted to monitoring toxic cyanobacteria and associated cyanotoxins. As such a broad search and review was not an efficient use of resources for the purpose of specifically answering this secondary question. The approach also considered whether a range of surrogates may offer an alternative to monitoring for specific toxins.

Question 2) A review of examples of guidelines, guidance, and implementation practices in place in comparable countries was carried out from grey literature searches for the websites from a range of national organisations and agencies and local jurisdictional agencies (i.e. states) to address Secondary Question 2. These searches were structured to gather and extract information on guidelines/guidance from other countries and sub-jurisdictions in addition to Australian states.

2.1.2 Population, Exposure, Comparator, Outcome (PECO) Table

The context for the review was set by the 'PECO' (Population, Exposure, Comparator, Outcome) assessment developed by the Committee. This was used to scope and guide the evidence collection and analysis. The PECO table is given in Table 2.

Table 2: PECO for the Narrative Review: Cyanobacteria and Algae (provided by the Committee).

Population	Exposure	Comparator	Outcomes
The general population *May also need to consider:* Do specific subpopulations need additional attention • Elderly • Infants and children • Pregnant women • Indigenous Australians (Aboriginal and Torres Strait Islander peoples) • Any groups that might be exposed more frequently as a result of inequity (e.g. geographic location, socioeconomic status) or lifestyle/occupation.	**Freshwater pelagic cyanobacteria** and toxins of interest: • *Cylindrospermopsis raciborskii, Microcystis spp., Dolichospermum circinale, Nodularia spumigena, Lyngbya wollei,* Total cyanobacteria. • Microcystins, cylindrospermopsins, saxitoxins, anatoxin-a, nodularin, LPS endotoxins	Control group of people with no exposure; where available/included and reported	• Gastrointestinal illness • Pneumonia-like symptoms • Hepatotoxicity • Neurotoxicity • Dermal irritation or allergic reaction • Inhalation-related symptoms (e.g. induction of asthma, shortness of breath)
As above.	**Freshwater benthic cyanobacteria** and toxins of interest: • *Phormidium, Geitlerinema, Nostoc, Oscillaroria, Schizothrix*, Total cyanobacteria. • Microcystins, cylindrospermopsins, saxitoxins, anatoxin-a, nodularin, LPS endotoxins	Control group of people with no exposure; where available/included and reported	• Gastrointestinal illness • Pneumonia-like symptoms • Hepatotoxicity • Neurotoxicity • Dermal irritation or allergic reaction
As above.	**Marine algae and cyanobacteria** and toxins of interest: • *Lyngbya majuscula, Oscillaroria, Trichodesmium, Karenia brevis, K. spp., Pfiesteria, Alexandrium, Gymnodinium, Dinophysis.* • lyngbyatoxin, applisiatoxin, pectenotoxin, saxitoxins, other marine toxins (e.g. brevetoxins, domoic acid).	Control group of people with no exposure; where available/included and reported	• Inhalation-related symptoms (e.g. induction of asthma, shortness of breath) • Dermal irritation or allergic reaction
Domestic, farm or wild animals exhibiting adverse health effects or death as evidence for the presence of toxin-producers in recreational waters.	**Algae or cyanobacteria** and toxins of interest: • Algae or cyanobacteria in general. • Any toxin type listed above or unidentified toxins.	Control group of animals with no exposure; where available/included and reported	• Gastrointestinal illness • Pneumonia-like symptoms • Hepatotoxicity • Neurotoxicity • Dermal irritation or allergic reaction • Inhalation-related symptoms (e.g. induction of asthma, shortness of breath)

2.1.3 Retrieval of Publications

Publications and reports were obtained via the University of Adelaide Library and from open access literature databases where available. Publications and reports downloaded were collated into a literature database using EndNote™ reference management software. This software was also used to manage bibliographies and references when writing the Narrative Review and Technical Report. The software version used was EndNote™ V9.3.3.

2.1.4 Process for Extracting and Presenting Data

Data was extracted from each paper for full review and presented in summary 'Metadata' files. These were compiled in Excel and have searchable filters. These files are both a compilation and analysis table which were principally designed to record details of study type and design, exposure categories and reported outcomes and include the contents of the PECO criteria. The units used in all data were checked and converted where required to achieve consistency. One table was developed for the freshwater cyanobacteria and algae studies and one for the marine cyanobacteria and algae studies.

The Metadata compilation tables were developed to record data from studies in a consistent manner and to guide the analysis. Their further value is as a legacy resource from the project, which can be readily interrogated using the filters to pull out studies into groups related to different categories of exposure (cyanobacteria and toxin types), water body types, type of health outcomes, etc.

These Metadata tables are not an analysis tool for risk of bias and results assessment and evidence quality, as this was achieved in more specific tables related to evidence evaluation for each research question.

2.1.5 Process for Critically Appraising the Evidence

Primary studies were used to answer the primary research question using a narrative review approach. One reviewer performed this assessment.

Studies selected for full review were critically appraised for relevance and suitability for the update of the NHMRC Guidelines. This appraisal consisted of both assessing the risk of bias of individual studies and assessing the certainty of the body of evidence where appropriate.

The studies included in this Narrative Review covered a range of types of evidence including peer-reviewed primary studies, existing guidelines or guidance and comprehensive reviews. The process of evaluation differed for each type of study and is summarised as follows:

- Primary studies: evidence was assessed separately against criteria that was used to evaluate how reliable the results were (see sections below).
- Guidelines or Guidance: assessment was made of how that guideline was developed.
- Comprehensive reviews: assessment was made of how the authors reviewed the evidence.

2.2 Search Strategy and Selection of Evidence

The strategy developed to find and select the evidence for the Primary Question involved the following elements and steps.

2.2.1 Databases

The databases searched were PubMed® and Scopus®. PubMed® is regarded as the primary search database for this review due to its coverage of biomedical journals and capacity for advanced searching. Scopus® was also used, and it claims to be the world's largest abstract and citation database of peer-reviewed literature. It is very broad-based, covering thousands of journals in the life sciences, the social sciences and humanities, the physical sciences, and the health sciences.

A small test search was run in Web of Science™. It proved to be not as flexible as PubMed® and Scopus® and was not pursued for this review.

2.2.2 Publication Dates and Language

The review considered papers and reports published from 2006 onwards. This allowed for the Guidelines update to include relevant new evidence and information since the publication of last revision of the Guidelines in 2008. Search results were restricted to English language publications only.

2.3 Search Protocol Development and Structure

Search terms and search-string combinations were defined based upon the PECO Table (Table 2) and the Research Questions for the review. The arrangement of search terms was based around search 'Concepts'. The advanced search was initially constructed using the PubMed® database. This is regarded as the most advanced and complex type of search and was used to develop and test the approach used and this was then followed for other searches with appropriate modifications for the Scopus® database.

The approach for this advanced search combined the three defined 'Concepts':

1. Cyanobacteria/Algae/Toxins
2. Recreation/Recreational
3. Health

These concepts were run as separate searches and then combined with the Boolean AND operator. These concepts are placed in a "Logic Grid" which is used to define the combination of search term key words and likely synonyms. The search terms for the preliminary logic grid based upon the PECO Table (Table 2) are given in Table 3.

Table 3: Preliminary Logic Grid for construction of an advanced search for the Primary Question: "What is the risk of any adverse health outcome for water users from exposure to cyanobacteria or algae in recreational water?".

Keys words and their variants to be searched based around each of the three concepts prior to their combination. Key words were initially chosen based upon the search terms suggested by the Committee for the PECO Table.		
Cyanobacteria/Algae/Toxins	**Recreation/Recreational**	**Health**
cyanobacteria blue-green algae algae cyanobacterial bloom/s algal bloom/s harmful algal blooms HAB/s cyanotoxin/s neurotoxin/s hepatotoxins/s microcystin/s saxitoxin/s cylindrospermopsin/s anatoxin-a nodularin/s *Cylindrospermopsis raciborskii* *Raphidiopsis* *Microcystis* *Dolichospermum circinale* *Anabaena circinalis* *Nodularia spumigena* *Lyngbya wollei* "total cyanobacteria"	recreation recreational swimming bathing wading paddling boating sailing wind surfing water skiing fishing kayaking canoeing jet-skiing	health health effects health outcome/s disease illness/es symptoms gastrointestinal nausea vomiting diarrhea pneumonia-like symptoms fever headache hay fever-like flu-like skin rash/es skin irritation eye irritation pruritus dermatologic allergic reaction/s neurotoxicity neurologic/al hepatotoxicity dermal irritation allergic reaction/s inhalation-related symptoms induction of asthma shortness of breath exposure oral inhalation
Note: This table illustrates the structure of the logic grid developed for the research protocol and does not include Index and MeSH terms and wildcard terms (*) which were added during development of the final search string combinations for each concept.		

The initial terms in the preliminary logic grid were assessed for their indexing status in PubMed® using its MeSH data base. MeSH (Medical Subject Headings) is the controlled vocabulary thesaurus used for indexing articles for PubMed® by the National Library of Medicine (USA). Each journal article included in MEDLINE is indexed with terms from the thesaurus to represent its subject content. MEDLINE is the National Library of Medicine's (NLM) premier bibliographic database that contains references to journal articles in life sciences, with a concentration on biomedicine. MEDLINE content is searchable via PubMed and constitutes the primary component of PubMed®. It is used for indexing, cataloguing, and searching of biomedical and health-related information. The MeSH terms and headings provide a consistent way to find content with different terminology but containing the same concepts. MeSH organizes its descriptors in a hierarchical structure so that broad searches will find articles indexed more narrowly.

The PubMed® MeSH database was also interrogated to find the appropriate alternative descriptors for terms that were originally specified for the searches in this review. The review of the database generated a range of alternative MeSH headings [mh] and Supplementary Concepts [nm] that may have been used to index a term or topic in the publications that were being sought by the searches. For example, for this search, many, but not all, of the major toxin or genus types from this search were indexed as MeSH terms (e.g. saxitoxin, *Microcystis*, *Aphanizomenon*, *Nostoc*, *Oscillatoria*, *Plectonema,* etc.). Other terms were indexed as Supplementary Concepts which are designed to include chemical, protocol, disease or organism terms. For example, within this search many of the toxin types and variants (e.g. microcystin, cylindrospermopsin, anatoxin a, nodularin, aplysiatoxin, beta-N-methylamino-L-alanine, pectenotoxins, brevetoxins, domoic acid, etc.) and generic or species names (e.g. *Cylindrospermopsis raciborskii*, *Nodularia spumigena, Dolichospermum circinale, Microseira wollei*, etc.) were indexed as supplementary concept terms. The evolution of the test searches provided a list of alternative MeSH and Supplementary Concept terms in PubMed® that were potentially associated with the key initial terms (Table 4), and these were included in final searches.

Table 4: Alternative and multiple MeSH and Supplementary Concept terms used in PubMed® searches related to the original terms specified for searching in the research protocol.

Term specified in research protocol	Topic description for the term	Alternative MeSH [mh] and Supplementary Concept [nm] terms from the database included in the searches
Cyanobacteria/Algae/Toxins Concept		
Cyanobacteria/Algae/Blooms	General and specific collective terms for the groups or classes of cyanobacteria and algal organisms	"Cyanobacteria"[mh] "Harmful Algal Bloom"[mh] "phytoplankton"[mh] "microalgae"[mh] "Chlorophyta"[mh] "Dinoflagellida"[mh] “Diatoms"[mh]
Anatoxins	Different types of Anatoxins	"anatoxin a"[nm] "anatoxin-a(s)"[nm] "homoanatoxin"[nm]
BMAA	Terms for BMAA	"beta-N-methylamino-L-alanine"[nm] "beta-(N-carboxy-N-methyl)aminoalanine"[nm]
Pectenotoxins	Different types of Pectenotoxins	"pectenotoxin-4"[nm] "pectenotoxin-2-seco acid"[nm] "pectenotoxin 2"[nm] "pectenotoxin 1"[nm] "pectenotoxin 11"[nm] "pectenotoxin 9"[nm] "pectenotoxin-11, Dinophysis acuta"[nm] "pectenotoxin-14"[nm] "pectenotoxin-13"[nm] "pectenotoxin 7"[nm] "pectenotoxin-8"[nm] "pectenotoxin 6"[nm]
Brevetoxin	Different types of Brevetoxins	"brevetoxin T17"[nm] "Brevetoxin"[nm] "brevetoxin 3, Karenia brevis"[nm] "brevetoxin 3"[nm] "brevetoxin 2"[nm] "Brevetoxin A"[nm] "brevetoxin B"[nm] "T34 toxin"[nm] "brevetoxin 7"[nm] "brevenal (polyether)"[nm]
Recreation/al Concept		
Water recreation	Collective broad MeSH index terms related to water recreational activities	"recreation"[mh] "Leisure Activities"[mh] "Water Sports"[mh]

Table 4: (continued)

Health Concept		
Health outcomes	Broad MeSH index terms related to health outcomes	"Health"[mh] "Public Health"[mh]
Gastrointestinal conditions	Range of MeSH index terms related to gastrointestinal conditions and related adverse health outcomes	"Gastroenteritis"[mh] "Vomiting"[mh] "Diarrhea"[mh]
Hay Fever-like conditions	MeSH index term related to hay fever-like conditions and related adverse health outcomes	"Rhinitis, Allergic"[mh]
Skin and dermatological conditions	Range of MeSH index terms related to skin and dermatologic conditions and related adverse health outcomes	"Exanthema"[mh] "Dermatitis"[mh] "Hypersensitivity"[mh] "Skin Manifestations"[mh] "Erythema"[mh] "Pruritus"[mh]
Neurotoxicity conditions	Range of MeSH index terms related to neurotoxicity conditions and related adverse health outcomes	"Neurotoxicity Syndromes"[mh] "Neurologic Manifestations"[mh]
Liver injury conditions	Range of MeSH index terms related to liver injury conditions and related adverse health outcomes	"Chemical and Drug Induced Liver Injury"[mh] "Liver Failure, Acute"[mh] "Massive Hepatic Necrosis"[mh]
Respiratory conditions	Range of MeSH index terms related to respiratory conditions and related adverse health outcomes	"Inhalation Exposure"[mh] "Asthma"[mh] "Respiratory Hypersensitivity"[mh] "Dyspnea"[mh]

Where a term is a PubMed® MeSH term it was included in the string using the following field code [mh:noexp]. This field code allowed for that term only to be searched without "exploding" to include a wide range of other synonyms and capturing extraneous material. In addition, the terms that were MeSH headings were also searched separately in article titles and abstracts. For example, "cyanobacteria" was searched using both "Cyanobacteria"[mh:noexp] or cyanobacteria*[tiab]. The reason for this was to capture recent material in PubMed® that was not yet indexed. In the case where articles were not yet indexed, there were no MeSH terms available to search, and it was necessary to look for words in titles and abstracts of articles. Also, in cases where a MeSH term had been added only recently, older material was searched using the titles and abstracts field code [tiab]. In addition, terms that were required for the search and were not MeSH terms were also searched for in titles and abstracts only, and not within the full text. The search strings also used truncated terms with wildcards for plurals variants where required: e.g. alga* for algae, algal.

It was initially anticipated that four separate searches would be required to fully cover the topics listed for review to update the Guidelines. These were:

- Freshwater pelagic cyanobacteria and toxins (Human exposure)
- Freshwater benthic cyanobacteria and toxins (Human exposure)
- Marine algae and cyanobacteria and toxins (Human exposure)

- Algae or cyanobacteria and toxins (Animal exposure).

Following initial searches in PubMed® it became clear that the requirement for the four searches was not necessary and was altered in favour of a single 'Super' search. This search was inclusive of these four topics and was developed and run in two databases (PubMed® and Scopus®). The justification for this was that the early test searches returned large amounts of material relevant to both pelagic and benthic freshwater and marine algae and cyanobacteria and their toxins and it was decided it would be more efficient to run and screen a single search. A time-limiting factor for undertaking the search procedure was the time required for multi-stage screening.

The development of search structure and content of multiple search iterations is given in Appendix 1. The approach adopted was to develop and test search terms and alternatives within each concept within the database. The completed and validated search in PubMed® was then translated with the appropriate syntax to be able to run in the Scopus® database.

The development of searches in PubMed® was carried out over a 3-month period (August-November 2020) and involved the following number of individual iterations for each concept: Cyanobacteria/Algae/Toxins: 17; Recreation/al: 7; Health: 5. The iterations involved a progressive process of testing and adding index terms, testing wildcards, adding the appropriate non-index terms required and correcting errors to arrive at the most efficient and comprehensive search structure for each concept. The date for each search iteration was recorded. In some cases, identical searches were run on different dates. It was found, as expected, that the size of searches (even for identical searches) increased over time due to more material being added to the databases. The results (numbers) for identical searches were found to change daily. See Appendix 1 for full details of this process and development of individual concept searches, combined searches and supplementary searches in each database.

The final combined searches in both PubMed® and Scopus® in November 2020 were named the Final Combined Search and were used to find and collate the literature to answer the Primary Question.

The combined single comprehensive 'Super' search with Logic Grids for the Final Combined Search in each of the three concepts (1: Cyanobacteria/Algae/Toxins; 2: Recreation/Recreational; 3: Health Outcomes) and their combination constructed for PubMed® in list form is given in Table 5. The terms for each concept listed as strings exactly as they were entered into the searches are given in Table 6. The results for the individual concept searches are also given in Table 5.

Equivalent individual and combined searches with the identical structure and the terms developed in PubMed® were translated directly across for application in Scopus®, also in November 2020 (17/11/2020). The Scopus® database does not use indexing language and the searches appear simpler in content but are no less comprehensive. The Logic Grid terms and search string terms for individual searches for Scopus® for the Final Combined Search are given in Tables 7 and 8.

An additional full set of individual and combined searches were run again as validation searches in both databases (Validating Combined Search) in April 2021 to check for new material for inclusion since the searches in November 2020.

Table 5: Logic Grid for construction of the Final Combined Search in PubMed® (11/11/2020) for the Primary Question: "What is the risk of any adverse health outcome for water users from exposure to cyanobacteria or algae in recreational water?". This search includes all Freshwater, Marine, Benthic Algae and Cyanobacteria (all known potentially toxic genera), and Freshwater and Marine toxins (Includes BMAA; does not include LPS/Endotoxins).

PubMed®		
Concept 1: Cyanobacteria/Algae/Toxins Includes: Freshwater, Marine, Benthic Algae and Cyanobacteria (all known potentially toxic genera); Freshwater and Marine toxins (Includes BMAA; does not include LPS/Endotoxins) **(PubMed® Code: Search #117;**	**Concept 2: Recreation/Recreational** **(PubMed® Code: Search #207)**	**Concept 3: Health Outcomes** **(PubMed® Code: Search #305)**
133 terms	25 terms	82 terms
"Cyanobacteria"[mh:noexp] cyanobacteri*[tiab] Blue-green alga*[tiab] toxic alga*[tiab] cyanobacteria bloom*[tiab] cyanobacterial bloom*[tiab] algae bloom*[tiab] algal bloom*[tiab] "Harmful Algal Bloom"[mh:noexp] harmful algal bloom*[tiab] HAB[tiab] "phytoplankton"[mh:noexp] phytoplankton*[tiab] "microalgae"[mh:noexp] microalga*[tiab] "Chlorophyta"[mh:noexp] chlorophyta[tiab] green alga*[tiab] "Dinoflagellida"[mh:noexp] dinoflagell*[tiab] "Pfiesteria piscicida"[mh:noexp] pfiesteria piscicida[tiab] "Diatoms"[mh:noexp] diatom*[tiab] brown alga*[tiab] marine alga*[tiab] cyanotoxin*[tiab] "microcystin"[nm:noexp] microcysti*[tiab] "Saxitoxin"[mh:noexp] saxitoxin*[tiab] "cylindrospermopsin"[nm:noexp] cylindrospermopsin*[tiab] "anatoxin a"[nm:noexp] "anatoxin-a(s)"[nm:noexp] anatoxin*[tiab] "homoanatoxin"[nm:noexp]	"recreation"[mh:noexp] recreation*[tiab] "Leisure Activities"[mh:noexp] Leisure Activities[tiab] "Water Sports"[mh] Water sport*[tiab] "swimming"[mh] swimming[tiab] bathing[tiab] wading[tiab] paddling[tiab] "diving"[mh:noexp] diving[tiab] scuba[tiab] boating[tiab] sailing[tiab] surfing[tiab] wind surfing[tiab] water skiing[tiab] angling[tiab] fishing[tiab] kayaking[tiab] canoeing[tiab] jet-skiing[tiab] rowing[tiab]	"Health"[mh:noexp] health[tiab] "Public Health"[mh:noexp] public health[tiab] "Epidemiology"[mh:noexp] epidemiology[tiab] "adverse effects"[sh:noexp] adverse effect*[tiab] "Disease"[mh:noexp] disease*[tiab] illness*[tiab] symptom*[tiab] "Poisoning"[mh:noexp] Poison*[tiab] "toxicity"[sh:noexp] toxi*[tiab] gastrointestinal[tiab] "Gastroenteritis"[mh:noexp] gastroenteritis[tiab] "Nausea"[mh:noexp] nausea*[tiab] "Vomiting"[mh:noexp] vomiting[tiab] "Diarrhea"[mh:noexp] diarrhea[tiab] diarrhoea[tiab] pneumonia like symptom*[tiab] "Fever"[mh:noexp] fever*[tiab] "Headache"[mh:noexp] headache*[tiab] "Rhinitis, Allergic"[mh:noexp] rhinitis[tiab] hay fever-like[tiab] flu-like[tiab] allergic reaction*[tiab] "Exanthema"[mh:noexp]

homoanatoxin*[tiab] “nodularin”[nm:noexp] nodularin*[tiab] BMAA[tiab] β-N-methylamino-L-alanine[tiab] “beta-N-methylamino-L-alanine”[nm:noexp] beta-N-methylamino-L-alanine[tiab] “beta-(N-carboxy-N-methyl)aminoalanine”[nm:noexp] “Lyngbya Toxins”[mh:noexp] Lyngbya toxin*[tiab] “aplysiatoxin”[nm:noexp] aplysiatoxin*[tiab] “debromoaplysiatoxin”[nm:noexp] Debromoaplysiatoxin*[tiab] “homoanatoxin-a”[nm:noexp] homoanatoxin-a[tiab] “cylindrospermopsis raciborskii”[nm:noexp] cylindrospermopsis raciborskii[tiab] “Microcystis”[mh:noexp] Microcystis[tiab] “Dolichospermum circinale”[nm:noexp] Dolichospermum circinale[tiab] Anabaena circinalis[tiab] “Nodularia spumigena”[nm:noexp] Nodularia spumigena[tiab] Anabaenopsis[tiab] “Aphanizomenon”[mh:noexp] Aphanizomenon[tiab] Aphanocapsa[tiab] Aphanothece[tiab] Arthrospira[tiab] Calothrix[tiab] Cuspidothrix issatschenkoi[tiab] Aphanizomenon issatschenkoi[tiab] geitlerinema[tiab] Hapalosiphon[tiab] Leptolyngbya[tiab] Lyngbya[tiab] Microcoleus[tiab] Microseira[tiab] “Microseira wollei”[nm:noexp] Moorea[tiab] “Nostoc”[mh:noexp] Nostoc*[tiab] “Oscillatoria”[mh:noexp] Oscillatoria*[tiab] Phormidium[tiab] Planktothrix[tiab] “Plectonema”[mh:noexp] Plectonema[tiab] Radiocystis[tiab] Raphidiopsis[tiab] Schizothrix[tiab]		exanthema[tiab] “Dermatitis”[mh:noexp] dermatitis[tiab] “Hypersensitivity”[mh:noexp] hypersensitiv*[tiab] skin rash*[tiab] dermal irrita*[tiab] skin irrita*[tiab] “Skin Manifestations”[mh:noexp] skin manifestation*[tiab] “Erythema”[mh:noexp] erythema[tiab] “Pruritus”[mh:noexp] pruriti*[tiab] dermatologic*[tiab] eye irrita*[tiab] “Neurotoxicity Syndromes”[mh:noexp] neurotoxicity syndrome*[tiab] “Neurologic Manifestations”[mh:noexp] neurologic manifestation*[tiab] neurotoxic*[tiab] neurologic*[tiab] “Chemical and Drug Induced Liver Injury”[mh:noexp] liver injury[tiab] “Liver Failure, Acute”[mh:noexp] liver failure[tiab] “Massive Hepatic Necrosis”[mh:noexp] hepatic necros*[tiab] hepatotoxi*[tiab] “Inhalation Exposure”[mh:noexp] inhalation exposure[tiab] shortness of breath[tiab] “Asthma”[mh:noexp] asthma*[tiab] “Respiratory Hypersensitivity”[mh:noexp] respiratory hypersensitiv*[tiab] “Dyspnea”[mh:noexp] dyspnea[tiab] exposure[tiab] oral[tiab] ingestion[tiab] dermal[tiab] inhalation[tiab] “Aerosols”[mh:noexp] aerosol*[tiab]

Scytonema[tiab] Heteroscytonema[tiab] Snowella[tiab] “Synechococcus”[mh:noexp] Synechococcus[tiab] “Synechocystis”[mh:noexp] Synechocystis[tiab] Tychonema[tiab] Umezakia[tiab] Woronichinia[tiab] “Trichodesmium”[mh:noexp] Trichodesmium[tiab] Karenia[tiab] Alexandrium[tiab] Gymnodinium[tiab] Dinophysis[tiab] “Marine Toxins”[mh:noexp] pectenotoxin*[tiab] “pectenotoxin-4”[nm:noexp] “pectenotoxin-2-seco acid”[nm:noexp] “pectenotoxin 2”[nm:noexp] “pectenotoxin 1”[nm:noexp] “pectenotoxin 11”[nm:noexp] “pectenotoxin 9”[nm:noexp] “pectenotoxin-11, Dinophysis acuta”[nm:noexp] “pectenotoxin-14”[nm:noexp] “pectenotoxin-13”[nm:noexp] “pectenotoxin 7”[nm:noexp] “pectenotoxin-8”[nm:noexp] “pectenotoxin 6”[nm:noexp] Brevetoxin*[tiab] “brevetoxin T17”[nm:noexp] “Brevetoxin”[nm:noexp] “brevetoxin 3, Karenia brevis”[nm:noexp] “brevetoxin 3”[nm:noexp] “brevetoxin 2”[nm:noexp] “Brevetoxin A”[nm:noexp] “brevetoxin B”[nm:noexp] “T34 toxin”[nm:noexp] “brevetoxin 7”[nm:noexp] “brevenal (polyether)”[nm:noexp] domoic acid[tiab] “domoic acid”[nm:noexp]		
Individual Concept Search Results (number of papers) and date periods		
Code: Search #117 Date Run: 11/11/2020	Code: Search #207 Date Run: 11/11/2020	Code: Search #305 Date Run: 11/11/2020
(1880-2021): 90,104 **(2006-2021): 60,517**	(1803-2021): 106,595 **(2006-2021): 65,623**	(1781-2021): 10,064,190 **(2006-2021): 5,706,671**

Table 6: The search terms listed as strings entered into PubMed® for each concept used for the Final Combined Search (11/11/2020) for the Primary Question: "What is the risk of any adverse health outcome for water users from exposure to cyanobacteria or algae in recreational water?"

PubMed®
Concept 1: Cyanobacteria/Algae/Toxins. (PubMed® Code: Search #117) Includes: Freshwater, Marine, Benthic Algae and Cyanobacteria (all known potentially toxic genera); Freshwater and Marine toxins (Includes BMAA; does not include LPS/Endotoxins)
"Cyanobacteria"[mh:noexp] OR cyanobacteri*[tiab] OR Blue-green alga*[tiab] OR toxic alga*[tiab] OR cyanobacteria bloom*[tiab] OR cyanobacterial bloom*[tiab] OR algae bloom*[tiab] OR algal bloom*[tiab] OR "Harmful Algal Bloom"[mh:noexp] OR harmful algal bloom*[tiab] OR HAB[tiab] OR "phytoplankton"[mh:noexp] OR phytoplankton*[tiab] OR "microalgae"[mh:noexp] OR microalga*[tiab] OR "Chlorophyta"[mh:noexp] OR chlorophyta[tiab] OR green alga*[tiab] OR "Dinoflagellida"[mh:noexp] OR dinoflagell*[tiab] OR "Pfiesteria piscicida"[mh:noexp] OR pfiesteria piscicida[tiab] OR "Diatoms"[mh:noexp] OR diatom*[tiab] OR brown alga*[tiab] OR marine alga*[tiab] OR cyanotoxin*[tiab] OR "microcystin"[nm:noexp] OR microcysti*[tiab] OR "Saxitoxin"[mh:noexp] OR saxitoxin*[tiab] OR "cylindrospermopsin"[nm:noexp] OR cylindrospermopsin*[tiab] OR "anatoxin a"[nm:noexp] OR "anatoxin-a(s)"[nm:noexp] OR anatoxin*[tiab] OR "homoanatoxin"[nm:noexp] OR homoanatoxin*[tiab] OR"nodularin"[nm:noexp] OR nodularin*[tiab] OR BMAA[tiab] OR β-N-methylamino-L-alanine[tiab] OR "beta-N-methylamino-L-alanine"[nm:noexp] OR beta-N-methylamino-L-alanine[tiab] OR "beta-(N-carboxy-N-methyl)aminoalanine"[nm:noexp] OR "Lyngbya Toxins"[mh:noexp] OR Lyngbya toxin*[tiab] OR "aplysiatoxin"[nm:noexp] OR aplysiatoxin*[tiab] OR "debromoaplysiatoxin"[nm:noexp] OR Debromoaplysiatoxin*[tiab] OR "homoanatoxin-a"[nm:noexp] OR homoanatoxin-a[tiab] OR "cylindrospermopsis raciborskii"[nm:noexp] OR cylindrospermopsis raciborskii[tiab] OR "Microcystis"[mh:noexp] OR Microcystis[tiab] OR "Dolichospermum circinale"[nm:noexp] OR Dolichospermum circinale[tiab] OR Anabaena circinalis[tiab] OR "Nodularia spumigena"[nm:noexp] OR Nodularia spumigena[tiab] OR Anabaenopsis[tiab] OR "Aphanizomenon"[mh:noexp] OR Aphanizomenon[tiab] OR Aphanocapsa[tiab] OR Aphanothece[tiab] OR Arthrospira[tiab] OR Calothrix[tiab] OR Cuspidothrix issatschenkoi[tiab] OR Aphanizomenon issatschenkoi[tiab] OR geitlerinema[tiab] OR Hapalosiphon[tiab] OR Leptolyngbya[tiab] OR Lyngbya[tiab] OR Microcoleus[tiab] OR Microseira[tiab] OR "Microseira wollei"[nm:noexp] OR Moorea[tiab] OR "Nostoc"[mh:noexp] OR Nostoc*[tiab] OR "Oscillatoria"[mh:noexp] OR Oscillatoria*[tiab] OR Phormidium[tiab] OR Planktothrix[tiab] OR "Plectonema"[mh:noexp] OR Plectonema[tiab] OR Radiocystis[tiab] OR Raphidiopsis[tiab] OR Schizothrix[tiab] OR Scytonema[tiab] OR Heteroscytonema[tiab] OR Snowella[tiab] OR "Synechococcus"[mh:noexp] OR Synechococcus[tiab] OR "Synechocystis"[mh:noexp] OR Synechocystis[tiab] OR Tychonema[tiab] OR Umezakia[tiab] OR Woronichinia[tiab] OR "Trichodesmium"[mh:noexp] OR Trichodesmium[tiab] OR Karenia[tiab] OR Alexandrium[tiab] OR Gymnodinium[tiab] OR Dinophysis[tiab] OR "Marine Toxins"[mh:noexp] OR pectenotoxin*[tiab] OR "pectenotoxin-4"[nm:noexp] OR "pectenotoxin-2-seco acid"[nm:noexp] OR "pectenotoxin 2"[nm:noexp] OR "pectenotoxin 1"[nm:noexp] OR "pectenotoxin 11"[nm:noexp] OR "pectenotoxin 9"[nm:noexp] OR "pectenotoxin-11, Dinophysis acuta"[nm:noexp] OR "pectenotoxin-14"[nm:noexp] OR "pectenotoxin-13"[nm:noexp] OR "pectenotoxin 7"[nm:noexp] OR "pectenotoxin-8"[nm:noexp] OR "pectenotoxin 6"[nm:noexp] OR Brevetoxin*[tiab] OR "brevetoxin T17"[nm:noexp] OR "Brevetoxin"[nm:noexp] OR "brevetoxin 3, Karenia brevis"[nm:noexp] OR "brevetoxin 3"[nm:noexp] OR "brevetoxin 2"[nm:noexp] OR "Brevetoxin A"[nm:noexp] OR "brevetoxin B"[nm:noexp] OR "T34 toxin"[nm:noexp] OR "brevetoxin 7"[nm:noexp] OR "brevenal (polyether)"[nm:noexp] OR domoic acid[tiab] OR "domoic acid"[nm:noexp]

Table 6: (continued)

Concept 2: Recreation/Recreational. (PubMed® Code: Search #207)
"recreation"[mh:noexp] OR recreation*[tiab] OR "Leisure Activities"[mh:noexp] OR Leisure Activities[tiab] OR "Water Sports"[mh] OR Water sport*[tiab] OR "swimming"[mh] OR swimming[tiab] OR bathing[tiab] OR wading[tiab] OR paddling[tiab] OR "diving"[mh:noexp] OR diving[tiab] OR scuba[tiab] OR boating[tiab] OR sailing[tiab] OR surfing[tiab] OR wind surfing[tiab] OR water skiing[tiab] OR angling[tiab] OR fishing[tiab] OR kayaking[tiab] OR canoeing[tiab] OR jet-skiing[tiab] OR rowing[tiab]
Concept 3: Health Outcomes (PubMed® Code: Search #305)
"Health"[mh:noexp] OR health[tiab] OR "Public Health"[mh:noexp] OR public health[tiab] OR "Epidemiology"[mh:noexp] OR epidemiology[tiab] OR "adverse effects"[sh:noexp] OR adverse effect*[tiab] OR "Disease"[mh:noexp] OR disease*[tiab] OR illness*[tiab] OR symptom*[tiab] OR "Poisoning"[mh:noexp] OR Poison*[tiab] OR "toxicity"[sh:noexp] OR toxi*[tiab] OR gastrointestinal[tiab] OR "Gastroenteritis"[mh:noexp] OR gastroenteritis[tiab] OR "Nausea"[mh:noexp] OR nausea*[tiab] OR "Vomiting"[mh:noexp] OR vomiting[tiab] OR "Diarrhea"[mh:noexp] OR diarrhea[tiab] OR diarrhoea[tiab] OR pneumonia like symptom*[tiab] OR "Fever"[mh:noexp] OR fever*[tiab] OR "Headache"[mh:noexp] OR headache*[tiab] OR "Rhinitis, Allergic"[mh:noexp] OR rhinitis[tiab] OR hay fever-like[tiab] OR flu-like[tiab] OR allergic reaction*[tiab] OR "Exanthema"[mh:noexp] OR exanthema[tiab] OR "Dermatitis"[mh:noexp] OR dermatitis[tiab] OR "Hypersensitivity"[mh:noexp] OR hypersensitiv*[tiab] OR skin rash*[tiab] OR dermal irrita*[tiab] OR skin irrita*[tiab] OR "Skin Manifestations"[mh:noexp] OR skin manifestation*[tiab] OR "Erythema"[mh:noexp] OR erythema[tiab] OR "Pruritus"[mh:noexp] OR pruriti*[tiab] OR dermatologic*[tiab] OR eye irrita*[tiab] OR "Neurotoxicity Syndromes"[mh:noexp] OR neurotoxicity syndrome*[tiab] OR "Neurologic Manifestations"[mh:noexp] OR neurologic manifestation*[tiab] OR neurotoxic*[tiab] OR neurologic*[tiab] OR "Chemical and Drug Induced Liver Injury"[mh:noexp] OR liver injury[tiab] OR "Liver Failure, Acute"[mh:noexp] OR liver failure[tiab] OR "Massive Hepatic Necrosis"[mh:noexp] OR hepatic necros*[tiab] OR hepatotoxi*[tiab] OR "Inhalation Exposure"[mh:noexp] OR inhalation exposure[tiab] OR shortness of breath[tiab] OR "Asthma"[mh:noexp] OR asthma*[tiab] OR "Respiratory Hypersensitivity"[mh:noexp] OR respiratory hypersensitiv*[tiab] OR "Dyspnea"[mh:noexp] OR dyspnea[tiab] OR exposure[tiab] OR oral[tiab] OR ingestion[tiab] OR dermal[tiab] OR inhalation[tiab] OR "Aerosols"[mh:noexp] OR aerosol*[tiab]

Table 7: Logic Grid for construction of the Final Combined Search in Scopus® (17/11/2020) for the Primary Question: "What is the risk of any adverse health outcome for water users from exposure to cyanobacteria or algae in recreational water?"

Scopus®		
Concept 1: Cyanobacteria/Algae/Toxins Includes: Freshwater, Marine, Benthic Algae and Cyanobacteria (all known potentially toxic genera); Freshwater and Marine toxins (Includes BMAA; does not include LPS/Endotoxins) **(Scopus® Code: Search CAT#1)**	**Concept 2: Recreation/Recreational** **(Scopus® Code: Search R#1)**	**Concept 3: Health Outcomes** **(Scopus® Code: Search H#1)**
75 terms	20 terms	53 terms
cyanobacteri* "Blue-green alga*" "toxic alga*" "cyanobacteria* bloom" "alga* bloom" "harmful algal bloom" {HAB} phytoplankton* microalga* chlorophyta "green alga*" dinoflagell* "pfiesteria piscicida" diatom "brown alga*" "marine alga*" cyanotoxin microcysti* saxitoxin cylindrospermopsin anatoxin homoanatoxin nodularin {BMAA} {β-N-methylamino-L-alanine} {beta-N-methylamino-L-alanine} "Lyngbya toxin*" aplysiatoxin debromoaplysiatoxin {homoanatoxin-a} "Cylindrospermopsis raciborskii" Microcystis "Dolichospermum circinale" "Anabaena circinalis" "Nodularia spumigena" Anabaenopsis Aphanizomenon Aphanocapsa	recreation* "leisure activit*" "water sport*" swimming bathing wading paddling diving scuba boating sailing surfing "wind surfing" "water skiing" angling fishing kayaking canoeing "jet skiing" rowing	health "public health" epidemiology "adverse effect*" disease* illness* symptom* poison* toxi* gastrointestinal gastroenteritis nausea* vomiting diarrhea diarrhoea "pneumonia like symptoms" fever* headache* rhinitis "hay fever like" {flu-like} "flu like" "allergic reaction*" exanthema dermatitis hypersensitiv* "skin rash*" "dermal irrita*" "skin irrita*" "skin manifestation*" erythema prurit* dermatologic* "eye irrita*" "neurotoxicity syndrome*" "neurologic manifestation*" neurotoxic* neurologic*

Aphanothece Arthrospira Calothrix “Cuspidothrix issatschenkoi” “Aphanizomenon issatschenkoi” geitlerinema Hapalosiphon Leptolyngbya Lyngbya Microcoleus Microseira Moorea Nostoc* Oscillatoria* Phormidium Planktothrix Plectonema Radiocystis Raphidiopsis Schizothrix Scytonema Heteroscytonema Snowella Synechococcus Synechocystis Tychonema Umezakia Woronichinia Trichodesmium Karenia Alexandrium Gymnodinium Dinophysis “Marine Toxin*” pectenotoxin Brevetoxin “domoic acid”		“liver injury” “liver failure” “hepatic necros*” hepatotoxi* “inhalation exposure” “shortness of breath” asthma* “respiratory hypersensitiv*” dyspnea exposure oral ingestion dermal inhalation aerosol*
Individual Concept Search Results (number of papers) and date periods		
Code: Search CAT#1 Date Run: 17/11/2020	Code: Search R#1 Date Run: 17/11/2020	Code: Search H#1 Date Run: 17/11/2020
(1835-2021): 228,681 **(2006-2021):** 141,664	**(2006-2021):** 191,287	(1863-2021): 17,556,021 **(2006-2022):** 9,739,949

Table 8: The search terms listed as strings for each concept used for the Final Combined Search in Scopus® (17/11/2020) for the Primary Question: "What is the risk of any adverse health outcome for water users from exposure to cyanobacteria or algae in recreational water?"

Scopus®
Concept 1: Cyanobacteria/Algae/Toxins Includes: Freshwater, Marine, Benthic Algae and Cyanobacteria (all known genera); Freshwater and Marine toxins (Includes BMAA; does not include LPS/Endotoxins). **(Scopus® Code: Search CAT#1)**
cyanobacteria* OR ("Blue-green alga*") OR ("toxic alga*") OR ("cyanobacteria* bloom") OR ("alga* bloom") OR ("harmful algal bloom") OR {HAB} OR phytoplankton* OR microalga* OR chlorophyta OR ("green alga*") OR dinoflagell* OR ("pfiesteria piscicida") OR Diatom OR ("brown alga*") OR ("marine alga*") OR cyanotoxin OR microcysti* OR saxitoxin OR cylindrospermopsin OR anatoxin OR homoanatoxin OR nodularin OR {BMAA} OR {β-N-methylamino-L-alanine} OR {beta-N-methylamino-L-alanine} OR ("Lyngbya toxin*") OR Aplysiatoxin OR Debromoaplysiatoxin OR {homoanatoxin-a} OR ("Cylindrospermopsis raciborskii") OR Microcystis OR ("Dolichospermum circinale") OR ("Anabaena circinalis") OR ("Nodularia spumigena") OR Anabaenopsis OR Aphanizomenon OR Aphanocapsa OR Aphanothece OR Arthrospira OR Calothrix OR ("Cuspidothrix issatschenkoi") OR ("Aphanizomenon issatschenkoi") OR Geitlerinema OR Hapalosiphon OR Leptolyngbya OR Lyngbya OR Microcoleus OR Microseira OR Moorea OR Nostoc* OR Oscillatoria* OR Phormidium OR Planktothrix OR Plectonema OR Radiocystis OR Raphidiopsis OR Schizothrix OR Scytonema OR Heteroscytonema OR Snowella OR Synechococcus OR Synechocystis OR Tychonema OR Umezakia OR Woronichinia OR Trichodesmium OR Karenia OR Alexandrium OR Gymnodinium OR Dinophysis OR ("Marine Toxin*") OR Pectenotoxin OR Brevetoxin OR ("domoic acid")
Concept 2: Recreation/Recreational **(Scopus® Code: Search R#1)**
recreation* OR ("leisure activit*") OR ("water sport*") OR swimming OR bathing OR wading OR paddling OR diving OR scuba OR boating OR sailing OR surfing OR ("wind surfing") OR ("water skiing") OR angling OR fishing OR kayaking OR canoeing OR ("jet skiing") OR rowing
Concept 3: Health Outcomes **(Scopus® Code: Search H#1)**
health OR ("public health") OR epidemiology OR ("adverse effect*") OR disease* OR illness* OR symptom* OR poison* OR toxi* OR gastrointestinal OR gastroenteritis OR nausea* OR vomiting OR diarrhea OR diarrhoea OR ("pneumonia like symptoms") OR fever* OR headache* OR rhinitis OR ("hay fever like") OR {flu-like} OR ("flu like") OR ("allergic reaction*") OR exanthema OR dermatitis OR hypersensitiv* OR ("skin rash*") OR ("dermal irrita*") OR ("skin irrita*") OR ("skin manifestation*") OR erythema OR prurit* OR dermatologic* OR ("eye irrita*") OR ("neurotoxicity syndrome*") OR ("neurologic manifestation*") OR neurotoxic* OR neurologic* OR ("liver injury") OR ("liver failure") OR ("hepatic necros*") OR hepatotoxi* OR ("inhalation exposure") OR ("shortness of breath") OR asthma* OR ("respiratory hypersensitiv*") OR dyspnea OR exposure OR oral OR ingestion OR dermal OR inhalation OR aerosol*

2.4 Accessing Evidence from Other Sources

In addition to the database searches, a range of publications was assessed to source reports and publications that would provide evidence that may be relevant to answer the questions. This was done by citation searching which involved review of the bibliography/reference lists of selected publications that were published within the date range for the review (2006-2021). The publications selected for assessment were based upon the reviewer's knowledge of the authoritative status of the author/s in the topic area and/or those papers that represented extensive or comprehensive reviews. The papers that were examined covered both the freshwater and marine areas are given in Table 9. This assessment of key publications also acted as a validation of the extent of coverage of the conventional literature searches in the databases.

Additional material sourced from these bibliography searches were processed by the same two-stage screening process and applying the inclusion and exclusion criteria (Table 10) used to select papers that would proceed to full-text review as used for the data base searches.

Table 9: Publications assessed to provide reports and publications for evidence in addition to the database searches. The bibliography/reference lists of the selected publications were examined for papers that were published within the date range for the review (2006-2021).

Reference	Reason for assessment of the reference list/bibliography
Freshwater Reference Sources	
Backer (2009)	General overview paper by authoritative scientist in field.
Backer *et al.* (2015)	Recent comprehensive review by authoritative scientists in the field.
Bownik (2010)	Recent review.
Buratti *et al.* (2017)	Recent comprehensive review by authoritative scientist.
Carmichael and Boyer (2016)	Recent review by authoritative scientists in the field.
Chorus and Testai (2021)	The most recent extensive and authoritative cyanobacterial recreational exposure and guideline review endorsed by WHO.
Funari *et al.* (2015)	Details of development of Italian guidelines.
Health Canada (2020)	Comprehensive review for development of guidelines.
Ibelings *et al.* (2014)	Comparison of guidance approaches in different countries by authoritative scientist in the field.
Koreiviene *et al.* (2014)	Recent review.
Nielsen and Jiang (2020)	Recent article about human skin penetration by cyanotoxins.
Quiblier *et al.* (2013)	Recent review.
Stewart *et al.* (2006)	Comprehensive review by authoritative Australian scientist.
Svirčev *et al.* (2017)	Recent comprehensive review by authoritative scientist.
Testai *et al.* (2016)	Recent comprehensive review by authoritative scientist in the field of cyanobacteria and recreational exposure.
Veal *et al.* (2018)	Review of management approach of using proxy indicators of cyanotoxin production rather than measurement of cyanotoxin directly.
Wood (2016)	Extensive literature review particularly the tables in Supplementary Material.

Table 9: (continued)

Marine Reference Sources	
Backer (2009)	Overview of research related to Florida red tides and brevetoxins by authoritative scientist in field.
Bean *et al*. (2011)	Publication that referred to several US studies on brevetoxins.
Fleming *et al.* (2011)	Overview of Florida red tides and brevetoxins by authoritative scientists in field.
Kirkpatrick *et al*. (2004)	Overview of Florida red tides and brevetoxins.
Osborne *et al*. (2001)	Australian study of *Lyngbya majuscula*.
Scardala *et al*. (2011)	Provided coverage of relevant papers from Italy.
Taylor *et al*. (2014)	Australian study of *Lyngbya majuscula* and tropical marine cyanobacteria.
Tubaro *et al*. (2011)	Review of marine palytoxins.

2.4.1 Screening Methods

Searches were processed by a two-stage screening process combined with a set of inclusion and exclusion criteria (Table 10) to select papers that would proceed to full-text review.

Stage 1: This involved assessment of relevance to answer the primary or secondary questions by examination of the title. In many cases papers could be readily rejected based upon clear lack of relevance to any of the review questions.

Stage 2: This involved further review of titles and abstracts for close relevance to the topic. Studies that had initially appeared relevant by inclusion of cyanobacteria, cyanotoxins, blooms, recreational water, monitoring, or exposure and adverse health outcomes in both freshwater and marine environments in titles were assessed more closely in this way.

Papers could be rejected based upon a range of limitations or criteria related to relevance. For example: not containing actual data and/or information related to health outcomes; were primarily ecological or occurrence studies of organisms or toxins; were management-related; were economic and social assessments; were related to analytical assays for organisms or toxins (see Table 10).

Table 10: Inclusion/exclusion criteria applied to select studies for full-text review.

Inclusion
Searched studies were required to closely match search concepts and elements developed from the PECO criteria. Amongst these the priorities for inclusion were: • Systematic Reviews and Literature Reviews – related to human exposure to cyanobacteria/algae/toxins in the natural environment; in particular those with reviews of evidence. • Primary studies (epidemiological, case series or case reports) with quantitative evidence of human exposure to the specified cyanobacteria, algae/toxins in recreational situations resulting in measured health outcomes (positive or negative). • Human and animal studies reporting exposure to benthic cyanobacteria in recreational water situations.
Exclusion
• Studies reporting exposure to cyanobacteria or algae where toxins were not identified. • Studies reporting exposure to cyanobacteria or algae where types were not identified. • No clear or weak evidence of exposure to cyanotoxins or cyanobacteria in recreational water • Studies with illness acquired from treated recreational water (e.g., swimming pools, spas, hot tubs) • Studies that were primarily ecological or occurrence studies of organisms or toxins; were management-related, were economic and social assessments. • Studies primarily related to analytical assays for organisms or toxins. • Non-peer reviewed studies as a general principle. Some were noted after review of the abstract or summary and retained if study appeared to contain relevant data.

2.5 Additional and Supplementary Searches

2.5.1 Endotoxins/LPS

A search for literature related to adverse health effects of Endotoxins/LPS was initially run as part of combined PubMed® searches. A series of terms were originally included in early PubMed® CAT concept searches (up to CAT Search #115), however these were subsequently removed from this concept for all final PubMed® searches.

The terms removed from the CAT concept were later run as single search string in PubMed® database only. This was agreed with the Committee. The search string was:

"Endotoxins"[mh:noexp] OR Endotoxi*[tiab] OR "Lipopolysaccharides"[mh] OR Lipopolysaccharide*[tiab] OR LPS[tiab]

A supplementary search for these terms was combined with the Recreation/al and Health outcomes concepts developed and used for the other full combined searches in PubMed® (Recreation #207 AND Health #305).

2.5.2 BMAA

The amino acid, β-methylamino-L-alanine (BMAA), which may be found in cyanobacteria was not initially included in the specific list of known toxins of interest in the PECO table for review. It was included after discussion with the Committee and added to the Cyanobacteria/Algae/Toxins (CAT) concept from search #113 onwards with the following search terms:

BMAA[tiab] OR β-N-methylamino-L-alanine[tiab] OR “beta-N-methylamino-L-alanine”[nm:noexp] OR beta-N-methylamino-L-alanine[tiab] OR “beta-(N-carboxy-N-methyl)aminoalanine”[nm:noexp]

BMAA was also searched in an abbreviated supplementary search with a limited range of terms for cyanobacteria to determine the extent of literature on this compound, although this search was not necessarily directed to capture health effects.

The cyanobacteria search string used was narrow and restricted to four terms related to cyanobacteria and blue-green algae:

“Cyanobacteria”[mh:noexp] OR cyanobacteria*[tiab] OR Blue-green alga*[tiab] OR toxic alga*[tiab]

This supplementary search was carried out in the PubMed® database only. This was regarded as sufficient to explore the relationship and extent of literature for this topic in the context of this review.

2.5.3 Search for Assessment of Significance of Topic for Indigenous Health

The searches for this review were combined with an indigenous search term string to determine the relevance of this topic to public health of Australian indigenous people/s.

A search string for Indigenous peoples based upon terms for indigenous groups associated with specific regions, states and territories and indigenous health services had been developed for other research purposes by the University of Adelaide library (M. Bell, pers. comm.). The search string was:

(Aborig*[tw] OR Indigenous[tw] OR (Torres Strait[tw] AND Islander*[tw]) OR health services, indigenous[mh] OR Oceanic Ancestry Group[mh] OR koori[tw] OR tiwi[tw]) AND (.au[ad] OR australia*[ad] OR Australia[mh] OR Australia*[tiab] OR Northern Territory[tiab] OR Northern Territory[ad] OR Tasmania*[tiab] OR Tasmania[ad] OR New South Wales[tiab] OR New South Wales[ad] OR Victoria*[tiab] OR Victoria[ad] OR Queensland[tiab] OR Queensland[ad])

This string was combined with two full combined searches in PubMed® (PM-C8: #116 AND #207 AND #305; 13/11/2020; PM-C11: #117 AND #207 AND #305; 04/04/2021) repeated at two different times with a 5-month interval between in November 2020 and April 2021. This represented an initial search and a validation search as was used for the other full combined searches to answer the primary question.

The Indigenous Search String alone was tested for validity or potential errors and returned the following number of results: 12,038 documents for an extended time period (1891-2021); and 8,792 documents for the specified period of the review (2006-2021) for a search on 04/04/2021.

2.5.4 Web of Science

A combined search using the three identical concepts and terms developed for PubMed® and Scopus® was carried out in Web of Science™ on 25/11/2020. This search produced combined results of 3,873 (for 2006-2021) prior to any screening. This was regarded as impractical to screen and suggested the advanced search structure and operational performance at least for this search provided much less discrimination than PubMed® and Scopus®. On this basis it was decided to not proceed further with using Web of Science™ and to restrict the combined primary searches to the two databases which have performed well, i.e. PubMed® and Scopus®.

2.6 Grey Literature

A grey literature search was conducted to identify studies not in the published, peer-reviewed literature and to source guideline values used for cyanobacteria in recreational fresh- and marine water in other jurisdictions. These searches were carried out specifically to gather information required to address Secondary Question 2: “What guidelines, guidance and implementation practices are in place in comparable countries to minimise or manage this/these hazards and risks/s?”

Key international agencies were searched for relevant reports. These organisations were:

- USA-American Water Works Association (AWWA)
- USA-Centers for Disease Control and Prevention (CDC)
- USA-The Interstate Technology and Regulatory Council (ITRC)
- USA-National Oceanic and Atmospheric Administration (NOAA)
- USA-United States Environmental Protection Agency (U.S. EPA)
- USA-United States Geological Survey (USGS)
- USA-Woods Hole Oceanographic Institution
- USA- each individual state Department of Environment (or equivalent)
- Europe-European Environment Agency
- UK- UK Health Protection Agency
- South Africa- Republic of South Africa Department of Environment, Forestry and Fisheries
- Germany – Umweltbundesamt (German Environment Agency)
- Global -United Nations Environment Programme (UNEP)
- Global- United Nations Educational Scientific and Cultural Organization (UNESCO)
- Global-World Health Organization (WHO)
- Australia-Water Research Australia (WaterRA)
- Australia-each state and territory Department of Environment
- Australia-each state and territory Department of Health
- Australia-each state and territory Department of Agriculture
- Australia-National Health and Medical Research Council (NHMRC)
- New Zealand-Ministry for the Environment, New Zealand Government
- Canada – Health Canada

In addition, a search using the Google search engine was made using the following keywords for the freshwater reports:

Guidelines for AND HABs OR harmful algal blooms OR blue-green algae OR cyanobacteria.

For marine searches the following keywords were used:

Marine algae OR marine cyanobacteria OR *Lyngbya* OR red tide OR seaweed disease OR swimmer's itch

These strings were initially used alone and then combined with the name of each Australian state or territory, each US state, each Canadian province, South Africa, NZ, UK, Scotland, Wales, Ireland and several European countries.

2.7 Assessment of the Study Quality (Risk of Bias) of Individual Studies

Definitions used here were provided by NHMRC as follows:

- "**Bias** refers to factors that can systematically affect the observations and conclusions of a study and cause them to be different from the truth"
- "**Risks of bias** (RoB) are the likelihood that features of the study design will give misleading results"

Reference: https://www.nhmrc.gov.au/guidelinesforguidelines/develop/assessing-risk-bias

The methodological quality of individual studies was assessed using an adaptation of the OHAT risk of bias tool (Appendix 2) (OHAT, 2019). Studies were evaluated on applicable risk of bias questions based on study design. The rating or answer to each risk of bias question was selected on an outcome basis from four options:

- definitely low risk of bias (++)
- probably low risk of bias (+)
- probably high risk of bias (-)
- definitely high risk of bias (--).

Data used to assess risk of bias was extracted using existing approaches/templates such as those available in the *OHAT Handbook* (OHAT, 2019). Study types that did not have an existing template (such as monitoring studies) were assessed against the usual risk of bias domains using questions such as those outlined in the OHAT framework: Table 4 (OHAT, 2019) where applicable.

Studies that were determined to have a high risk of bias or serious concerns with study quality were excluded from the review. Their removal was recorded with justification in the PRISMA Flow Diagram.

Conflicts of interest and funding data from the study characteristics tables were considered when assessing whether these might have affected any of the risk of bias domains (e.g. selection of comparators, selective reporting of results). If there were serious overall concerns, these were noted under 'Other sources of bias' in Appendix 2.

The outcome of the risk of bias assessments are presented in the in Section 5.1.2 of the Evidence Evaluation Report, together with a discussion of the overall quality of each study.

A template for questions for assessing the risk of bias in studies in this review is provided in Table 11. These questions followed exactly the domains given in OHAT (2019) apart from modifications to questions in the domain for Detection Bias. In this domain a series of six custom questions were developed to adequately cover exposure characterisation to cyanobacteria, algae and their toxins based upon their unique characteristics and behaviour. This was designed to reflect the natural tendency of algae and cyanobacteria to show a high degree of spatial variability often over short periods of time within water bodies. The questions were designed to determine if a study was designed adequately to account for this inherent variability in characterising exposure. The questions covered determining the adequacy of sampling and monitoring to account for potential spatial distribution characteristics of the organisms; assessing the suitability of identification and quantification techniques for cyanobacteria/algae and their toxins; and determining the degree of confidence in matching measures of exposure with adverse health outcomes in relation to potential time lags between sampling and exposure (Table 11).

Table 11: Template of questions used for assessing risk of bias in individual studies.

Qn.	Selection bias	
1	Randomization	Not applicable to cohort, observational and case studies.
2	Allocation concealment	Not applicable to cohort, observational and case studies.
3	Comparison groups appropriate	
	Confounding bias	
4	Confounding (design/analysis)	
	Performance bias	
5	Identical experimental conditions	Not applicable to cohort, observational and case studies.
6	Blinding of researchers during study?	Not applicable to cohort, observational and case studies.
	Attrition/exclusion bias	
7	Missing outcome data	
	Detection bias	
8	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	
9	Outcome assessment	
	Selective reporting bias	
10	Outcome reporting	
	Other sources of bias	
11	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol	

2.8 Assessment of the Certainty in the Body of Evidence

A process based on the OHAT (2019) approach to using the GRADE system was used to assess the certainty of a body of evidence. The GRADE system to assess the certainty of the evidence as recommended by NHMRC is described at: https://www.nhmrc.gov.au/guidelinesforguidelines/develop/assessing-certainty-evidence.

In this approach the evidence streams for each research question are tabulated together by outcome if possible. It was anticipated that the summary tables would include evidence streams for multiple studies and be grouped together to present evidence for the four topics listed for review to update the guidelines. These were: Freshwater pelagic cyanobacteria and toxins (Human exposure); Freshwater benthic cyanobacteria and toxins (Human exposure); Marine algae and cyanobacteria and toxins (Human exposure); Algae or cyanobacteria and toxins (Animal exposure).

An overall certainty rating was assigned to each evidence stream after the domains used to assess certainty in the GRADE framework were applied to the body of evidence: overall risk of bias across studies, unexplained inconsistency, imprecision, indirectness, publication bias. Under the GRADE system, the overall quality of the evidence for an outcome is categorised as high, moderate, low or very low.

Each evidence stream was assigned an initial certainty rating similar to that described in the OHAT Handbook (OHAT, 2019). For example, evidence from randomised controlled trials is initially graded as high certainty and evidence from observational studies is initially graded as low certainty. If there are any study types that do not have an initial rating, an appropriate initial rating is determined by the reviewer in a similar manner to the approach used in OHAT (2019).

The certainty of the evidence can be downgraded or upgraded from the initial rating if any of the conditions in the Table 12 are met. If none are met, the initial certainty rating is retained. These domains are explained in more detail in OHAT (2019). Conflicts of interest and funding sources were also be considered as a reason to downgrade if there are serious concerns that these have influenced the findings from the body of evidence.

Table 12: Approach used to downgrade or upgrade the certainty of the evidence from the initial rating (Based upon Figure 6 in the OHAT (2019)).

Reasons to Downgrade	Reasons to Upgrade
• **Risk of bias** - Serious or very serious concerns about study quality across the body of evidence (reliability) (see Appendix 2) • **Unexplained inconsistency** - Important inconsistency of results across the included studies that can't be explained by study design • **Indirectness** - Some or major uncertainty about directness (relevance to the research question that is being answered) • **Imprecision** - Imprecise or sparse data • **Publication bias** - High probability of reporting bias (selective reporting of results across the body of evidence that might skew results)	• **Consistency** - Strong or very strong evidence of association based on consistent evidence from two or more observational studies, with no plausible confounders • **Magnitude of effect** - Very strong evidence of association based on direct evidence with no major threats to validity • **Dose-response** - Evidence of a dose-response gradient • **Residual confounding** - All plausible confounders would have reduced the effect • **Other reasons** – any topic-specific reasons as determined by experts in the field

The results of the certainty assessment process were tabulated in a similar manner to that described in the OHAT (2019) framework. Where a conclusion was unable to be made by the reviewer around any of the domains (e.g. inconsistency and imprecision may be difficult to ascertain with the kind of evidence that will be included in the review) this was recorded as 'not applicable' or 'unknown'. A Table summarising the results for each outcome is included in the Evidence Evaluation Report (Table 7)

3 Results

3.1 Primary Question Search

As described in the methods the searches were developed using logic grids for three individual concepts: Cyanobacteria/Algae/Toxins; Recreation/Recreational; Health Outcomes.

The concepts were combined into single comprehensive 'Super' searches which were performed twice.

The Final Combined Searches in both PubMed® and Scopus® were carried out in November 2020 for the initial gathering and assessment of evidence to answer the primary question. The searches were then repeated in April 2021 as the Validating Combined Searches for comparison to earlier searches.

3.1.1 Individual Concept Searches

The results for the individual concepts for Final Combined Searches in November 2020 for PubMed® are given in Table 5 and for Scopus® in Table 7.

3.1.2 Combined Searches

The results for combined searches in both PubMed® and Scopus®, Final Combined Search (November 2020) and Validating Combined Searches (April 2021) are given in Table 13.

A comparison of the Final and Validating searches showed that the validating searches did not produce any new or additional papers that would require further assessment by full-text review to answer either the Primary or Secondary questions after the first full set of searches in November 2020. This was regarded as satisfactory validation of structure and performance of the searches in both databases in November 2020.

Table 13: Results from all full combined searches in PubMed® and Scopus®, and results for Stage 1 and 2 screening to select papers for full-text review to answer the Primary Question for both freshwater and marine cyanobacteria and algae. The table also includes papers found by the searches that were not relevant to the Primary Question but were placed into categories for further review to provide evidence to address aspects of the secondary questions, or in the case of the topics of BMAA were set aside to hold for advice of the Committee.

Final Combined Search		
Database	**PubMed®**	**Scopus®**
Combined Search Code specific to database	PM-C7[1.]	S-C1[2.]
Search Date	11/11/2020	17/11/2020
Results Breakdown – number of papers		
Full Search - Prior to screening	641	1032
Screen Stage 1 – sorted by Title for potential relevance	140	140
Screen Stage 2 – sorted by Abstract for relevance for full-text review	41	34
Additional papers not relevant to Primary Question sorted to Topic Categories and retained for further review		
Dogs-benthics/poisoning BMAA	10 1	10 1
Validating Combined Search		
Database	**PubMed®**	**Scopus®**
Combined Search Code specific to database	PM-C10[3.]	S-C2[4.]
Search Date	4/04/2021	5/04/2021
Results Breakdown – number of papers		
Full Search - Prior to screening	523	1278
Screen Stage 1 – sorted by Title for potential relevance	130	145
Screen Stage 2 – sorted by Abstract for relevance for full-text review	Not required – no new papers found from comparison with PM-C7 above	Not required – no new papers found from comparison with S-C1 above

Codes for individual Concept Searches that were used to make up the Combined Searches within the respective databases:

1. PM-C7 (PubMed®): #117 Cyanobacteria/Algae/Toxins AND #207 Recreation AND #305 Health
2. S-C1 (Scopus®): CAT#1 AND R#1 AND H#1
3. PM-C10 (PubMed®): #117 Cyanobacteria/Algae/Toxins AND #207 Recreation AND #305 Health
4. S-C2 (Scopus®): CAT#1 AND R#1 AND H#1

3.2 Inclusion/Exclusion of Literature and PRISMA Flow Diagram

The Prisma Flow Diagram (Figure 1) summarises the process for identification, screening and eligibility assessment of literature used for the evidence evaluation and the narrative review.

The first stage for the identification of studies involved combining the results of the database searches for PubMed® (PM-C7: 11/11/2020) and Scopus® (S-C1: 17/11/2020) given in Table 13 and the studies identified from other sources (Table 9; Section 3.3). This produced 1,693 records. After removal of duplicates (n=456) the number of records identified to proceed to screening was 1,237.

Screening involved the application of the two-stage process described in Section 2.4.1. The inclusion and exclusion criteria which form part of this screening process (Table 10) were applied to the selected papers that proceeded to full-text review (n=143). This number of records assessed by full-text review for eligibility to provide evidence to answer the primary question was comprised of 89 freshwater studies and 54 marine studies.

The aim of the full-text review was to identify primary studies that contained suitable data that could be included in the assessment for risk of bias and further exclude other studies that did not meet this criterion.

The definition of primary studies applied here was those studies that contain original primary data which report measurements of effects or observations of health outcomes from exposure to cyanobacteria, algae or their toxins. This is opposed to secondary reporting and publication of data taken from primary studies.

A list of freshwater and marine studies that were excluded from further assessment after full-text review with reasons for exclusion is given in Appendix 3.

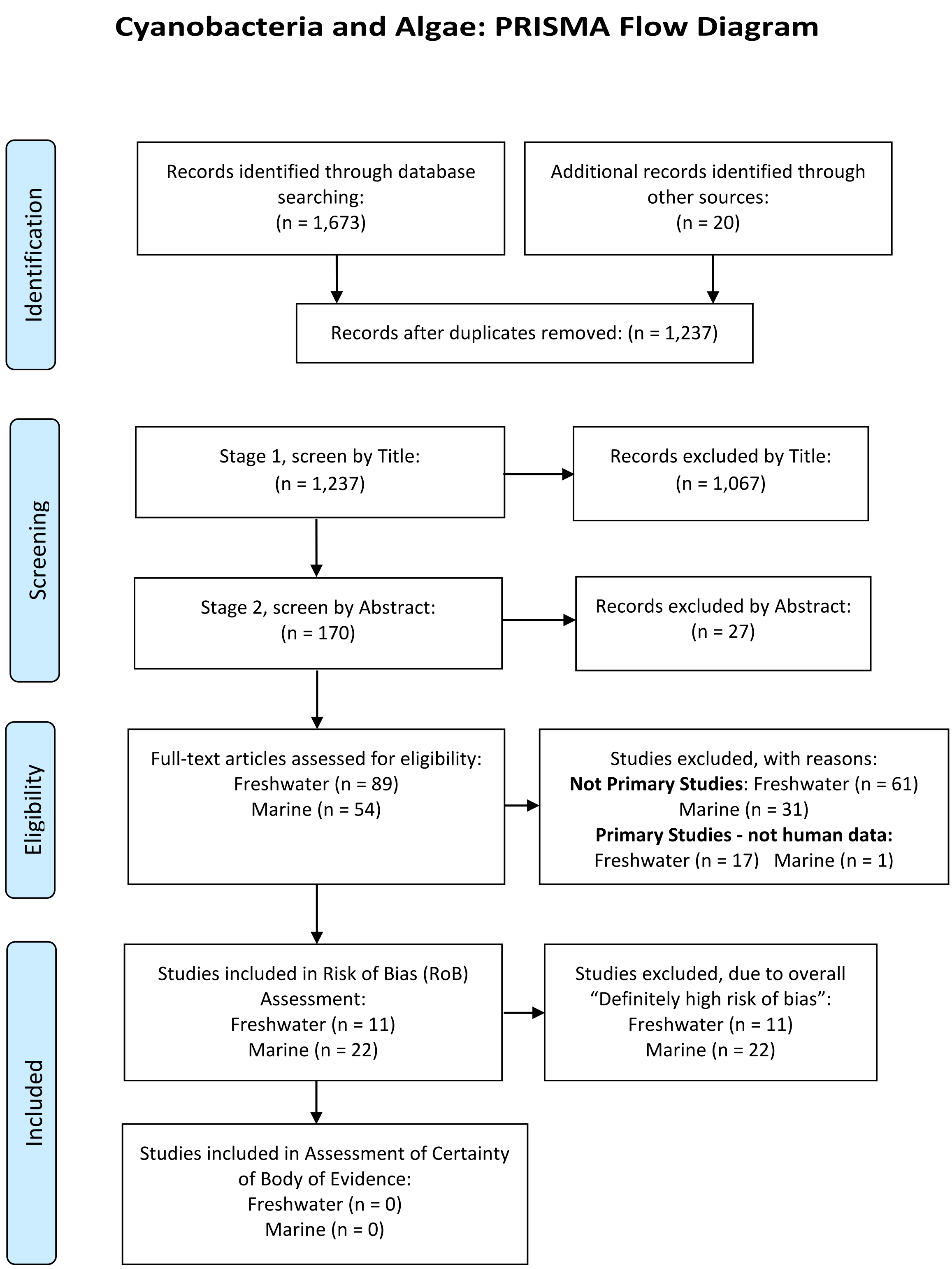
The output from the full-text review identified 51 studies that were regarded as primary studies that contained suitable data that could potentially be included in the assessment for risk of bias. However, only the human exposure studies were included in the risk of bias assessment, and this excluded a further 18 studies (11 freshwater; 1 marine). The numbers of primary studies therefore that proceeded through the full risk of bias assessment were 11 freshwater and 22 marine studies. The other primary studies which were not related to human exposure provided data that was useful for answering the Secondary Questions in some cases. A list of the primary freshwater and marine studies excluded from the risk of bias assessment is given in Appendix 4 with explanations for their exclusion.

All studies assessed for risk of bias assessment were determined to have overall "definitely high risk of bias". A subsequent assessment of certainty in the body of evidence was done and an overall certainty rating was assigned to each evidence stream as 'very low confidence' across all study types. This was based on downgrading any evidence streams with an initial 'low' or 'very low' confidence rating to 'very low' across the board for serious risk of bias.

These shortcomings considered together led to the conclusion that there was insufficient confidence in the findings of the available studies. It is worth noting that methods and approaches for systematic reviews of environmental health evidence is still an area of research and development, and further modification of the available frameworks and tools is beyond the scope of services required for this review.

This is explained in further detail in Section 5.1.3 of the Evidence Evaluation Report.

Figure 1: PRISMA flow diagram outlining the identification and screening of literature and assessment for study quality to identify and evaluate evidence from the studies.



3.3 Additional and Supplementary Searches

3.3.1 Endotoxins/LPS

A supplementary search for Endotoxins/LPS (narrow search terms) was developed to combine with the Recreation/al and Health outcomes concept developed for the full combined searches in PubMed® (Recreation #207 AND Health #305) (Table 14).

Table 14: Supplementary search for Endotoxin/LPS combined with the Recreation and Health concepts developed within PubMed®.

Search Name	Date	Contains Searches	Individual Search Results (2006-2021)	Combined Results
Endotoxins/LPS AND Recreation AND Health	15/11/2020	Endotoxins/LPS AND Recreation #207 AND Health #305	Endotoxins/LPS: 86,282 #207: 65,692 #305: 5,713,018	Endotoxins/LPS AND #207 AND #305: 170 documents (2006-2021) The 170 papers were screened for relevance to the topic (Endotoxins/LPS AND Recreation AND Health) and this returned only 6 potentially relevant papers.

This individual search string for Endotoxins/LPS produced 86, 282 results (2006-2021). Analysis of the results for an earlier extended time period showed that the research field started to increase in publication rate from 1980, with a further steady increase from 2000 and again from 2010.

The results for the combined search (Endotoxins/LPS AND Recreation #207 AND Health #305) were low – only 170 studies/papers and these were of very limited or no relevance to environmental exposure to Endotoxins/LPS in recreational water situations. The search returned many physiological studies with animals (rodents) related to the ability of LPS to induce depression and assess the effect of a range of agents to counter this. It is not clear why the search captured these studies as they do not have appear to have a clear link to the Recreation/al terms string.

The 170 results were screened based upon titles and 6 studies were selected that related to LPS/Endotoxins in natural water and potential for human exposure and adverse health outcomes. The six potentially relevant papers were: Berg *et.al.*, 2011; Lévesque *et.al.*, 2016; de Man *et.al.*, 2014; Mohamed, 2008; Mohamed and Shehri, 2007; Sattar *et.al.*, 2019.

These were further reviewed and narrowed to only two relevant studies that mentioned cyanobacteria and Endotoxins/LPS.

Of the four studies excluded, one study related to use of an *in vitro* culture assay that reflects the level of LPS in water samples; one study related to exposure to contaminated aerosols and water originating from water features that may pose public health risks; and two other studies by the same author related to the occurrence of cyanobacteria in water bodies in Saudi Arabia.

The two relevant studies were:

Berg, K.A., Lyra, C., Niemi, R.M., Heens, B., Hoppu, K., Erkomaa, K., Sivonen, K. and Rapala, J. (2011). *Virulence genes of Aeromonas isolates, bacterial endotoxins and cyanobacterial toxins from recreational water samples associated with human health symptoms*. Journal of Water and Health, 9, 670-679.

Lévesque, B., Gervais, M.-C., Chevalier, P., Gauvin, D., Anassour-Laouan-Sidi, E., Gingras, S., Fortin, N., Brisson, G., Greer, C. and Bird, D. (2016). *Exposure to cyanobacteria: acute health effects associated with endotoxins.* Public Health*,* 134**,** 98-101.

The paper by Berg *et al*. 2011 undertook analysis of endotoxins and cyanotoxins in recreational water samples (n = 38) taken from sites where cyanobacteria were suspected to have caused human health symptoms. The toxins analyses for (cyanobacterial hepatotoxins and neurotoxins, and bacterial endotoxins) were not detectable or were present in only low concentrations in the majority of the samples. The results indicated that the toxins were unlikely to be the main cause of the reported adverse health effects, whereas more attention should be paid to bacteria associated with cyanobacteria as a source of health effects.

3.3.2 BMAA

The supplementary search for the potentially toxic amino acid BMAA combined with a limited range of terms for cyanobacteria to determine the extent of literature on this compound is given in Table 15.

Table 15: Supplementary search for the amino acid BMAA combined with a limited range of terms for cyanobacteria.

Search Name	Date	Contains Searches	Individual Search Results	Combined Results
BMAA and Cyanobacteria	14/11/2020	Cyanobacteria AND BMAA	Cyanobacteria: 27,727 (1901-2021) BMAA: 399 (2006-2020)	Cyanobacteria AND BMAA: 234 (2006-2020)

The specific individual search for BMAA terms (5 terms) returned 399 results (from 2006-2020). The individual search for cyanobacteria was unconstrained to a time period and returned 27,727 results (from 1901-2020).

The combined Cyanobacteria and BMAA search returned 234 results for (2006-2020). This combined result of 234 suggested that the association of BMAA with cyanobacteria is a recent popular research topic and approximately 60% of the publications from 2006 that mentioned BMAA also mentioned cyanobacteria (234 from 399). Note this search return is for the terms cyanobacteria and BMAA found in titles and abstracts only, and the relevance of this for the public health hazard of BMAA can only be confirmed by a detailed assessment of these publications.

The combined search also indicated that publications associating BMAA with cyanobacteria first occurred in 2003 and accelerated in 2008 and 2009. Note, this does not necessarily mean that all publications were related to BMAA in cyanobacteria. They may only have contained these terms in titles and abstracts.

3.3.3 Search for Assessment of Significance of the Topic for Indigenous Health

The indigenous search terms string obtained from the University of Adelaide library was combined with two full combined searches in PubMed® (PM-C8: #117 AND #207 AND #305; 13/11/2020; PM-C11: #117 AND #207 AND #305; 04/04/2021). This was repeated at two different times at a 5-month interval in November 2020 and April 2021, representing an initial search and a validation search as was used for the other full combined searches to answer the primary question.

This search was tested only within PubMed® as the low number results were regarded as a sufficient indication that there is limited or no published literature on this topic in conventional databases.

PM-C8 (13/11/2020)

The combined Search (#117 AND #207 AND #305) was run prior to the indigenous string and generated 478 documents (2006-2021). This was then combined with the indigenous search string. This generated 0 documents (2006-2021); i.e. no results were found.

For a further validation this was repeated for the full time period (from ~1880) for all of these searches, and this also generated no results.

A further iteration was then carried out with the removal of the Recreation concept (#207) and a combination of Cyanobacteria/Algae/Toxins, Health and Indigenous (CAT #117 AND Health #305 AND Indigenous). This generated 13 documents, 12 of which were considered not relevant. Only one paper (Sadgrove, 2012) mentioned cyanobacteria, and this was not health-related but was related to aboriginal and early European encounters with cyanobacterial blooms.

PM-C11 (04/04/2021)

PM-C11 (#117 AND #207 AND #305 AND Indigenous) was a repeat and validation of PM-C8 to test the combined search and the Indigenous concept (2006-2021) after a 5-month interval.

No results related to indigenous studies or health outcomes and the Primary Question were found from this updated combined search.

3.4 Assessment of Primary Studies and Grey Literature

3.4.1 Assessment of Primary Studies with Regard to the Primary Question

A detailed assessment of the primary freshwater and marine studies selected for full-text review was made and data for each study was extracted and recorded in Excel meta-databases (provided separately to NHMRC). The databases were both a data compilation and also an analysis tool for the review and were compiled in Excel with searchable filters. The databases were designed to record details of study type and design, exposure categories and reported outcomes. The units used in all data were checked and converted where required to achieve consistency. Separate databases were developed for the freshwater cyanobacteria and algae studies and for the marine cyanobacteria and algae studies. A summary of the key parameters assessed for each study and a breakdown of the number of papers falling into a range of criteria are given in Tables 16 and 17.

In order to answer Secondary Question 5 regarding benthic cyanobacteria with reference to dog deaths, one of the filters applied was to discriminate animal and human studies. To achieve this the data in Tables 16 and 17 were divided into animal or human studies. The study by Trevino-Garrison *et al.* (2015) contained data for both humans and animals, explaining why the sum of human and animal freshwater studies (28) exceeds the total number of freshwater studies assessed (27).

The majority of the papers assessed were peer-reviewed with the exception of 3 freshwater and 1 marine study, and all of the studies were from field observations with no lab-based investigations as would be expected for recreational exposure situations (Table 16). All of the human exposure studies assessed (9 studies) were from exposure to planktonic organisms apart from 3 where the type was not given. This contrasted to animal studies where the split was 9 benthic: 5 planktonic: 1 mixed and 2 not given (Table 16). This reflects the situation that poisonings due to ingestion of benthic cyanobacteria represent the majority of the published primary studies for animal exposure. The majority of human exposure to cyanobacteria occurred in lakes in the freshwater environment (9), whereas poisoned animals could be exposed in freshwater lakes, rivers or ponds (Table 16).

Studies were assessed to indicate where toxins or their surrogates were determined or analysed for both within the exposure environment and/or within the subject of the exposure (Table 17). Surrogates included cell counts, chlorophyll-a, cell surface area, or the alanine aminotransferase (ALT) test which is a serum liver enzyme biomarker to determine liver injury. Toxins or surrogates could be measured within subjects for example in tissues, organs, or blood.

The breakdown of numbers showed that for freshwater human studies, toxins and/or surrogates were determined in the environment in 73% of studies (8/11). Toxins were determined in the human subjects in only 36% of the studies (4/11), and surrogates were not determined within any human subjects (Table 17). This contrasted to freshwater animal studies where toxins were confirmed in the environment for the majority (15/17: 88%) of animal poisonings, and surrogates were determined in a slightly lower proportion (11/17: 65%). Also, for animals, toxins were determined within a high proportion of poisoned animals (11/17: 65%) (Table 17). Surrogates were determined within a lower proportion of animals (6/17: 35%), which often represented looking for cells within stomach contents. These latter figures relating to published studies of poisoned animals represent a situation where the medical assessment was the subject of examination by veterinarians who often undertook a range of diagnostic tests to confirm the nature of the poisoning.

For the marine primary studies with humans, toxins were determined in the environment in only 50% of studies (11/22) and surrogates were determined in 68% of studies (15/22). This represents a low proportion of the studies that assessed whether it is possible to potentially attribute exposure to any known toxin or toxic organism. Similarly, the human studies had very low proportion of toxin determinations within subjects (3/22: 14%) and only one study with a determination of a surrogate within a human (Table 17). The single animal poisoning in the marine environment reported toxins measured within the environment but no other assessments relating to toxins or surrogates within the animal.

The type and degree of health assessment undertaken and reported from human primary studies is given in Table 18. This breakdown of numbers showed that in moderate proportions of studies the outcomes were self-reported rather than being properly medically diagnosed by trained personnel. For freshwater primary studies, the proportion medically diagnosed was 33% (5/15), and for marine studies the proportion was greater with 70% (16/23) of assessments being medically diagnosed. Health outcomes reported for the range of freshwater and marine studies covered a broad spectrum of diagnoses from respiratory, gastrointestinal (GI), irritation (ear, nose, or skin), fever or headache to cognitive symptoms (Table 18).

As indicated above the secondary question relating to animal deaths, in particular dog poisonings and benthic cyanobacteria, was addressed by the analysis of studies captured in the literature search for the primary question. The search produced twenty-five papers on animal studies and 18 of these were included as primary studies. A detailed description of these 18 primary source papers for the animal literature is given in Table A10-1 in Appendix 10. From the 18 primary animal studies, 9 reported exposure to benthic cyanobacteria, 6 to planktonic cyanobacteria (1 marine), 1 to a mixture of cyanobacteria and 2 did not report the habitat type. The majority of the studies were from the USA (8), followed by New Zealand (3), the Netherlands (2) and 1 each from Canada, Finland (marine) France, Germany and Switzerland. The exposure scenario was predominantly direct immersion with one direct non-immersion and one unspecified. The majority of studies reported ingestion as the exposure pathway with one also reporting dermal exposure. The marine study was uncertain about exposure, but ingestion was suspected. Health assessment and outcomes from these primary animal studies are summarised in Table 19. The range of adverse health outcomes for animals encompassed a similar range of symptoms to reports from human exposure including gastrointestinal (GI), irritation, or neurotoxicity symptoms. The animal primary studies also included a relatively high number (14/18: 78%) that recorded death as the end point (Table 19).

The assessment of the primary animal studies contrasted to human studies in that all animal studies were diagnosed by a trained professional such as a veterinarian (Table 19). This reflects that these studies were case reports or case series that set out to report the investigation of novel animal poisonings and achieved publication in medical or veterinary science journals.

Table 16: Breakdown of the numbers of primary freshwater and marine studies in relation to peer-review status, study type, cyanobacterial growth habit and water source type.

	Freshwater (total 27)		**Marine (total 23)**	
Category	Human[1.]	Animal[1.]	Human	Animal
Total papers	11	17	22	1
Peer reviewed				
Y	9	16	21	1
N	2	1	1	0
Study type				
Field	11	17	22	1
Lab	0	0	0	0
Cyanobacterial growth habit				
Benthic	0	9	3	0
Planktonic	9	5	18	1
Mixed	0	1	0	0
Not given	3	2	1	0
Water source type				
Sea	0	0	20	1
River	0	4	1 (estuarine)	0
Lake	9	9	0	0
Pond	0	3	0	0
Mixed	1	0	0	0
Not given	2	1	1	0

[1] Trevino-Garrison *et al.*, 2015 contained data for both humans and animals, and the total for studies with human and animal data is therefore 28, one more than total number of freshwater studies.

Table 17: Breakdown of the numbers of primary freshwater and marine studies to indicate where either toxins or surrogates were measured both in the exposure environment and within the subject.

		Freshwater (total 27)		**Marine (total 23)**	
Category		Human (11)	Animal (17)	Human (22)	Animal (1)
Toxin[1.] measured in the environment	Y	8	15	11	0
	N	4	2	11	1
Toxin[2.] determined in within the subject	Y	4	11	3	1
	N	8	6	19	0
Surrogate/s[3.] measured in the environment	Y	8	11	15	0
	N	4	6	7	1
Surrogate/s determined within the subject	Y	0	6	1	0
	N	11	11	21	1

The number of freshwater papers was only 27, however

[1] Trevino-Garrison *et al.*, 2015 reported both Y and N;

[2.] Vidal *et al.*, 2017 reported both Y and N;

[3.] Surrogates included cell counts, chlorophyll-a, cell surface area, alanine aminotransferase (ALT) test which is a serum liver enzyme biomarker to determine liver injury.

Table 18: Breakdown of numbers of primary freshwater and marine human exposure studies indicating the type of health assessment undertaken and the health outcomes reported.

	Freshwater	**Marine**
Health Assessment Type		
Medically diagnosed[1.]	5	16
Self-reported[2.]	7	7
Mixed	1	0
Not given or not applicable	2	0
Health Outcome Reported		
Respiratory	6	17
GI	7	5
Irritation[3.]	6	7
Fever or headache	4	3
Cognitive	0	1
Mastoiditis	0	1
No symptoms	2[4]	0
Not given	1	0

[1] medically diagnosed was determined by a doctor, nurse, veterinarian or other qualified health-practitioner;

[2] self-reported;

[3] irritation included eye, ear, nose and skin irritation;

[4] Backer *et al.*, 2008 and 2010 - Participants reported no symptom increases following exposure.

Table 19: Breakdown of numbers of primary freshwater and marine exposure studies in animals indicating the type of health assessment undertaken and the health outcomes reported.

Health assessment	Medically diagnosed[1.]	18
	Self-reported[2.]	0
Health outcome	Respiratory	0
	GI	4
	Irritation[3.]	1
	Fever or headache	0
	Neurotoxicosis	1
	Death	15

[1] medically diagnosed is defined as the health outcome assessment was determined by a doctor, nurse, veterinarian or other qualified health practitioner;
[2] self-reported by the animal owner;
[3] irritation included eye, ear, nose and skin irritation.

3.4.2 Assessment of Grey Literature with regard to the Secondary Questions

The results of the assessment of the grey literature that were used to contribute to answering the Secondary Questions are given below.

Secondary Question 1

What are the indicators/surrogates of this/these hazard/s? What are the advantages and disadvantages of using surrogates versus monitoring specific toxins?

Secondary Question 1 was addressed by a review of selected reviews (see Section 2.1.1). This is discussed in full in Section 5.1.4 of the Evidence Evaluation Report. However, as part of the grey literature search a broad range of information was found in relation to indicators or measures that were used as surrogates for toxin hazards in a range of published guideline values. This information is given here to provide a comprehensive overview of usage and application across jurisdictions. The three surrogates that were used in published guidelines were cell counts, chlorophyll-a concentration and biovolume measurement. Details of the jurisdictions that used these surrogates within their guidelines are given in Table 20.

Table 20: Jurisdictions that use a range of measures as surrogates in freshwater and marine recreational guidelines. Those that use surrogates only and not cyanotoxin concentration values are indicated by (*). The table identifies US state guidelines separately as a group as they represent a large number of individual states that have separately published guidelines.

Freshwater			**Marine**		
Cell counts	**Chlorophyll-a**	**Biovolume**	**Cell counts**	**Chlorophyll-a**	**Biovolume**
Australia[1.] NSW (*) ACT (*) Vic (*) Tas Canada Czech Republic (*) France Italy Turkey Scotland (*) WHO 2003 (removed in 2021)	Netherlands (*) Turkey Scotland (*) WHO 2003 WHO 2021[2.]	Australia NSW (*) ACT (*) Vic (*) Tas NZ Netherlands (*) WHO 2021[2.]	Australia[1] (*) NSW (*) WA (*)		
USA States					
California Connecticut (*) Idaho (*) Indiana Kansas Massachusetts Montana New Jersey Ohio Rhode Island Utah Virginia Wisconsin	New York Ohio		Florida (*)		

[1.] NHMRC (2008)

[2.] Chorus and Testai (2021)

Secondary Question 2

What guidelines, guidance and implementation practices are in place in comparable countries to minimise or manage this/these hazards and risks/s?

The grey literature search found recreational water quality guidelines for freshwater cyanobacteria and cyanobacterial toxins for 42 jurisdictions. These can be divided into a cross section of 17 jurisdictions which represented international and national agencies and 25 jurisdictions within the USA (2 Federal and 23 states). The US information was collated and presented separately for the individual states as in some cases it represented a diversity of approaches which were useful to capture individually. Not all documents provided full details of the derivation of the guideline values. The collation of derivations and the associated recreational water guideline values for freshwater cyanobacteria and cyanotoxins from various countries and Australian states is given in Appendix 6.

The derivations of the tolerable daily intake (TDI) or reference dose (RfD) for the range of cyanotoxins: microcystin, saxitoxin, anatoxin-a and cylindrospermopsin that were available are given in Table A6-1 (Appendix 6). The derivation of guideline values in the different countries and jurisdictions from these TDI or RfD values are also given in Table A6-2 (Appendix 6). Compilation of the derivation of recreational water guidelines in terms of cyanobacterial cell counts for the countries, jurisdictions, and Australian states where this is given in Table A6-3 (Appendix 6). A collation of recreational water guideline values developed for marine algae and cyanobacteria from Australian and international sources is given in Table A6-4 (Appendix 6).

The guidelines found from the search were assessed to collate the differing values of toxin concentration, cell counts, and other surrogates used for the Alert and Action levels and these are compiled in Appendix 7. The concept of 'Guidance' or 'Alert' levels related to recreational exposure guidelines was first developed and widely promoted by Chorus and Bartram (1999). Following this approach many countries have used this guidance approach as a basis for implementing guidelines or action levels for assessing health risks from cyanobacteria through recreational usage of waterbodies. In general, the jurisdictions have often employed three alert levels associated with advice, warnings and action related to site usage and/or closure. There are however often considerable differences in the toxin concentrations or cell count levels triggering them and in their assessments of the health risk arising from exposure.

For the purposes of this review the range of national and local jurisdiction guidelines were assessed to extract an 'Alert' and 'Action' level for comparative purposes. The Alert level was defined as stage where some form of initial advisory or advice was issued, and the Action level was generally the point of declaring the requirement for site or waterbody closure. It was not always easy to find a precise fit to these levels, however the comparison was instructive to achieve a view on the application of guidelines in different jurisdictions. Not all jurisdictions distinguished between Alert and Action values, so where only one value was given, this was listed as an Action value. As part of this assessment information on the use of the presence of cyanobacterial scums as Action levels was noted. This can be regarded as an imprecise estimate of hazard, and the advice terms used for the assessment of scums reflect this. The descriptive terms varied and included "scums being persistent"; "high probability of scums"; "visible thick scums"; "scums well-established"; "scums containing toxic cyanobacteria" as examples.

Compilation of recreational water guideline values expressed as Action and Alert levels for specific freshwater cyanotoxins, cell counts and other surrogates from Australian and international sources (excluding USA) is given in Table A7-1 (Appendix 7). A separate table of the equivalent information for the US federal and state jurisdictions is provided in Table A7-2 (Appendix 7). An administrative and technical assessment of existing guidelines from selected jurisdictions (New Zealand, Canada, U.S. EPA, WHO, California, Massachusetts, Oregon, and Washington) is given in Appendix 8. This assessment protocol was developed by NHMRC based upon assessment criteria outlined in the AGREE Reporting Checklist (citation: https://www.bmj.com/content/352/bmj.i1152).

Secondary Question 3

What are the specific exposure scenarios that might increase risk for sub-populations (e.g. infants playing in shallow waters in presence of benthic mats, water skiers/beach goers inhaling aerosolised cells/toxins) and how are these managed by other organisations?

The literature search found no studies specifically related to indigenous groups or to exposure of infants in relation to benthic mats. However, there were several marine studies that investigated adverse effects of aerosolised cell material and toxins upon asthmatics. This is discussed in detail in the Discussion.

Secondary Question 4

What is the extent of evidence of adverse effects due to recreational exposure to marine cyanobacteria or algae (e.g. skin irritation due to *Lyngbya majuscula* or inhalation-related symptoms due to cells/toxins aerosolised by wave action, boats, jet-skis, etc.)? Are there any existing guidelines that address these exposure risks?

The assessment of the results for marine studies that were captured in the literature search for the primary question is given in Section 3.4.1 above. The grey literature search for guidelines found only four recreational water quality guidelines for marine algae and cyanobacteria and no guidelines for marine algal or cyanobacterial toxins. It is important to note that no national or local jurisdiction has yet to develop any guidelines for specific marine toxins for recreation water quality in the marine environment. The four existing guidelines consisted of cell number guidelines for the dinoflagellate *Karenia brevis* from Florida, USA, and cell number guidelines for dinoflagellates and various marine cyanobacteria from three Australian sources (NHMRC, 2008; Water NSW and Western Australian Department of Health) (Table 21). None of these guidelines included any other surrogates or indicators in addition to cell counts. Not all jurisdictions distinguished between Alert and Action values, so where only one value was given this value was listed as an Action value in Table 21.

Secondary Question 5

Much of the evidence for freshwater benthic cyanotoxin production in Australia is anecdotal and often linked to dog deaths following swimming in water bodies (e.g. at least 4 dog deaths in Lake Burley Griffin). It would be useful to try to collate the grey literature evidence to provide a clearer picture of the extent of any risk.

This Secondary Question relating to animal deaths, in particular dog poisonings, was addressed by the analysis of studies captured in the literature search for the primary question. These studies were regarded as being likely to provide potentially higher quality evidence which related to toxin and cyanobacterial types associated with the dog poisonings along with comprehensive veterinary assessment of adverse health outcomes rather than information from anecdotal grey literature reports. These results are covered in Section 3.4.1 above.

Table 21: Collation of derivations of recreational water guideline values for marine algae and cyanobacteria from international and Australian sources.

Source	Organism	Cell count [1.]		Comment
		Alert[2.]	**Action[3.]**	
UNITED STATES				
Florida Fish and Wildlife Research Institute 2021	*Karenia brevis*	>10,000 cells/L – 100,000 cells/L (LOW)	>100,000 cells/L – 1,000,000 cells/L (MED) >1,000,000 cells/L (HIGH)	LOW, MED and HIGH-respiratory irritation No information about derivation of levels
AUSTRALIA				
National NHMRC 2008	*Karenia brevis*	≤1 cell/mL	>1 - <10 cells/mL (Tier 1) ≥10 cells/mL (Tier 2)	NHMRC 2008 Table 7.3
	Lyngbya majuscula *Pfiesteria* sp.		Present in: Low numbers (Tier 1) High numbers (Tier 2)	'low' and 'high' not defined
Water NSW 2021	*Karenia brevis*		10 cells/mL	
	Lyngbya *Pfiesteria*		High numbers	'High' not defined
Western Australia Department of Health, Public Health and Clinical Services 2021	*Lyngbya majuscula*	Detected	Relative widespread visible presence of algal filaments	NHMRC, 2008
	Trichodesmium		Presence of algal scums	NHMRC, 2008
	Other cyanobacteria	>5,000 cells/L	>15,000 cells/L	
	Karenia brevis	>5,000 cells/L	>10,000 cells/L	
	Karenia sp.	>50,000 cells/L	>100,000 cells/L	
	Pfiesteria	Detected	Presence of algal scums	NHMRC, 2008

[1.] Cell count based on all total potentially toxic cyanobacteria unless specified;
[2.] .Alert = health advisory; [3.] Action = health warning/guideline/health advisory; where sources did not distinguish between Alert and Action values the value was listed as Action

3.4.3 Material from Grey Literature related to the Implementation of Guidelines

A range of resources from different jurisdictions was identified during the grey literature search. These are considered to have potential value for agencies and organisations (e.g. state agencies, local government, lake managers, etc.) that are required to implement recreational guidelines or for others that may have to deal with the range of impacts on both humans or animals (e.g. physicians, veterinarians, dog owners, farmers, etc.). A selection of examples of material that may provide useful resources for information and advice is given in Appendix 9. These examples are not exhaustive but are provided as a guide. The resource material covers the following topics: local action plans, field identification of cyanobacteria, fact sheets about cyanobacterial blooms, sampling and monitoring advice, and advice for veterinarians, dog owners, physicians, general homeowners, irrigators and livestock owners.

4 Declared Interests

The author of this review (Michael D Burch) has the following declared interests:

Interest	Interest Details
NHMRC	The reviewer was involved in the development of the previous version of the NHMRC guidelines (The Guidelines for Managing Risks in Recreational Water. 2008). This was initially as a volunteer member of the steering Committee and subsequently as chair of the Committee (2004-2006).
Visiting Associate Professor in the School of Biological Sciences in the Faculty of Sciences at the University of Adelaide	The reviewer participates in research projects with university staff and students; publishes journal articles with University affiliation. This includes publications on cyanobacteria and algae.
Director, Australis Water Consulting Pty Ltd.	The reviewer is the Director and Principal of an Australian water consulting company that provides advice on water management and research management to a range of Australian and international clients, including government agencies, water authorities, research Institutions, Universities and local government organisations.
Professional association with members of the NHMRC Recreational Water Quality Advisory Committee (RWQAC) (the Committee)	The reviewer has professional scientific relationships with several members (three members) of the Committee which has included joint research and producing joint publications at different times over the last 30 years.
Member of Water Research Australia through affiliation with the University of Adelaide, and as a consultant.	The reviewer provides professional and scientific advice to Water RA staff on research project design and management. This may be as a consultancy on a normal commercial basis.
The reviewer is a joint author on the following paper which was included in the review: Pilotto, L. S., Douglas, R. M., Burch, M. D., Cameron, S., Beers, M., Rouch, G. J., Robinson, P., Kirk, M., Cowie, C. T., Hardiman, S., Moore, C. and Attewell, R. G. (1997). Health effects of exposure to cyanobacteria (blue-green algae) during recreational water-related activities. Australian and New Zealand Journal of Public Health 21, 562-566.	The study by Pilotto *et al*., (1997) was included in the review although it was outside the date range specified (2006-2021). This was because it was a highly relevant Australian epidemiological study designed at the time to gather information to inform exposure to toxic cyanobacteria in recreational water environments.

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6 Appendices

6.1 Appendix 1 Development of Literature Searches

Appendix 1 outlines the development of literature searches in the PubMed® and Scopus® databases to collect evidence to answer the questions for this review. It is a compilation of the search structure, terms, and results for all searches as they progressively evolved and were refined. Final versions of searches are given in the Technical Report.

This Appendix contains the following:

Table A1-1: PubMed® individual concept searches in sequence for development of the searches in the Cyanobacteria/Algae/Toxins (CAT) concept.

Table A1-2: PubMed® individual concept searches in sequence for development of the searches in the Recreation/al (R) concept.

Table A1-3: PubMed® individual concept searches in sequence for development of the searches in the Health (H) concept.

Table A1-4: PubMed® Combined Searches (Code PM-C)

Table A1-5: Scopus® individual concept searches in sequence for development of the searches in Cyanobacteria/Algae/Toxins; Recreation/al; Health concepts.

Table A1-6: Scopus® combined searches (Code S-C).

Table A1-7: PubMed® searches for individual Endotoxin/LPS and BMAA concepts.

Table A1-8: PubMed® combined searches related to Endotoxin/LPS and BMAA concepts.

Searches for the individual concepts (Cyanobacteria/Algae/Toxins; Recreation/al; Health) and the variations and iterations in their development and their inclusion in subsequent combined searches were identified by codes and associated numbers. A different system of identifier codes was used for PubMed® and Scopus® searches.

Table A1-1: Details and sequence of the development of the individual searches for Cyanobacteria/Algae/Toxins concept in PubMed®

Search Number for Concept	Search Code number	Part of Combined SEARCH code #	Date of Search/s	Description, Search String and Results
1, 2	#101 and #102		19/08/2020	This search uses the initial search terms specified in the PECO by the Committee and listed in the research protocol. These initial searches made limited use of indexing terms ("Cyanobacteria"[mh:noexp]; "harmful algal bloom"[mh] only), wild cards or restriction of searching to titles and abstracts. **Search String:** "Cyanobacteria"[mh:noexp] OR cyanobacteria* OR Blue-green algae OR cyanobacteria [tiab] OR alga* OR cyanobacterial bloom* OR algal bloom* OR "harmful algal bloom"[mh] OR Cyanotoxin* OR Neurotoxin* OR Hepatotoxin* OR Microcystin* OR Saxitoxin* OR Cylindrospermopsin* OR Anatoxin* OR Nodularin* OR Cylindrospermopsis raciborskii OR Raphidiopsis OR Microcystis OR Dolichospermum circinale OR Anabaena circinalis OR Nodularia spumigena OR Lyngbya wollei OR "total cyanobacteria" **Results:** 19/08/2020: 77,726 (2006-2021)
3	#103		19/08/2020	Update to Search #102 restricting the searches for terms to titles and abstracts. The effect can be seen in the reduction of search results from 77,726 down to 54,903 for the nominated period (2006-2021). **Search String:** "Cyanobacteria"[mh:noexp] OR cyanobacteria*[tiab] OR alga*[tiab] OR cyanobacterial bloom* OR algal bloom* OR "harmful algal bloom"[mh] OR Cyanotoxin*[tiab] OR Neurotoxin*[tiab] OR Hepatotoxin*[tiab] OR Microcystin*[tiab] OR Saxitoxin*[tiab] OR Cylindrospermopsin*[tiab] OR Anatoxin*[tiab] OR Nodularin*[tiab] OR Cylindrospermopsis raciborskii[tiab] OR Raphidiopsis[tiab] OR "Microcystis"[mh] OR Dolichospermum circinale[tiab] OR Anabaena circinalis[tiab] OR Nodularia spumigena[tiab] OR Lyngbya wollei[tiab] OR "total cyanobacteria"[tiab] **Results:** 19/08/2020: 54,903 (2006-2021)
4	#104		19/08/2020	Update to Search #103 restricting all search terms to title and abstracts. The effect is minimal. **Search String:** "Cyanobacteria"[mh:noexp] OR cyanobacteria*[tiab] OR alga*[tiab] OR cyanobacterial bloom*[tiab] OR algal bloom*[tiab] OR "harmful algal bloom"[mh] OR Cyanotoxin*[tiab] OR Neurotoxin*[tiab] OR Hepatotoxin*[tiab] OR Microcystin*[tiab] OR Saxitoxin*[tiab] OR Cylindrospermopsin*[tiab] OR Anatoxin*[tiab] OR Nodularin*[tiab] OR Cylindrospermopsis raciborskii[tiab] OR Raphidiopsis[tiab] OR "Microcystis"[mh] OR Dolichospermum circinale[tiab] OR Anabaena circinalis[tiab] OR Nodularia spumigena[tiab] OR Lyngbya wollei[tiab] OR "total cyanobacteria"[tiab] **Results:** 19/08/2020: 54,851 (2006-2021)

Table A1-1: (continued)

5-7	#105, #106, #107		20/08/2020	Update to Search #104 as follows: • Add back Blue-green algae*[tiab]. Incorporate further MeSH term search terms: “harmful algal bloom*”[mh:noexp], “neurotoxin”[mh:noexp], “microcystin”[mh:noexp], “saxitoxin*”[mh:noexp] • Other minor variations were made to add or remove wildcards within MeSH terms to determine effects. This has a minor impact upon the number of results (Increase of approximately 1,000 results from 54,851 to 55,890) **Search String:** “cyanobacteria”[mh:noexp] OR cyanobacteria*[tiab] OR Blue-green alga*[tiab] OR alga*[tiab] OR toxic alga*[tiab] OR cyanobacterial bloom*[tiab] OR algal bloom*[tiab] OR “harmful algal bloom*”[mh:noexp] OR harmful algal bloom*[tiab] OR cyanotoxin*[tiab] OR “neurotoxin”[mh:noexp] OR neurotoxin*[tiab] OR hepatotoxin*[tiab] OR “microcystin”[mh:noexp] OR microcystin*[tiab] OR “saxitoxin*”[mh:noexp] OR saxitoxin*[tiab] OR cylindrospermopsin*[tiab] OR anatoxin*[tiab] OR nodularin*[tiab] OR cylindrospermopsis raciborskii[tiab] OR raphidiopsis[tiab] OR “microcystis”[mh:noexp] OR microcystis[tiab] OR dolichospermum circinale[tiab] OR anabaena circinalis[tiab] OR nodularia spumigena[tiab] OR lyngbya wollei[tiab] OR total cyanobacteria*[tiab] **Results:** 20/08/2020: 55,890 (2006-2020)
8	#108		21/08/2020	Update to Search #107: • Add a range of terms related to LPS and endotoxins as follows using OR “Lipopolysaccharides”[mh:noexp] OR lipopolysaccharide*[tiab] OR LPS[tiab] OR “endotoxin”[mh:noexp] OR endotoxin[tiab] Error Message: *Quoted phrases not found: "endotoxin"* – indicating that this is not a MeSH term. This search generated a very large increase in results indicating the extent of the literature related to LPS and endotoxins. The number of results increased by approximately 80,000 publications from 55,890 to 135,420. **Search String:** "cyanobacteria"[mh:noexp] OR cyanobacteria*[tiab] OR Blue-green alga*[tiab] OR alga*[tiab] OR toxic alga*[tiab] OR cyanobacterial bloom*[tiab] OR algal bloom*[tiab] OR "harmful algal bloom"[mh:noexp] OR harmful algal bloom*[tiab] OR HAB[tiab] OR cyanotoxin*[tiab] OR neurotoxin*[tiab] OR hepatotoxin*[tiab] OR microcystin*[tiab] OR "microcystin"[mh:noexp] OR "neurotoxin"[mh:noexp] OR "saxitoxin"[mh:noexp] OR saxitoxin*[tiab] OR cylindrospermopsin*[tiab] OR anatoxin*[tiab] OR nodularin*[tiab] OR cylindrospermopsis raciborskii[tiab] OR raphidiopsis[tiab] OR "microcystis"[mh:noexp] OR microcystis[tiab] OR dolichospermum circinale[tiab] OR anabaena circinalis[tiab] OR nodularia spumigena[tiab] OR lyngbya wollei[tiab] OR total cyanobacteria*[tiab] OR “Lipopolysaccharides”[mh:noexp] OR lipopolysaccharide*[tiab] OR LPS[tiab] OR “endotoxin”[mh:noexp] OR endotoxin[tiab] **Results:** 21/08/2020: 135,420 (2006-2020)

Table A1-1: (continued)

9	#109		21/08/2020	Update and variation to Search #108 as follows: • Add the LPS and endotoxins terms from #108 using the AND operator. AND "Lipopolysaccharides"[mh:noexp] OR lipopolysaccharide*[tiab] OR LPS[tiab] OR "endotoxin"[mh:noexp] OR endotoxin[tiab] Note the bracketing or syntax for PubMed® may not be correct. This alteration resulted in a significant reduction in numbers, down from 135,420 to 74,921. **Search String:** "cyanobacteria"[mh:noexp] OR cyanobacteria*[tiab] OR Blue-green alga*[tiab] OR alga*[tiab]OR toxic alga*[tiab] OR cyanobacterial bloom*[tiab] OR algal bloom*[tiab] OR "harmful algal bloom"[mh:noexp] OR harmful algal bloom*[tiab] OR HAB[tiab] OR cyanotoxin*[tiab] OR neurotoxin*[tiab] OR hepatotoxin*[tiab] OR microcystin*[tiab] OR "microcystin"[mh:noexp] OR "neurotoxin"[mh:noexp] OR "saxitoxin"[mh:noexp] OR saxitoxin*[tiab] OR cylindrospermopsin*[tiab] OR anatoxin*[tiab] OR nodularin*[tiab] OR cylindrospermopsis raciborskii[tiab] OR raphidiopsis[tiab] OR "microcystis"[mh:noexp] OR microcystis[tiab] OR dolichospermum circinale[tiab] OR anabaena circinalis[tiab] OR nodularia spumigena[tiab] OR lyngbya wollei[tiab] OR total cyanobacteria*[tiab] AND "Lipopolysaccharides"[mh:noexp] OR lipopolysaccharide*[tiab] OR LPS[tiab] OR "endotoxin"[mh:noexp] OR endotoxin[tiab] **Results:** 21/08/2020: 74,921 (2006–2021)
10	#110		21/08/2020	Update and variation to Search #109 as follows: • Test to remove a number of terms for individual cyanobacterial genera and species and individual cyanotoxin types to make a reduced search string. The terms removed were: "saxitoxin"[mh:noexp] OR saxitoxin*[tiab] OR cylindrospermopsin*[tiab] OR anatoxin*[tiab] OR nodularin*[tiab] OR cylindrospermopsis raciborskii[tiab] OR raphidiopsis[tiab] OR "microcystis"[mh:noexp] OR microcystis[tiab] OR dolichospermum circinale[tiab] OR anabaena circinalis[tiab] OR nodularia spumigena[tiab] OR lyngbya wollei[tiab] Results of this search appear to be almost identical to #109 above, indicating that it appears to make little difference to exclude all of the chosen species and genus names and the specific terms for individual toxins etc. It is assumed that the publications are captured by general indexed terms for such as cyanobacteria, toxic alga*, or harmful algal blooms, etc. **Search String:** "cyanobacteria"[mh:noexp] OR cyanobacteria*[tiab] OR Blue-green alga*[tiab] OR alga*[tiab]OR toxic alga*[tiab] OR cyanobacterial bloom*[tiab] OR algal bloom*[tiab] OR "harmful algal bloom"[mh:noexp] OR harmful algal bloom*[tiab] OR HAB[tiab] OR cyanotoxin*[tiab] OR neurotoxin*[tiab] OR total cyanobacteria*[tiab] AND "Lipopolysaccharides"[mh:noexp] OR lipopolysaccharide*[tiab] OR LPS[tiab] OR "endotoxin"[mh:noexp] OR endotoxin[tiab] **Results:** 21/08/2020: 74,920 (2006–2021)

Table A1-1: (continued)

11	#111		24/08/2020	This was a further variation to Search #109 as follows: • Include the Endotoxin/LPS terms with the OR operator: OR "Endotoxins"[mh:noexp] OR Endotoxin*[tiab] OR "Lipopolysaccharides"[mh] OR Lipopolysaccharide*[tiab] OR LPS[tiab] • Add a range of Anatoxin-related terms as follows: "anatoxin"[mh:noexp] OR "anatoxin a"[mh:noexp] OR "anatoxin-a(s)"[mh:noexp] OR anatoxin*[tiab] OR "homoanatoxin"[mh:noexp] OR homoanatoxin*[tiab] This search generated a larger number of results which is assumed to be primarily due to the inclusion of endotoxin/LPS terms. This was checked by removal of the terms again in the next Search #112. **Search String:** "Cyanobacteria"[mh:noexp] OR cyanobacteria*[tiab] OR Blue-green alga*[tiab] OR alga*[tiab] OR toxic alga*[tiab] OR cyanobacterial bloom*[tiab] OR algal bloom*[tiab] OR "Harmful Algal Bloom"[mh:noexp] OR harmful algal bloom*[tiab] OR HAB[tiab] OR cyanotoxin*[tiab] OR "Neurotoxins"[mh:noexp] OR neurotoxin*[tiab] OR hepatotoxin*[tiab] OR "microcystin"[mh:noexp] OR microcystin*[tiab] OR "Saxitoxin"[mh:noexp] OR saxitoxin*[tiab] OR "cylindrospermopsin"[mh:noexp] OR cylindrospermopsin*[tiab] OR "anatoxin"[mh:noexp] OR "anatoxin a"[mh:noexp] OR "anatoxin-a(s)"[mh:noexp] OR anatoxin*[tiab] OR "homoanatoxin"[mh:noexp] OR homoanatoxin*[tiab] OR "nodularin"[mh:noexp] OR nodularin*[tiab] OR "Endotoxins"[mh:noexp] OR Endotoxin*[tiab] OR "Lipopolysaccharides"[mh] OR Lipopolysaccharide*[tiab] OR LPS[tiab] OR "Cylindrospermopsis raciborskii"[mh:noexp] OR cylindrospermopsis raciborskii[tiab] OR raphidiopsis[tiab] OR "Microcystis"[mh:noexp] OR Microcystis[tiab] OR "Dolichospermum circinale"[mh:noexp] OR Dolichospermum circinale[tiab] OR "Anabaena circinalis"[mh:noexp] OR Anabaena circinalis[tiab] OR "Nodularia spumigena"[mh:noexp] OR Nodularia spumigena[tiab] OR total cyanobacteria*[tiab] **Results:** 24/08/2020: 143,301 (2006-2021) This search generated a number of error messages: *Quoted phrases not found: "microcystin", "cylindrospermopsin", "anatoxin", "anatoxin a", "anatoxin-a(s)", "homoanatoxin", "nodularin", "Cylindrospermopsis raciborskii", "Dolichospermum circinale", "Anabaena circinalis", "Nodularia spumigena". These were investigated and corrected in Search #113.*

Table A1-1: (continued)

12	#112		24/08/2020	This search was to reproduce Search #111 with the removal of the endotoxin and LPS terms. The result was a significant reduction in results (from 143,301 to 59, 686) **Search String:** "Cyanobacteria"[mh:noexp] OR cyanobacteria*[tiab] OR Blue-green alga*[tiab] OR alga*[tiab] OR toxic alga*[tiab] OR cyanobacterial bloom*[tiab] OR algal bloom*[tiab] OR "Harmful Algal Bloom"[mh:noexp] OR harmful algal bloom*[tiab] OR HAB[tiab] OR cyanotoxin*[tiab] OR "Neurotoxins"[mh:noexp] OR neurotoxin*[tiab] OR hepatotoxin*[tiab] OR "microcystin"[mh:noexp] OR microcystin*[tiab] OR "Saxitoxin"[mh:noexp] OR saxitoxin*[tiab] OR "cylindrospermopsin"[mh:noexp] OR cylindrospermopsin*[tiab] OR "anatoxin"[mh:noexp] OR "anatoxin a"[mh:noexp] OR "anatoxin-a(s)"[mh:noexp] OR anatoxin*[tiab] OR "homoanatoxin"[mh:noexp] OR homoanatoxin*[tiab] OR "nodularin"[mh:noexp] OR nodularin*[tiab] OR "Cylindrospermopsis raciborskii"[mh:noexp] OR cylindrospermopsis raciborskii[tiab] OR raphidiopsis[tiab] OR "Microcystis"[mh:noexp] OR Microcystis[tiab] OR "Dolichospermum circinale"[mh:noexp] OR Dolichospermum circinale[tiab] OR "Anabaena circinalis"[mh:noexp] OR Anabaena circinalis[tiab] OR "Nodularia spumigena"[mh:noexp] OR Nodularia spumigena[tiab] OR total cyanobacteria*[tiab] **Results:** 24/08/2020: 59,686 (2006-2021 The following error message was given: *"Quoted phrases not found: "microcystin", "cylindrospermopsin", "anatoxin", "anatoxin a", "anatoxin-a(s)", "homoanatoxin", "nodularin", "Cylindrospermopsis raciborskii", "Dolichospermum circinale", "Anabaena circinalis", "Nodularia spumigena"*
13	#113		3/11/2020	This search was a major update to all previous searches to incorporate a more comprehensive range of cyanobacterial types and toxins and to correct indexing term errors. Some terms were also deleted as being not relevant to the concept. Corrections and alterations to #111 and further comments are as follows: • include a wider range of cyanobacterial and algal genera, types and names, A comprehensive list of all known toxic types – genera and species was developed from the recent WHO-sponsored updated publication Chorus and Welker, 2021. • Delete the terms "Neurotoxins"[mh:noexp] OR neurotoxin*[tiab] OR hepatotoxin*[tiab] – this was major alteration. Early test searches with these toxin terms in the CAT search generated very large results of papers that were not related to cyanobacteria or algae and to the topic. This was particularly important relevant when these terms were combined with Recreation and Health, as it captures publications related to neurotoxins and hepatotoxins which are unrelated to the topic and the primary question. • Add a range of benthic types (genera and species). • Add more general collective terms for algal types, groups and some species, e.g. phytoplankton, microalgae, chlorophyta, Dinoflagellida, *Pfiesteria piscicida*, Diatoms.

				• The following terms were reviewed in the MeSH Database: microcystins, nodularins, cylindrospermopsin, anatoxin-a and homoanatoxin-a, anatoxin-a(S), saxitoxins, lipopolysaccharides. Many of these toxins and some species names had been entered incorrectly in earlier searches as MeSH terms [mh] and should have been coded as Supplementary Concepts [nm]. These were entered for next searches as follows: “cylindrospermopsin”[nm:noexp] OR “anatoxin”[nm:noexp] OR “homoanatoxin”[nm:noexp] OR “nodularin”[nm:noexp] OR “Cylindrospermopsis raciborskii”[nm:noexp] OR raphidiopsis[tiab] OR “Dolichospermum circinale”[nm:noexp] • Add wildcard: microcysti*[tiab]. This will capture microcystis[tiab] OR microcystin[tiab]. Leave Microcystis[tiab] in the search. • Remove Raphidiopsis. Not a MeSH term and it defaults to Cylindrospermopsis raciborskii [Supplementary Concept] • alga*[tiab] will also capture green alga*[tiab]; benthic alga*[tiab]; marine alga*[tiab]; brown alga*[tiab] • Note: below alga*[tiab] will capture toxic alga*[tiab]; algal bloom*[tiab]; blue-green alga*[tiab] These are however still included in the search. • alga*[tiab] will not capture alga* bloom*[tiab] • cyanobacteria*[tiab] will capture toxic cyanobacteria*[tiab]; benthic cyanobacteria*[tiab]; total cyanobacteria*[tiab] • Leave out total cyanobacteria*[tiab] • phytoplankton*[tiab] will capture marine phytoplankton*[tiab]; toxic phytoplankton*[tiab] • dinoflagell*[tiab] will capture marine dinoflagell*[tiab]; toxic dinoflagell*[tiab] • Nostoc*[tiab] and Oscillatoria*[tiab] captures more than Nostoc[tiab] and Oscillatoria[tiab] • Microcoleus[tiab] captures Microcoleus autumnalis[tiab]. Can leave out Microcoleus autumnalis[tiab] • Microseira[tiab] captures Microseira wollei[tiab]. Can leave out Microseira wollei[tiab]. • Phormidium[tiab] captures Phormidium autumnale[tiab]. Leave out Phormidium autumnale[tiab] • Add BMAA; β-N-methylamino-L-alanine. **Search String:** "Cyanobacteria"[mh:noexp] OR cyanobacteria*[tiab] OR Blue-green alga*[tiab] OR alga*[tiab] OR toxic alga*[tiab] OR cyanobacteria* bloom*[tiab] OR alga* bloom*[tiab] OR "Harmful Algal Bloom"[mh:noexp] OR harmful algal bloom*[tiab] OR HAB*[tiab] OR "phytoplankton"[mh:noexp] OR phytoplankton*[tiab] OR "microalgae"[mh:noexp] OR microalga*[tiab] OR "Chlorophyta"[mh:noexp] OR chlorophyta[tiab] OR "Dinoflagellida"[mh:noexp] OR dinoflagell*[tiab] OR "Pfiesteria piscicida"[mh:noexp] OR pfiesteria piscicida[tiab] OR "Diatoms"[mh:noexp] OR diatom*[tiab] OR cyanotoxin*[tiab] OR "Microcystin"[mh:noexp] OR microcysti*[tiab] OR "Saxitoxin"[mh:noexp] OR saxitoxin*[tiab] OR "cylindrospermopsin"[nm:noexp] OR cylindrospermopsin*[tiab]

				OR "anatoxin a"[nm:noexp] OR "anatoxin-a(s)"[nm:noexp] OR anatoxin*[tiab] OR "homoanatoxin"[nm:noexp] OR homoanatoxin*[tiab] OR "nodularin"[nm:noexp] OR nodularin*[tiab] OR "Endotoxins"[mh:noexp] OR Endotoxi*[tiab] OR "Lipopolysaccharides"[mh] OR Lipopolysaccharide*[tiab] OR LPS[tiab] OR BMAA[tiab] OR β-N-methylamino-L-alanine[tiab] OR "beta-N-methylamino-L-alanine"[nm:noexp] OR beta-N-methylamino-L-alanine[tiab] OR "beta-(N-carboxy-N-methyl)aminoalanine"[nm:noexp] OR "beta-(N-carboxy-N-methyl)aminoalanine[tiab] OR "Cylindrospermopsis raciborskii"[nm:noexp] OR cylindrospermopsis raciborskii[tiab] OR "Microcystis"[mh:noexp] OR Microcystis[tiab] OR "Dolichospermum circinale"[nm:noexp] OR Dolichospermum circinale[tiab] OR "Anabaena circinalis"[mh:noexp] OR Anabaena circinalis[tiab] OR "Nodularia spumigena"[mh:noexp] OR Nodularia spumigena[tiab] OR Anabaenopsis[tiab] OR "Aphanizomenon"[mh:noexp] OR Aphanizomenon[tiab] OR Aphanocapsa[tiab] OR Aphanothece[tiab] OR Arthrospira[tiab] OR Calothrix[tiab] OR "Cuspidothrix issatschenkoi"[nm:noexp] OR Cuspidothrix issatschenkoi[tiab] OR Aphanizomenon issatschenkoi[tiab] OR Geitlerinima[tiab] OR Hapalosiphon[tiab] OR Leptolyngbya[tiab] OR Lyngbya[tiab] OR Microcoleus[tiab] OR Microseira[tiab] OR "Microseira wollei"[nm:noexp] OR Moorea[tiab] OR "Nostoc"[mh:noexp] OR Nostoc*[tiab] OR "Oscillatoria"[mh:noexp] OR Oscillatoria*[tiab] OR Phormidium[tiab] OR "Phormidium autumnale"[nm:noexp] OR Planktothrix[tiab] OR "Plectonema"[mh:noexp] OR Plectonema[tiab] OR Radiocystis[tiab] OR Raphidiopsis[tiab] OR Schizothrix[tiab] OR Scytonema[tiab] OR Scytonema cf crispum[tiab] OR Heteroscytonema crispum[tiab] OR Snowella[tiab] OR "Synechococcus"[mh:noexp] OR Synechococcus[tiab] OR "Synechocystis"[mh:noexp] OR Synechocystis[tiab] OR Tychonema[tiab] OR Umezakia[tiab] OR Woronichinia[tiab] **Results:** #113 string generated multiple errors which required further corrections in #114.

Table A1-1: (continued)

14	#114		8/11/2020	Corrections/modifications to Search #113 to deal with multiple further errors related mainly to indexing were incorporated into Search #114: • Delete alga*[tiab] This was deleted as a wildcard * cannot be used with words of less than 5 letters. • Change cyanobacteria* bloom*[tiab] to to cyanobacteria bloom*[tiab] OR cyanobacterial bloom*[tiab] • alga* bloom*[tiab] truncates alga* to alga. Change to algae bloom*[tiab] OR algal bloom*[tiab] • "Microcystin"[mh:noexp] is not a MeSH heading; change to "microcystin"[nm:noexp] Supplementary Concept • Delete beta-(N-carboxy-N-methyl)aminoalanine[tiab] as a [tiab] search; leave [nm:noexp] • "Anabaena circinalis" is not found as MeSH [mh:noexp]; therefore delete "Anabaena circinalis"[mh:noexp] • "Nodularia spumigena"[mh:noexp] is not a MeSH term and should be a Supplementary Concept. Change to "Nodularia spumigena"[nm:noexp] • "Cuspidothrix issatschenkoi"[nm:noexp] was not found as a Supplementary Concept. Delete "Cuspidothrix issatschenkoi"[nm:noexp]. Leave Cuspidothrix issatschenkoi[tiab] • Geitlerinima[tiab] spelling was incorrect. Change to geitlerinema[tiab] • Delete "Phormidium autumnale"[nm:noexp] as it is captured by Phormidium[tiab] • Delete Scytonema cf crispum[tiab] as it is captured by Scytonema[tiab] • Delete Heteroscytonema crispum[tiab] as it is captured by Heteroscytonema[tiab] • Change HAB*[tiab] to HAB[tiab]. This makes no difference as HAB* defaults to HAB **Search String:** “Cyanobacteria”[mh:noexp] OR cyanobacteria*[tiab] OR Blue-green alga*[tiab] OR toxic alga*[tiab] OR cyanobacteria bloom*[tiab] OR cyanobacterial bloom*[tiab] OR algae bloom*[tiab] OR algal bloom*[tiab] OR “Harmful Algal Bloom”[mh:noexp] OR harmful algal bloom*[tiab] OR HAB[tiab] OR “phytoplankton”[mh:noexp] OR phytoplankton*[tiab] OR “microalgae”[mh:noexp] OR microalga*[tiab] OR “Chlorophyta”[mh:noexp] OR chlorophyta[tiab] OR green alga*[tiab] OR “Dinoflagellida”[mh:noexp] OR dinoflagell*[tiab] OR “Pfiesteria piscicida”[mh:noexp] OR pfiesteria piscicida[tiab] OR “Diatoms”[mh:noexp] OR diatom*[tiab] OR brown alga*[tiab] OR marine alga*[tiab] OR cyanotoxin*[tiab] OR "microcystin"[nm:noexp] OR microcysti*[tiab] OR “Saxitoxin”[mh:noexp] OR saxitoxin*[tiab] OR “cylindrospermopsin”[nm:noexp] OR cylindrospermopsin*[tiab] OR “anatoxin a”[nm:noexp] OR “anatoxin-a(s)”[nm:noexp] OR anatoxin*[tiab] OR “homoanatoxin”[nm:noexp] OR homoanatoxin*[tiab] OR “nodularin”[nm:noexp] OR nodularin*[tiab] OR “Endotoxins”[mh:noexp] OR Endotoxi*[tiab] OR “Lipopolysaccharides”[mh] OR Lipopolysaccharide*[tiab] OR LPS[tiab] OR BMAA[tiab] OR β-N-methylamino-L-alanine[tiab] OR “beta-N-methylamino-L-alanine”[nm:noexp] OR beta-N-methylamino-L-alanine[tiab] OR “beta-(N-carboxy-N-methyl)aminoalanine”[nm:noexp] OR “cylindrospermopsis raciborskii”[nm:noexp] OR cylindrospermopsis raciborskii[tiab] OR “Microcystis”[mh:noexp] OR Microcystis[tiab] OR

				"Dolichospermum circinale"[nm:noexp] OR Dolichospermum circinale[tiab] OR Anabaena circinalis[tiab] OR "Nodularia spumigena"[nm:noexp] OR Nodularia spumigena[tiab] OR Anabaenopsis[tiab] OR "Aphanizomenon"[mh:noexp] OR Aphanizomenon[tiab] OR Aphanocapsa[tiab] OR Aphanothece[tiab] OR Arthrospira[tiab] OR Calothrix[tiab] OR Cuspidothrix issatschenkoi[tiab] OR Aphanizomenon issatschenkoi[tiab] OR geitlerinema[tiab] OR Hapalosiphon[tiab] OR Leptolyngbya[tiab] OR Lyngbya[tiab] OR Microcoleus[tiab] OR Microseira[tiab] OR "Microseira wollei"[nm:noexp] OR Moorea[tiab] OR "Nostoc"[mh:noexp] OR Nostoc*[tiab] OR "Oscillatoria"[mh:noexp] OR Oscillatoria*[tiab] OR Phormidium[tiab] OR Planktothrix[tiab] OR "Plectonema"[mh:noexp] OR Plectonema[tiab] OR Radiocystis[tiab] OR Raphidiopsis[tiab] OR Schizothrix[tiab] OR Scytonema[tiab] OR Heteroscytonema[tiab] OR Snowella[tiab] OR "Synechococcus"[mh:noexp] OR Synechococcus[tiab] OR "Synechocystis"[mh:noexp] OR Synechocystis[tiab] OR Tychonema[tiab] OR Umezakia[tiab] OR Woronichinia[tiab] **Results:** 8/11/2020: 143,870 (2006-2021); Full time period: 250,960 (1880 to 2021)
15	#115	PM-C7	10/11/2020 11/11/2020	This search is the next update to Search #114. It is modified to include the additional marine toxins below: "Lyngbya Toxins"[mh:noexp] OR Lyngbya toxin*[tiab] OR "aplysiatoxin"[nm:noexp] OR aplysiatoxin[tiab] OR "debromoaplysiatoxin"[nm:noexp] OR debromoaplysiatoxin[tiab] OR "homoanatoxin-a"[nm:noexp] OR homoanatoxin-a[tiab] The marine toxins were added to complement the addition of the marine genera and type names. This is intended to make this a comprehensive search encompassing: • General terms for cyanobacteria, blue-green algae, blooms, HAB, • phytoplankton (Freshwater and Marine), microalgae • Freshwater cyanobacterial genera (pelagic and benthic) • All classes and individual toxins (including marine toxins) • A range of benthic genera • Marine cyanobacteria and algal genera • All other potential types or classes of algae (green, brown, dinoflagellates) • Note that homoanatoxin-a[nm:noexp] and homoanatoxin[nm:noexp] are included separately as they are different Supplementary Concepts **Search String:** "Cyanobacteria"[mh:noexp] OR cyanobacteria*[tiab] OR Blue-green alga*[tiab] OR toxic alga*[tiab] OR cyanobacteria bloom*[tiab] OR cyanobacterial bloom*[tiab] OR algae bloom*[tiab] OR algal bloom*[tiab] OR "Harmful Algal Bloom"[mh:noexp] OR harmful algal bloom*[tiab] OR HAB[tiab] OR "phytoplankton"[mh:noexp] OR phytoplankton*[tiab] OR "microalgae"[mh:noexp] OR microalga*[tiab] OR "Chlorophyta"[mh:noexp] OR chlorophyta[tiab] OR green alga*[tiab] OR "Dinoflagellida"[mh:noexp] OR dinoflagell*[tiab] OR "Pfiesteria piscicida"[mh:noexp] OR pfiesteria piscicida[tiab] OR "Diatoms"[mh:noexp] OR diatom*[tiab] OR brown alga*[tiab] OR marine alga*[tiab] OR cyanotoxin*[tiab] OR

				"microcystin"[nm:noexp] OR microcysti*[tiab] OR “Saxitoxin”[mh:noexp] OR saxitoxin*[tiab] OR “cylindrospermopsin”[nm:noexp] OR cylindrospermopsin*[tiab] OR “anatoxin a”[nm:noexp] OR “anatoxin-a(s)”[nm:noexp] OR anatoxin*[tiab] OR “homoanatoxin”[nm:noexp] OR homoanatoxin*[tiab] OR “nodularin”[nm:noexp] OR nodularin*[tiab] OR “Endotoxins”[mh:noexp] OR Endotoxi*[tiab] OR “Lipopolysaccharides”[mh] OR Lipopolysaccharide*[tiab] OR LPS[tiab] OR BMAA[tiab] OR β-N-methylamino-L-alanine[tiab] OR “beta-N-methylamino-L-alanine”[nm:noexp] OR beta-N-methylamino-L-alanine[tiab] OR “beta-(N-carboxy-N-methyl)aminoalanine”[nm:noexp] OR “Lyngbya Toxins”[mh:noexp] OR Lyngbya toxin*[tiab] OR “aplysiatoxin”[nm:noexp] OR aplysiatoxin[tiab] OR “debromoaplysiatoxin”[nm:noexp] OR debromoaplysiatoxin[tiab] OR “homoanatoxin-a”[nm:noexp] OR homoanatoxin-a[tiab] OR “cylindrospermopsis raciborskii”[nm:noexp] OR cylindrospermopsis raciborskii[tiab] OR “Microcystis”[mh:noexp] OR Microcystis[tiab] OR “Dolichospermum circinale”[nm:noexp] OR Dolichospermum circinale[tiab] OR Anabaena circinalis[tiab] OR “Nodularia spumigena”[nm:noexp] OR Nodularia spumigena[tiab] OR Anabaenopsis[tiab] OR “Aphanizomenon”[mh:noexp] OR Aphanizomenon[tiab] OR Aphanocapsa[tiab] OR Aphanothece[tiab] OR Arthrospira[tiab] OR Calothrix[tiab] OR Cuspidothrix issatschenkoi[tiab] OR Aphanizomenon issatschenkoi[tiab] OR geitlerinema[tiab] OR Hapalosiphon[tiab] OR Leptolyngbya[tiab] OR Lyngbya[tiab] OR Microcoleus[tiab] OR Microseira[tiab] OR “Microseira wollei”[nm:noexp] OR Moorea[tiab] OR “Nostoc”[mh:noexp] OR Nostoc*[tiab] OR “Oscillatoria”[mh:noexp] OR Oscillatoria*[tiab] OR Phormidium[tiab] OR Planktothrix[tiab] OR “Plectonema”[mh:noexp] OR Plectonema[tiab] OR Radiocystis[tiab] OR Raphidiopsis[tiab] OR Schizothrix[tiab] OR Scytonema[tiab] OR Heteroscytonema[tiab] OR Snowella[tiab] OR “Synechococcus”[mh:noexp] OR Synechococcus[tiab] OR “Synechocystis”[mh:noexp] OR Synechocystis[tiab] OR Tychonema[tiab] OR Umezakia[tiab] OR Woronichinia[tiab] **Results:** 10/11/2020: 143,905 (2006-2021); Full time period: 251,277 (1880-2021) 11/11/2020: 143,995 (2006-2021); Full time period: 251,367 (1880-2021)
16	#116		13/11/2020	This search is the next update to Search #115. It was modified as follows: • **Remove LPS/Endotoxin terms.** These are a combination of abbreviations, full chemical structure names, either as title and abstract search [tiab] or as MeSH terms [mh:noexp] as appropriate. Terms removed: “Endotoxins”[mh:noexp] OR Endotoxi*[tiab] OR “Lipopolysaccharides”[mh] OR Lipopolysaccharide*[tiab] OR LPS[tiab] Removal of these LPS and Endotoxin terms reduces the size of the search results as follows: Results: 13/11/2020: 144,098 down to 58,162 (2006-2021) after the removal of the 5 terms Full time period: 251,470 down to 85,189 (1880-2021) after the removal of the 5 terms

				• **Leave BMAA terms**. These are a combination of abbreviations, full chemical structure names, either as title and abstract search [tiab] or as supplementary concept terms [nm:noexp] as appropriate. BMAA[tiab] OR β-N-methylamino-L-alanine[tiab] OR “beta-N-methylamino-L-alanine”[nm:noexp] OR beta-N-methylamino-L-alanine[tiab] OR “beta-(N-carboxy-N-methyl)aminoalanine”[nm:noexp] **Search String:** "Cyanobacteria"[mh:noexp] OR cyanobacteria*[tiab] OR Blue-green alga*[tiab] OR toxic alga*[tiab] OR cyanobacteria bloom*[tiab] OR cyanobacterial bloom*[tiab] OR algae bloom*[tiab] OR algal bloom*[tiab] OR "Harmful Algal Bloom"[mh:noexp] OR harmful algal bloom*[tiab] OR HAB[tiab] OR "phytoplankton"[mh:noexp] OR phytoplankton*[tiab] OR "microalgae"[mh:noexp] OR microalga*[tiab] OR "Chlorophyta"[mh:noexp] OR chlorophyta[tiab] OR green alga*[tiab] OR "Dinoflagellida"[mh:noexp] OR dinoflagell*[tiab] OR "Pfiesteria piscicida"[mh:noexp] OR pfiesteria piscicida[tiab] OR "Diatoms"[mh:noexp] OR diatom*[tiab] OR brown alga*[tiab] OR marine alga*[tiab] OR cyanotoxin*[tiab] OR "microcystin"[nm:noexp] OR microcysti*[tiab] OR "Saxitoxin"[mh:noexp] OR saxitoxin*[tiab] OR "cylindrospermopsin"[nm:noexp] OR cylindrospermopsin*[tiab] OR "anatoxin a"[nm:noexp] OR "anatoxin-a(s)"[nm:noexp] OR anatoxin*[tiab] OR "homoanatoxin"[nm:noexp] OR homoanatoxin*[tiab] OR "nodularin"[nm:noexp] OR nodularin*[tiab] OR BMAA[tiab] OR β-N-methylamino-L-alanine[tiab] OR "beta-N-methylamino-L-alanine"[nm:noexp] OR beta-N-methylamino-L-alanine[tiab] OR "beta-(N-carboxy-N-methyl)aminoalanine"[nm:noexp] OR "Lyngbya Toxins"[mh:noexp] OR Lyngbya toxin*[tiab] OR "aplysiatoxin"[nm:noexp] OR aplysiatoxin[tiab] OR "debromoaplysiatoxin"[nm:noexp] OR debromoaplysiatoxin[tiab] OR "homoanatoxin-a"[nm:noexp] OR homoanatoxin-a[tiab] OR "cylindrospermopsis raciborskii"[nm:noexp] OR cylindrospermopsis raciborskii[tiab] OR "Microcystis"[mh:noexp] OR Microcystis[tiab] OR "Dolichospermum circinale"[nm:noexp] OR Dolichospermum circinale[tiab] OR Anabaena circinalis[tiab] OR "Nodularia spumigena"[nm:noexp] OR Nodularia spumigena[tiab] OR Anabaenopsis[tiab] OR "Aphanizomenon"[mh:noexp] OR Aphanizomenon[tiab] OR Aphanocapsa[tiab] OR Aphanothece[tiab] OR Arthrospira[tiab] OR Calothrix[tiab] OR Cuspidothrix issatschenkoi[tiab] OR Aphanizomenon issatschenkoi[tiab] OR geitlerinema[tiab] OR Hapalosiphon[tiab] OR Leptolyngbya[tiab] OR Lyngbya[tiab] OR Microcoleus[tiab] OR Microseira[tiab] OR "Microseira wollei"[nm:noexp] OR Moorea[tiab] OR "Nostoc"[mh:noexp] OR Nostoc*[tiab] OR "Oscillatoria"[mh:noexp] OR Oscillatoria*[tiab] OR Phormidium[tiab] OR Planktothrix[tiab] OR "Plectonema"[mh:noexp] OR Plectonema[tiab] OR Radiocystis[tiab] OR Raphidiopsis[tiab] OR Schizothrix[tiab] OR Scytonema[tiab] OR Heteroscytonema[tiab] OR Snowella[tiab] OR "Synechococcus"[mh:noexp] OR Synechococcus[tiab] OR "Synechocystis"[mh:noexp] OR Synechocystis[tiab] OR Tychonema[tiab] OR Umezakia[tiab] OR Woronichinia[tiab] **Results:** 13/11/2020: 58,162 (2006-2021). Full time period: 85,189 (1880-2021)

Table A1-1: (continued)

17	#117	PM-C7 PM-C8 PM-C10	11/11/2020	**Search #117 is the final version of the Cyanobacteria/Algae/Toxins concept and was used for all final combined searches.** This search is the next update to #115 and #116. It was modified as follows: • **Remove LPS/Endotoxin terms.** These are a combination of abbreviations, full chemical structure names, either as title and abstract search [tiab] or as MeSH terms [mh:noexp] as appropriate. Terms removed: "Endotoxins"[mh:noexp] OR Endotoxi*[tiab] OR "Lipopolysaccharides"[mh] OR Lipopolysaccharide*[tiab] OR LPS[tiab] • **Leave BMAA terms**. These are a combination of abbreviations, full chemical structure names, either as title and abstract search [tiab] or as supplementary concept terms [nm:noexp] as appropriate: BMAA[tiab] OR β-N-methylamino-L-alanine[tiab] OR "beta-N-methylamino-L-alanine"[nm:noexp] OR beta-N-methylamino-L-alanine[tiab] OR "beta-(N-carboxy-N-methyl)aminoalanine"[nm:noexp] • Include a range of additional terms related to marine cyanobacteria and algae (dinoflagellates) and their specific toxins that had not been initially included from the research protocol: The terms specified in the research protocol that related to exposure to marine algae and their toxins were: "Marine algae and cyanobacteria and toxins of interest: • *Lyngbya majuscula, Oscillatoria, Trichodesmium, Karenia brevis, K. spp., Pfiesteria, Alexandrium, Gymnodinium, Dinophysis.* • lyngbyatoxin, aplysiatoxin, pectenotoxin, saxitoxins, other marine toxins (e.g. brevetoxins, domoic acid)." This update allowed the development of a single exhaustive Cyanobacteria, Algae and Toxins "Super Search". The additional terms required that were related to marine cyanobacteria, algae and their toxins were: *Trichodesmium, Karenia brevis, K. spp., Alexandrium, Gymnodinium, Dinophysis*, and the toxins pectenotoxin, brevetoxins, domoic acid. Note that some marine cyanobacteria, algae and toxins were already included in #116. These were: *Lyngbya majuscula, Oscillatoria, Pfiesteria,* lyngbyatoxin, aplysiatoxin, saxitoxins. The additional terms that were required are given in a search string format which was added to the end of #115 and #116 to comprise the updated Search #117: "Trichodesmium"[mh:noexp] OR Trichodesmium[tiab] OR Karenia[tiab] OR Alexandrium[tiab] OR Gymnodinium[tiab] OR Dinophysis[tiab] OR "Marine Toxins"[mh:noexp] OR pectenotoxin*[tiab] OR "pectenotoxin-4"[nm:noexp] OR "pectenotoxin-2-seco acid"[nm:noexp] OR "pectenotoxin 2"[nm:noexp] OR

				“pectenotoxin 1”[nm:noexp] OR “pectenotoxin 11”[nm:noexp] OR “pectenotoxin 9”[nm:noexp] OR “pectenotoxin-11, Dinophysis acuta”[nm:noexp] OR “pectenotoxin-14”[nm:noexp] OR “pectenotoxin-13”[nm:noexp] OR “pectenotoxin 7”[nm:noexp] OR “pectenotoxin-8”[nm:noexp] OR “pectenotoxin 6”[nm:noexp] OR Brevetoxin*[tiab] OR “brevetoxin T17”[nm:noexp] OR “Brevetoxin”[nm:noexp] OR “brevetoxin 3, Karenia brevis”[nm:noexp] OR “brevetoxin 3”[nm:noexp] OR “brevetoxin 2”[nm:noexp] OR “Brevetoxin A”[nm:noexp] OR “brevetoxin B”[nm:noexp] OR “T34 toxin”[nm:noexp] OR “brevetoxin 7”[nm:noexp] OR “brevenal (polyether)”[nm:noexp] OR domoic acid[tiab] OR “domoic acid”[nm:noexp] • An additional change was made to the cyanobacteria term to capture plurals: cyanobacteria*[tiab] was changed to cyanobacteri*[tiab] to capture cyanobacteria and cyanobacterium. **Search String:** "Cyanobacteria"[mh:noexp] OR cyanobacteri*[tiab] OR Blue-green alga*[tiab] OR toxic alga*[tiab] OR cyanobacteria bloom*[tiab] OR cyanobacterial bloom*[tiab] OR algae bloom*[tiab] OR algal bloom*[tiab] OR "Harmful Algal Bloom"[mh:noexp] OR harmful algal bloom*[tiab] OR HAB[tiab] OR "phytoplankton"[mh:noexp] OR phytoplankton*[tiab] OR "microalgae"[mh:noexp] OR microalga*[tiab] OR "Chlorophyta"[mh:noexp] OR chlorophyta[tiab] OR green alga*[tiab] OR "Dinoflagellida"[mh:noexp] OR dinoflagell*[tiab] OR "Pfiesteria piscicida"[mh:noexp] OR pfiesteria piscicida[tiab] OR "Diatoms"[mh:noexp] OR diatom*[tiab] OR brown alga*[tiab] OR marine alga*[tiab] OR cyanotoxin*[tiab] OR "microcystin"[nm:noexp] OR microcysti*[tiab] OR "Saxitoxin"[mh:noexp] OR saxitoxin*[tiab] OR "cylindrospermopsin"[nm:noexp] OR cylindrospermopsin*[tiab] OR "anatoxin a"[nm:noexp] OR "anatoxin-a(s)"[nm:noexp] OR anatoxin*[tiab] OR "homoanatoxin"[nm:noexp] OR homoanatoxin*[tiab] OR"nodularin"[nm:noexp] OR nodularin*[tiab] OR BMAA[tiab] OR β-N-methylamino-L-alanine[tiab] OR "beta-N-methylamino-L-alanine"[nm:noexp] OR beta-N-methylamino-L-alanine[tiab] OR "beta-(N-carboxy-N-methyl)aminoalanine"[nm:noexp] OR "Lyngbya Toxins"[mh:noexp] OR Lyngbya toxin*[tiab] OR "aplysiatoxin"[nm:noexp] OR aplysiatoxin*[tiab] OR "debromoaplysiatoxin"[nm:noexp] OR Debromoaplysiatoxin*[tiab] OR "homoanatoxin-a"[nm:noexp] OR homoanatoxin-a[tiab] OR "cylindrospermopsis raciborskii"[nm:noexp] OR cylindrospermopsis raciborskii[tiab] OR "Microcystis"[mh:noexp] OR Microcystis[tiab] OR "Dolichospermum circinale"[nm:noexp] OR Dolichospermum circinale[tiab] OR Anabaena circinalis[tiab] OR "Nodularia spumigena"[nm:noexp] OR Nodularia spumigena[tiab] OR Anabaenopsis[tiab] OR "Aphanizomenon"[mh:noexp] OR Aphanizomenon[tiab] OR Aphanocapsa[tiab] OR Aphanothece[tiab] OR Arthrospira[tiab] OR Calothrix[tiab] OR Cuspidothrix issatschenkoi[tiab] OR Aphanizomenon issatschenkoi[tiab] OR geitlerinema[tiab] OR Hapalosiphon[tiab] OR Leptolyngbya[tiab] OR Lyngbya[tiab] OR Microcoleus[tiab] OR Microseira[tiab] OR "Microseira wollei"[nm:noexp] OR Moorea[tiab] OR "Nostoc"[mh:noexp] OR Nostoc*[tiab] OR "Oscillatoria"[mh:noexp] OR Oscillatoria*[tiab] OR Phormidium[tiab] OR Planktothrix[tiab] OR "Plectonema"[mh:noexp] OR Plectonema[tiab] OR

				Radiocystis[tiab] OR Raphidiopsis[tiab] OR Schizothrix[tiab] OR Scytonema[tiab] OR Heteroscytonema[tiab] OR Snowella[tiab] OR "Synechococcus"[mh:noexp] OR Synechococcus[tiab] OR "Synechocystis"[mh:noexp] OR Synechocystis[tiab] OR Tychonema[tiab] OR Umezakia[tiab] OR Woronichinia[tiab] OR "Trichodesmium"[mh:noexp] OR Trichodesmium[tiab] OR Karenia[tiab] OR Alexandrium[tiab] OR Gymnodinium[tiab] OR Dinophysis[tiab] OR "Marine Toxins"[mh:noexp] OR pectenotoxin*[tiab] OR "pectenotoxin-4"[nm:noexp] OR "pectenotoxin-2-seco acid"[nm:noexp] OR "pectenotoxin 2"[nm:noexp] OR "pectenotoxin 1"[nm:noexp] OR "pectenotoxin 11"[nm:noexp] OR "pectenotoxin 9"[nm:noexp] OR "pectenotoxin-11, Dinophysis acuta"[nm:noexp] OR "pectenotoxin-14"[nm:noexp] OR "pectenotoxin-13"[nm:noexp] OR "pectenotoxin 7"[nm:noexp] OR "pectenotoxin-8"[nm:noexp] OR "pectenotoxin 6"[nm:noexp] OR Brevetoxin*[tiab] OR "brevetoxin T17"[nm:noexp] OR "Brevetoxin"[nm:noexp] OR "brevetoxin 3, Karenia brevis"[nm:noexp] OR "brevetoxin 3"[nm:noexp] OR "brevetoxin 2"[nm:noexp] OR "Brevetoxin A"[nm:noexp] OR "brevetoxin B"[nm:noexp] OR "T34 toxin"[nm:noexp] OR "brevetoxin 7"[nm:noexp] OR "brevenal (polyether)"[nm:noexp] OR domoic acid[tiab] OR "domoic acid"[nm:noexp] **Results:** 11/11/2020: 60,517 (2006-2021); Full time period: 90,104 (1880-2021)

Table A1-2: Details and sequence of the development of the individual searches for the Recreation/al concept in PubMed®

Search Number for Concept	Search Code number	Part of combined SEARCH code #	Date of Search/s	Description, Search String and Results
1	#201		05/08/2020	Searches #201 to #204 were iterations on the Initial search terms in the research protocol. #201 has a range of MeSH terms and Title and abstract only terms. A variation selected was to leave out “swimming”[mh:noexp] as it is covered in “water sports’[mh] **Search String:** “recreation”[mh:noexp] OR Recreation*[tiab] OR “Water sports”[mh] OR bathing[tiab] OR wading[tiab] OR paddling[tiab] OR boating[tiab] OR sailing[tiab] OR wind surfing[tiab] OR water skiing[tiab] OR fishing[tiab] OR kayaking[tiab] OR canoeing[tiab] OR jet-skiing[tiab] **Results:** 05/08/2020: 45,570 (2006-2021)
2	#202		5/08/2020	Search #202 is an update to #201 to remove the SCUBA diving as a subset of “water sports” by adding NOT diving[mh] Diving was added back to future searches from #205. The result was a reduction in results. **Search String:** "recreation”[mh:noexp] OR Recreation*[tiab] OR “Water sports”[mh] OR bathing[tiab] OR wading[tiab] OR paddling[tiab] OR boating[tiab] OR sailing[tiab] OR wind surfing[tiab] OR water skiing[tiab] OR fishing[tiab] OR kayaking[tiab] OR canoeing[tiab] OR jet-skiing[tiab] NOT diving[mh] **Results:** 05/08/2020: 40,210 (2006-2021)
3	#203		05/08/2020	Search #203 was same as #202 but leaving out OR fishing to see if it is important as a passive activity. The result was a further reduction from 40,210 to 34,744. **Search String:** "recreation”[mh:noexp] OR Recreation*[tiab] OR “Water sports”[mh] OR bathing[tiab] OR wading[tiab] OR paddling[tiab] OR boating[tiab] OR sailing[tiab] OR wind surfing[tiab] OR water skiing[tiab] OR kayaking[tiab] OR canoeing[tiab] OR jet-skiing[tiab] NOT diving[mh **Results:** 05/08/2020: 34,744 (2006-2021)
4	#204		05/08/2020	Search #204 was the same as #203 but with Recreation*[tiab] removed. It led to a large reduction in results and was added back in future searches. **Search String:** "recreation”[mh:noexp] OR “Water sports”[mh] OR bathing[tiab] OR wading[tiab] OR paddling[tiab] OR boating[tiab] OR sailing[tiab] OR wind surfing[tiab] OR water skiing[tiab] OR kayaking[tiab] OR canoeing[tiab] OR jet-skiing[tiab] NOT diving[mh] **Results:** 5/08/2020: 17,758 (2006-2020)

Table A1-2: (continued)

5 and 6	#205 #206		05/08/2020 22/08/2020	Search #205 was major update to #204 to incorporate more MeSH terms including "Water Sports"[mh] which was allowed to "explode to include many other entry terms for activities such as swimming, diving etc. Most of these are then also covered by the specific activity[tiab] search terms for non-indexed papers. Search #206 is a repeat of #205 at a later time (+17 days) **Search String:** "recreation"[mh:noexp] OR recreation*[tiab] OR "Water Sports"[mh] OR "Swimming"[mh] OR swimming[tiab] OR bathing[tiab] OR wading[tiab] OR paddling[tiab] OR "Diving"[mh:noexp] OR diving[tiab] OR scuba[tiab] OR boating[tiab] OR sailing[tiab] OR surfing[tiab] OR wind surfing[tiab] OR water skiing[tiab] OR angling[tiab] OR fishing[tiab] OR kayaking[tiab] OR canoeing[tiab] OR jet-skiing[tiab] OR rowing[tiab] **Results:** #205 - 05/08/2020: 57,535 (2006-2020) #206 - 22/08/2020: 57,831 (2006-2021)
7	#207	PM-C5 PM-C7 PM-C8 PM-C10	25/08/2020 11/11/2020; 13/11/2020; 30/11/2020; 04/04/2021	**Search #207 is the final version of the Recreation/al concept and was used for all final combined searches.** This search is the next update to #206: • Addition of the high level terms "Leisure Activities"[mh:noexp] OR Leisure Activities[tiab] • Addition of Water sport*[tiab] • A range of terms were tested to determine that they would capture multiple activities: surfing[tiab] will capture wind surfing; fishing[tiab] will capture fly fishing; sailing will capture parasailing. **Search String:** "recreation"[mh:noexp] OR recreation*[tiab] OR "Leisure Activities"[mh:noexp] OR Leisure Activities[tiab] OR "Water Sports"[mh] OR Water sport*[tiab] OR "swimming"[mh] OR swimming[tiab] OR bathing[tiab] OR wading[tiab] OR paddling[tiab] OR "diving"[mh:noexp] OR diving[tiab] OR scuba[tiab] OR boating[tiab] OR sailing[tiab] OR surfing[tiab] OR wind surfing[tiab] OR water skiing[tiab] OR angling[tiab] OR fishing[tiab] OR kayaking[tiab] OR canoeing[tiab] OR jet-skiing[tiab] OR rowing[tiab] **Results:** 25/08/2020: 64,102 (2006-2021) 10/11/2020: 65,557 (2006-2021); Full time period: 106,529 (1803-2021) 11/11/2020: 65,623 (2006-2021); Full time period: 106,595 (1803-2021) 30/11/2020: 65,976 (2006-2021); Full time period: 106,948 (1803-2021) 04/04/2021: 68,532 (2006-2021); Full time period: 109,508 (1803-2021)

Table A1-3: Details and sequence of the development of the individual searches for the Health concept in PubMed®

Search Number for Concept	Search Code number	Part of combined SEARCH code #	Date of Search/s	Description, Search String and Results
1	#301		19/08/2020	This search is the first search for the Health Concept: • Contains the initial list of terms developed from the PECO Table and the terms proposed by the Committee and included in the research protocol. • Includes MeSH terms, but not Supplementary Concept terms which were progressively added in later searches. • Does not include limiting searching of terms to Titles and Abstracts [tiab], i.e., it was allowed to include all fields. • Contains some wildcards, but not all. **Search String:** Health OR health effect* OR health outcome* OR adverse effect* OR disease* OR illness* OR symptom* OR gastrointestinal OR gastroenteritis OR nausea OR vomiting OR diarrhea OR pneumonia-like symptom* OR fever OR headache OR hay fever-like OR flu-like OR skin rash* OR skin irritation OR pruritis OR dermatologic OR dermal irritation OR eye irritation OR allergic reaction* OR neurotoxicity OR neurologic* OR hepatotoxicity OR inhalation-related symptom* OR induction of asthma OR shortness of breath OR exposure OR oral OR ingestion OR dermal OR inhalation OR aerosol* OR “public health”[mh:noexp] OR “epidemiology”[mh:noexp] OR “adverse effects”[mh:noexp] OR “poisoning”[mh:noexp] OR “toxicity”[mh:noexp] OR “disease”[mh:noexp] OR “Rhinitis, Allergic”[mh:noexp] OR “Exanthema”[mh:noexp] OR “dermatitis”[mh:noexp] OR “hypersensitivity”[mh:noexp] OR “Neurotoxicity Syndromes”[mh:noexp] OR “Neurologic Manifestations”[mh:noexp] OR “Chemical and Drug Induced Liver Injury”[mh:noexp] OR “Inhalation Exposure”[mh:noexp] OR “Respiratory Hypersensitivity”[mh:noexp] OR “Dyspnea”[mh:noexp] OR “Inhalation Exposure”[mh:noexp] OR “Aerosols”[mh:noexp] **Results:** 19/8/2020: 7,493,239 results (Note this is for all fields)

Table A1-3: (continued)

2	#302		20/08/2020	This is a modification to Search #301 as follows: • Addition of more MeSH terms that had been obtained from the PubMed® MeSH (Medical Subject Headings) Database; for example terms related to Health"[mh:noexp], "public health"[mh:noexp], "epidemiology"[mh:noexp]; "adverse effects"[mh:noexp], "disease"[mh:noexp], "poisoning"[mh:noexp], etc. • Restrict the searching for both MeSH and non-mesh terms to titles and abstracts only i.e. [tiab]. • Remove the terms: Induction of asthma; shortness of breath as these are regarded as too colloquial and can be captured by MeSH terms. • Add Asthma both as MeSH and non-mesh terms “asthma”[mh:noexp] OR Asthma[tiab], and additional respiratory illness terms such as "Respiratory Hypersensitivity"[mh:noexp] OR "Dyspnea"[mh:noexp]. **Search String:** Health"[mh:noexp] OR Health[tiab] OR "public health"[mh:noexp] OR public health[tiab] OR "epidemiology"[mh:noexp] OR Epidemiology[tiab] OR health effect*[tiab] OR health outcome*[tiab] OR "adverse effects"[mh:noexp] OR adverse effect*[tiab] OR "disease"[mh:noexp] OR disease*[tiab] OR illness*[tiab] OR symptom*[tiab] OR "poisoning"[mh:noexp] OR Poisoning[tiab] OR "toxicity"[mh:noexp] OR Toxicity[tiab] OR gastrointestinal[tiab] OR "gastroenteritis"[mh:noexp] OR gastroenteritis[tiab] OR "nausea"[mh:noexp] OR nausea[tiab] OR "vomiting"[mh:noexp] OR vomiting[tiab] OR "diarrhea"[mh:noexp] OR diarrhea[tiab] OR pneumonia-like symptom*[tiab] OR "fever"[mh:noexp] OR fever[tiab] OR "headache"[mh:noexp] OR headache[tiab] OR "Rhinitis, Allergic"[mh:noexp] OR hay fever-like[tiab] OR flu-like[tiab] OR allergic reaction*[tiab] OR "Exanthema"[mh:noexp] OR "dermatitis"[mh:noexp] OR dermatitis[tiab] OR "hypersensitivity"[mh:noexp] OR hypersensitivity[tiab] OR skin rash*[tiab] OR dermal irritation[tiab] OR skin irritation[tiab] OR "pruritis"[mh:noexp] OR pruritis[tiab] OR dermatologic*[tiab] OR eye irritation[tiab] OR "Neurotoxicity Syndromes"[mh:noexp] OR "Neurologic Manifestations"[mh:noexp] OR neurotoxicity[tiab] OR neurologic*[tiab] OR "Chemical and Drug Induced Liver Injury"[mh:noexp] OR hepatotoxicity[tiab] OR "Inhalation Exposure"[mh:noexp] OR Inhalation Exposure[tiab] OR "asthma"[mh:noexp] OR Asthma[tiab] OR "Respiratory Hypersensitivity"[mh:noexp] OR "Dyspnea"[mh:noexp] OR Dyspnea[tiab] OR exposure[tiab] OR oral[tiab] OR ingestion[tiab] OR dermal[tiab] OR inhalation[tiab] OR "Aerosols"[mh:noexp] OR aerosol*[tiab] **Results:** 20/08/2020: 4,955,464 (2006-2021)

Table A1-3: (continued)

3 and 4	#303 and #304	PM-C5	21/08/2020; 22/08/2020	These are modifications to Search #302: • The term back shortness of breath[tiab] that had been deleted from #302 was added back as it had been seen in some titles and abstracts. **Search String:** "Health"[mh:noexp] OR Health[tiab] OR "public health"[mh:noexp] OR public health[tiab] OR "epidemiology"[mh:noexp] OR Epidemiology[tiab] OR health effect*[tiab] OR health outcome*[tiab] OR "adverse effects"[mh:noexp] OR adverse effect*[tiab] OR "disease"[mh:noexp] OR disease*[tiab] OR illness*[tiab] OR symptom*[tiab] OR "poisoning"[mh:noexp] OR Poisoning[tiab] OR "toxicity"[mh:noexp] OR Toxicity[tiab] OR gastrointestinal[tiab] OR "gastroenteritis"[mh:noexp] OR gastroenteritis[tiab] OR "nausea"[mh:noexp] OR nausea[tiab] OR "vomiting"[mh:noexp] OR vomiting[tiab] OR "diarrhea"[mh:noexp] OR diarrhea[tiab] OR pneumonia-like symptom*[tiab] OR "fever"[mh:noexp] OR fever[tiab] OR "headache"[mh:noexp] OR headache[tiab] OR "Rhinitis, Allergic"[mh:noexp] OR hay fever-like[tiab] OR flu-like[tiab] OR allergic reaction*[tiab] OR "Exanthema"[mh:noexp] OR "dermatitis"[mh:noexp] OR dermatitis[tiab] OR "hypersensitivity"[mh:noexp] OR hypersensitivity[tiab] OR skin rash*[tiab] OR dermal irritation[tiab] OR skin irritation[tiab] OR "pruritis"[mh:noexp] OR pruritis[tiab] OR dermatologic*[tiab] OR eye irritation[tiab] OR "Neurotoxicity Syndromes"[mh:noexp] OR "Neurologic Manifestations"[mh:noexp] OR neurotoxicity[tiab] OR neurologic*[tiab] OR "Chemical and Drug Induced Liver Injury"[mh:noexp] OR hepatotoxicity[tiab] OR "Inhalation Exposure"[mh:noexp] OR Inhalation Exposure[tiab] OR shortness of breath[tiab] OR "asthma"[mh:noexp] OR Asthma[tiab] OR "Respiratory Hypersensitivity"[mh:noexp] OR "Dyspnea"[mh:noexp] OR Dyspnea[tiab] OR exposure[tiab] OR oral[tiab] OR ingestion[tiab] OR dermal[tiab] OR inhalation[tiab] OR "Aerosols"[mh:noexp] OR aerosol*[tiab] **Results:** 21/08/2020: 4,956,439 (2006-2021) 22/08/2020: 4,958,189 (2006-2021) The error messages displayed: Quoted phrases not found: "adverse effects", "toxicity", "pruritis" (Incorrect spelling of pruritus)
5	#305	PM-C7 PM-C8 PM-C10	11/11/2020; 15/11/2020; 30/11/2020; 04/04/2021	**Search #305 is the final version of the Health concept and was used for all final combined searches.** This search is the next update to #304. • It was modified to include a much wider and more exhaustive range of MeSH headings and Supplementary Concepts relevant to diseases and their symptoms. • From earlier lists the following were considered not to be required as they are covered under entry terms for other headings: • health effect*[tiab]; health outcome*[tiab] were not required and have been removed. • dermatologic[tiab] is considered not to be required, but has been left in the full search. • Leave out - inhalation-related symptom*[tiab] OR induction of asthma[tiab] (as per #302). • Include Asthma (as per #302).

				• Had removed shortness of breath[tiab] but it was subsequently added back as it had been seen in some titles and abstracts (as per #303 and #304) • This list also includes English and American variations of spelling for diarrhea[tiab] OR diarrhoea[tiab]. • dermal irrita*[tiab] OR skin irrita*[tiab] have been truncated to capture irritant and irritation. **Search String:** “Health”[mh:noexp] OR health[tiab] OR “Public Health”[mh:noexp] OR public health[tiab] OR “Epidemiology”[mh:noexp] OR epidemiology[tiab] OR “adverse effects”[sh:noexp] OR adverse effect*[tiab] OR “Disease”[mh:noexp] OR disease*[tiab] OR illness*[tiab] OR symptom*[tiab] OR “Poisoning”[mh:noexp] OR Poison*[tiab] OR “toxicity”[sh:noexp] OR toxi*[tiab] OR gastrointestinal[tiab] OR “Gastroenteritis”[mh:noexp] OR gastroenteritis[tiab] OR “Nausea”[mh:noexp] OR nausea*[tiab] OR “Vomiting”[mh:noexp] OR vomiting[tiab] OR “Diarrhea”[mh:noexp] OR diarrhea[tiab] OR diarrhoea[tiab] OR pneumonia like symptom*[tiab] OR “Fever”[mh:noexp] OR fever*[tiab] OR “Headache”[mh:noexp] OR headache*[tiab] OR “Rhinitis, Allergic”[mh:noexp] OR rhinitis[tiab] OR hay fever-like[tiab] OR flu-like[tiab] OR allergic reaction*[tiab] OR “Exanthema”[mh:noexp] OR exanthema[tiab] OR “Dermatitis”[mh:noexp] OR dermatitis[tiab] OR “Hypersensitivity”[mh:noexp] OR hypersensitiv*[tiab] OR skin rash*[tiab] OR dermal irrita*[tiab] OR skin irrita*[tiab] OR “Skin Manifestations”[mh:noexp] OR skin manifestation*[tiab] OR “Erythema”[mh:noexp] OR erythema[tiab] OR “Pruritus”[mh:noexp] OR pruriti*[tiab] OR dermatologic*[tiab] OR eye irrita*[tiab] OR “Neurotoxicity Syndromes”[mh:noexp] OR neurotoxicity syndrome*[tiab] OR “Neurologic Manifestations”[mh:noexp] OR neurologic manifestation*[tiab] OR neurotoxic*[tiab] OR neurologic*[tiab] OR “Chemical and Drug Induced Liver Injury”[mh:noexp] OR liver injury[tiab] OR “Liver Failure, Acute”[mh:noexp] OR liver failure[tiab] OR “Massive Hepatic Necrosis”[mh:noexp] OR hepatic necros*[tiab] OR hepatotoxi*[tiab] OR “Inhalation Exposure”[mh:noexp] OR inhalation exposure[tiab] OR shortness of breath[tiab] OR “Asthma”[mh:noexp] OR asthma*[tiab] OR “Respiratory Hypersensitivity”[mh:noexp] OR respiratory hypersensitiv*[tiab] OR “Dyspnea”[mh:noexp] OR dyspnea[tiab] OR exposure[tiab] OR oral[tiab] OR ingestion[tiab] OR dermal[tiab] OR inhalation[tiab] OR “Aerosols”[mh:noexp] OR aerosol*[tiab] **Results:** 11/11/20: 5,706,671 (2006-2021); Full time period: 10,064,190 (1781-2021) 15/11/20: 5,713,018 (2006-2021); Full time period: 10,070,541 (1781-2021) 30/11/20: 5,741,386 (2006-2021); Full time period: 10,098,907 (1781-2021) 04/04/21: 5,980,614 (2006-2021); Full time period: 10,338,533 (1781-2021)

Table A1-4: PubMed® Combined searches (Code PM-C)

Combined Search Number	Date	Contains Concept Searches	Individual Search Results	Results
PM-C5	25/08/2020	#111 AND #207 AND #304	#111 CAT: 143,362 (2006-2021); 263,330 (1846-2021) #207 Rec: 64,121 (2006-2021); 105,077 (1803-2021) #304 Health: 4,964,148 (2006-2021);8,546,758 (1781-2021)	This was an early search to combine the 3 concepts which were still in development. It contained a range of errors in phrases within Search #111. The results indicated that the combined search was functioning and capturing a realistic number of results. The main error noted was within the Cyanobacteria/algae/toxins concept ((#111 CAT), which was designed capture classes of cyanotoxin*[tiab]. This included some specific types of toxins entered as follows: “Neurotoxins”[mh:noexp] OR neurotoxin*[tiab] OR hepatotoxin*[tiab] It was subsequently recognised that this also captures a range of substances that are toxins with these modes of action and then matches them to recreation and then to the health outcomes in this combined search. These terms were removed from later searches for this concept. **Results:** 573 documents (2006-2021) This total of 573 was screened to 135 papers based upon titles and in some cases abstracts to assess relevance to both the primary and secondary questions. 76 were further selected for full-text review related to the primary question based upon more extensive review of their abstracts. 18 were rejected from the 135 papers based upon this review of abstracts. Others were assessed and put into different categories below. This was for further full-text review related to the secondary questions. These groups and the number of papers were: Surrogates and Monitoring: 17; Animal Poisoning (i.e. specifically Dogs): 7; Marine Cyanobacteria/Algae/Toxins: 15; BMAA: 2

Table A1-4: (continued)

PM-C7	11/11/20	#117 AND #207 AND #305	#117 CAT: 60,517 (2006-2021) #207 Rec: 65,623 (2006-2021) #305 Health: 5,706,671 (2006-2021)	**This search is referred to as the Final Combined Search in PubMed® ®** **Results:** 641 documents (2006-2021) prior to screening **Stage 1** Screen: 140 selected from 641. This involved assessment of relevance to answer the primary or secondary questions by examination of the title. In many cases papers could be readily rejected based upon lack of clear relevance to the review questions. **Stage 2** Screen: 41 selected from 140 for full-text review. This involved review of both Titles and Abstracts for close relevance to the topic. Abstracts for studies that had initially appeared relevant by inclusion of cyanobacteria, cyanotoxins, blooms, recreational water, marine monitoring, or exposure and adverse health outcomes in both freshwater and marine environments in titles were assessed. 62 studies were rejected from the 140 papers based upon this review of abstracts. Papers could be rejected based upon a range of limitations or relevance criteria, for example: • not containing primary data and/or information related to health outcomes. • were primarily ecological or occurrence studies of organisms or toxins. • were management-related or economic and social assessments. • were related to analytical assays for organisms or toxins. In addition to those selected for full-text review in relation to the primary question, other papers were placed into groups (categories) for later careful assessment of relevance to secondary questions. These groups and the number of papers were: Surrogates and Monitoring: 9; Animal Poisoning (i.e., specifically Dogs): 10; Marine Cyanobacteria/Algae/Toxins: 13; BMAA: 1; LPS/Endotoxins: 2

Table A1-4: (continued)

PM-C8 (Incorporates Indigenous search string)	13/11/20	#117 AND #207 AND #305 (2006-2021) AND Indigenous	#117 CAT: 60,642 (2006-2021) #207 Rec: 65,692 (2006-2021) #305 Health: 5,713,018 (2006-2021)	**PM-C8 is a combined search run prior testing with the Indigenous terms string.** **Results:** 478 documents (2006-2021); (#117 AND #207 AND #305) The purpose of this was not to further screen these results but to use them for combination with the Indigenous Search String The combined search output above was then run with the Indigenous string. **Results:** 0 documents (2006-2021). No results were found. For a further validation this was repeated for the full time period (from ~1880) for all of these searches, and this still also generated no additional results. A further iteration was then carried out with the removal of the Recreation concept (#207) and a combination of Cyanobacteria/Algae/Toxins, Health and indigenous: CAT #117 AND Health #305 AND Indigenous. **Results**: 13 documents. 12 of these were considered not relevant. Only 1 mentioned Cyanobacteria and this was not health-related and was related to with aboriginal and early European encounters with cyanobacterial blooms. (Sadgrove NJ. A 'cold-case' review of historic aboriginal and European Australian encounters with toxic blooms of cyanobacteria. Ecohealth. 2012 Sep;9(3):315-27. doi: 10.1007/s10393-012-0782-6. Epub 2012 Jul 10. PMID: 22777052).

Table A1-4: (continued)

PM-C10	04/04/21	Updated combined search comprised of #117 AND #207 AND #305	#117 CAT: 62,688 (2006-2021) #207 Rec: 68,532 (2006-2021) #305 Health: 5,980,614 (2006-2021)	**This Search is referred to as the Validating Combined Search in PubMed® ®** The purpose of this search was to validate earlier Combined Searches PM-C7 from November 2020, to determine if any additional publications could be found in a consolidated and complete "Super Search" after an additional 5-month time period. **Results**: 523 documents (2006-2021) **Stage 1 Screen:** 130 selected from 523. This involved assessment of relevance to answer the primary or secondary questions by examination of the title. In many cases papers could be readily rejected based upon lack of clear relevance to the review questions. **Stage 2 Screen**: this involved a comparison of the Stage 1 Screen (130 results) to the Stage 1 Screen (140 results) obtained from PM-C7. This comparison did not produce any new or additional papers that would require further assessment by full-text review to answer either the Primary or Secondary questions. This was regarded as a good validation of Search PM-C7
PM-C11 (Incorporates Indigenous search string)	04/04/2021	Combined SEARCH #117 AND #207 AND #305 (2006-2021) AND Indigenous (2006-2021)	Indigenous Search String alone results: 04/04/2021: 8,792 (2006-2021).	**This search was an update to PM-C8 to test the more comprehensive combined search #117 AND #207 AND #305 AND the Indigenous concept (2006-2021) after an additional 5-month period.** No Results related to indigenous studies and the Primary Question were found for this combined search.

Indigenous String

(Aborig*[tw] OR Indigenous[tw] OR (Torres Strait[tw] AND Islander*[tw]) OR health services, indigenous[mh] OR Oceanic Ancestry Group[mh] OR koori[tw] OR tiwi[tw]) AND (.au[ad] OR australia*[ad] OR Australia[mh] OR Australia*[tiab] OR Northern Territory[tiab] OR Northern Territory[ad] OR Tasmania*[tiab] OR Tasmania[ad] OR New South Wales[tiab] OR New South Wales[ad] OR Victoria*[tiab] OR Victoria[ad] OR Queensland[tiab] OR Queensland[ad])

Results: Indigenous Search alone 4/04/2021: 12,038 documents (1891-2021); 8,792 documents (2006-2021).

Table A1-5: Scopus® individual concept searches in sequence for evolution of the searches in Cyanobacteria/Algae/Toxins; Recreation/al; Health respectively.

Concept	Code name	Part of combined Search	Date of Search/es	Description, Search string and Results
Cyanobacteria/ Algae/ Toxins	CAT#1	S-C1 and S-C2	17/11/2020 05/04/2021	This search is the translation of the PubMed® Cyanobacteria/Algae/Toxins Search #117 CAT directly across to the Scopus® format. • This involves the removal of all indexing language codes (MeSH term headings and sub-headings) • Searching for the terms is by the Scopus® default Title/Abstract/Keyword search. • The Scopus® search CAT#1 is comprised of 75 terms. • The search was rerun in April 2021 to check differences after 5 months. This gave higher results as expected (approximately 5,000 more papers). Search String cyanobacteria* OR (“Blue-green alga*”) OR (“toxic alga*”) OR (“cyanobacteria* bloom”) OR (“alga* bloom”) OR (“harmful algal bloom”) OR {HAB} OR phytoplankton* OR microalga* OR chlorophyta OR (“green alga*”) OR dinoflagell* OR (“pfiesteria piscicida”) OR Diatom OR (“brown alga*”) OR (“marine alga*”) OR cyanotoxin OR microcysti* OR saxitoxin OR cylindrospermopsin OR anatoxin OR homoanatoxin OR nodularin OR {BMAA} OR {β-N-methylamino-L-alanine} OR {beta-N-methylamino-L-alanine} OR (“Lyngbya toxin*”) OR Aplysiatoxin OR Debromoaplysiatoxin OR {homoanatoxin-a} OR (“Cylindrospermopsis raciborskii”) OR Microcystis OR (“Dolichospermum circinale”) OR (“Anabaena circinalis”) OR (“Nodularia spumigena”) OR Anabaenopsis OR Aphanizomenon OR Aphanocapsa OR Aphanothece OR Arthrospira OR Calothrix OR (“Cuspidothrix issatschenkoi”) OR (“Aphanizomenon issatschenkoi”) OR Geitlerinema OR Hapalosiphon OR Leptolyngbya OR Lyngbya OR Microcoleus OR Microseira OR Moorea OR Nostoc* OR Oscillatoria* OR Phormidium OR Planktothrix OR Plectonema OR Radiocystis OR Raphidiopsis OR Schizothrix OR Scytonema OR Heteroscytonema OR Snowella OR Synechococcus OR Synechocystis OR Tychonema OR Umezakia OR Woronichinia OR Trichodesmium OR Karenia OR Alexandrium OR Gymnodinium OR Dinophysis OR (“Marine Toxin*”) OR Pectenotoxin OR Brevetoxin OR (“domoic acid”) Results: 17/11/2020: 141,664 (2006-2021); Full time period: 228,681 (1835-2021) 05/04/2021: 146,963 (2006-2021); Full time period: 234,038 (1835-2021)

Table A1-5: (continued)

	R#1	S-C1 and S-C2	17/11/2020 05/04/2021	This search is the translation of the PubMed® Health Search # 207 R directly across to the Scopus® format. • This involves the removal of all indexing language codes (MeSH term headings and sub-headings) • Searching for the terms is by the Scopus® default Title/Abstract/Keyword search. • The Scopus® search R#1 is comprised of 20 terms. • R#1 was rerun after an additional 5-month time period. • The search returned more results after 5 months, approximately 21,000 increase (05/04/2021: 212,560; 17/11/2020: 191,287). Search String: recreation* OR (“leisure activit*”) OR (“water sport*”) OR swimming OR bathing OR wading OR paddling OR diving OR scuba OR boating OR sailing OR surfing OR (“wind surfing”) OR (“water skiing”) OR angling OR fishing OR kayaking OR canoeing OR (“jet skiing”) OR rowing Results: 17/11/2020: 191,287 (2006-2021) 05/04/2021: 212,560 (2006-2022)
Health	H#1	S-C1 and S-C2	17/11/2020 05/04/2021	This search is the translation of the PubMed® Health Search #305 H directly across to the Scopus® format. • This involves the removal of all indexing language codes (MeSH term headings and sub-headings) • Searching for the terms is by the Scopus® default Title/Abstract/Keyword search. • The Search is for the period 2006-2022. • The Scopus® search H#1 is comprised of 53 terms. • The search returned more results after 5 months, approximately 430,000 increase (05/04/2021: 10,170,384; 17/11/2020: 9,739,949) Search String: health OR (“public health”) OR epidemiology OR (“adverse effect*”) OR disease* OR illness* OR symptom* OR poison* OR toxi* OR gastrointestinal OR gastroenteritis OR nausea* OR vomiting OR diarrhea OR diarrhoea OR (“pneumonia like symptoms”) OR fever* OR headache* OR rhinitis OR (“hay fever like”) OR {flu-like} OR (“flu like”) OR (“allergic reaction*”) OR exanthema OR dermatitis OR hypersensitiv* OR (“skin rash*”) OR (“dermal irrita*”) OR (“skin irrita*”) OR (“skin manifestation*”) OR erythema OR prurit* OR dermatologic* OR (“eye irrita*”) OR (“neurotoxicity syndrome*”) OR (“neurologic manifestation*”) OR neurotoxic* OR neurologic* OR (“liver injury”) OR (“liver failure”) OR (“hepatic necros*”) OR hepatotoxi* OR (“inhalation exposure”) OR (“shortness of breath”) OR asthma* OR (“respiratory hypersensitiv*”) OR dyspnea OR exposure OR oral OR ingestion OR dermal OR inhalation OR aerosol* Results: 17/11/2020: 9,739,949 results (2006-2022); Full time period: 17,556,021 (1863-2022) 05/04/2021: 10,170,384 documents (2006-2022); 18,031,867 documents (1863-2022)

Table A1-6: Scopus® combined searches (Code S-C).

Combined Search Number	**Date**	**Contains Scopus® Searches**	**Equivalent PubMed® Searches**	**Individual Search Results**	**Results**
S-C1	17/11/2020	CAT#1 R#1 H#1	#117 CAT #207 R #305 H Search PM-C8 (13/11/2020) Results: 478	CAT#1: 17/11/20 141,664 (2006-2021) R#1: 17/11/20 191,287 (2006-2021) H#1: 17/11/20 9,739,949 (2006-2022)	**Results:** 1032 documents (2006-2021) prior to screening (**Comparison PubMed® PM-C8**; 13/11/2020; Results: 478) **Stage 1 Screen:** 140 selected from 1032. This involved assessment of relevance to answer the primary or secondary questions by examination of the title. In many cases papers could be readily rejected based upon lack of clear relevance to the review questions. In some cases, the Abstract was also reviewed to confirm this. **Stage 2 Screen:** 34 selected from 140 for full-text review. This involved review of both Titles and Abstracts for close relevance to the topic. Abstracts for studies that had initially appeared relevant by inclusion of cyanobacteria, cyanotoxins, blooms, recreational water, marine monitoring, or exposure and adverse health outcomes in both freshwater and marine environments in titles were assessed. 71 studies were rejected from the 140 papers based upon this review of abstracts. Papers could be rejected based upon a range of limitations or relevance criteria, for example: • not containing primary data and/or information related to health outcomes. • were primarily ecological or occurrence studies of organisms or toxins. • were management-related or economic and social assessments. • were related to analytical assays for organisms or toxins. In addition to those selected for full-text review in relation to the primary question, other papers were placed into groups (categories) for later careful assessment of relevance to secondary questions. These groups and the number of papers were: Surrogates and Monitoring: 3; Animal Poisoning (i.e., specifically Dogs): 10; Marine Cyanobacteria/Algae/Toxins: 19; BMAA: 1; LPS/Endotoxins: 2

Table A1-6: (continued)

S-C2	05/04/2021	CAT#1 R#1 H#1	#117 CAT #207 R #305 H Search PM-C10 (04/04/2021) Results: 523	CAT#1: 5/04/21 160,573 (2006-2021) R#1: 5/04/21 212,560 (2006-2021) H#1: 5/04/21 10,170,384 (2006-2022)	**Results:** 1,278 documents (2006-2021) prior to screening (Comparison PubMed® Search PM-C10; 04/04/2021; Results: 523) The purpose of this search was to validate earlier S-C1 from 17/11/2020, to determine if any additional publications could be found in a consolidated and complete "Super" Search after an additional 5-month time period. This updated S-C2 produced a higher result than S-C1. **Stage 1 Screen:** 145 selected from 1278. This involved assessment of relevance to answer the primary or secondary questions by examination of the title. In many cases papers could be readily rejected based upon lack of clear relevance to the review questions. In some cases, the abstract was also reviewed to confirm this. **Stage 2 Screen:** this involved a comparison of the Stage 1 Screen (145 results) to the Stage 1 Screen (140 results) from S-C1. This comparison did not produce any new or additional papers that would require further assessment by full-text review to answer either the Primary or Secondary questions. This was regarded as good validation of Search S-C1 in November 2020.

Table A1-7: PubMed® searches for individual Endotoxin/LPS and BMAA concepts

Search number	Date of Search/s	Description, Search string and Results
Endotoxins/LPS	14/11/2020	This Search was run alone to determine the extent of the literature for this topic. This was agreed with the Committee. **Search String:** "Endotoxins"[mh:noexp] OR Endotoxi*[tiab] OR "Lipopolysaccharides"[mh] OR Lipopolysaccharide*[tiab] OR LPS[tiab] These terms and string were originally included in the CAT Searches and subsequently removed from CAT SEARCH # 115. This search string produces a very large number of results – 86, 282 (2006-2021). Analysis of the results for an extended time-period shows that the research field started to increase in publication rate from 1980, with a further steady increase from 2000 and again from 2010. **Results:** 166,724 for the full time period (1909-2021)
BMAA	14/11/2020	**Search String:** BMAA[tiab] OR β-N-methylamino-L-alanine[tiab] OR “beta-N-methylamino-L-alanine”[nm:noexp] OR beta-N-methylamino-L-alanine[tiab] OR “beta-(N-carboxy-N-methyl)aminoalanine”[nm:noexp] This is a relatively recent research and publication topic with records commencing in 1986. It accelerated from around 2005. It has been steady for a decade from around 2012. **Results:** 399 (from 2006-2020); 510 (from 1986-2020)

Table A1-8: PubMed® combined searches related to Endotoxin/LPS and BMAA concepts

Search Name	Date	Contains Searches	Individual Search Results	Results
Endotoxins/LPS AND Recreation AND Health	15/11/2020	Endotoxins/LPS AND Recreation #207 AND Health #305	Endotoxins/LPS 86,282 (2006-2021) 166,725 (1909-2021) #207 65,692 (2006-2021) #305 5,713,018 (2006-2021	**Results:(** Endotoxins/LPS AND #207 AND #305) 170 documents (2006-2021) Analysis: The 170 papers were screened for relevance to the topic (Endotoxins/LPS AND Recreation AND Health) and this returned only 6 potentially relevant papers, namely: Berg *et al.* (2011); Lévesque *et al.* (2016); de Man *et al.* (2014); Mohamed and Al Shehri (2007); Mohamed (2008); Sattar *et al.* (2019). The 170 studies/papers for the full search and were of very limited relevance to environmental exposure to Endotoxins/LPS in recreational water situations. The search returned many animal physiological studies (with rodents) related to the impact of LPS in inducing depression and the effect of a range of agents to counter this. It is not clear why the search captured these studies as they do not have appear to have a clear link to the Recreation/al terms string.
BMAA and Cyanobacteria	14/11/2020	Cyanobacteria AND BMAA	Cyanobacteria 27,727 (1901-2021) BMAA: 399 (2006-2020)	The purpose of this search to determine relationship of the research and publication output between BMAA with cyanobacteria. **Search String**s: **BMAA:** BMAA[tiab] OR β-N-methylamino-L-alanine[tiab] OR "beta-N-methylamino-L-alanine"[nm:noexp] OR beta-N-methylamino-L-alanine[tiab] OR "beta-(N-carboxy-N-methyl)aminoalanine"[nm:noexp] **Cyanobacteria:** "Cyanobacteria"[mh:noexp] OR cyanobacteria*[tiab] OR Blue-green alga*[tiab] OR toxic alga*[tiab] The combined search indicates that publications associating BMAA and cyanobacteria first occurred in 2003 and accelerated in 2008 and 2009. Note, this does not necessarily mean that all publications were related to BMAA in cyanobacteria. They may just have contained the terms in Title and Abstracts. **Results:** BMAA: 399 (2006-2020) Combined Cyanobacteria AND BMAA: 234 (2006-2020) This comparison suggests that approximately 60% of the publications from 2006 that mentioned BMAA also mentioned Cyanobacteria (234 from 399). Note that this is in Titles and Abstracts.

6.2 Appendix 2 Risk of Bias Assessment Table

Table A2-1 Questions from OHAT (2019) used to assess risk of bias for individual primary studies.

Study ID:		Risk of bias: Yes/No Unknown N/A	Notes	Risk of bias rating (++/+/-/--)
Study Type:				
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate			
	Cofounding bias			
4.	Confounding (design/analysis)			
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data			
	Detection Bias			
8.	Exposure characterisation 7. Was the sampling and monitoring sufficiently close to the exposure zone? 8. Was there sufficient sample replication? 9. Was there recognition and accounting for spatial variance? 10. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 11. Were cyanotoxins identified and quantified by appropriate methods? 12. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?			

Table A2-1: (continued)

9.	Outcome assessment			
	Selective Reporting Bias			
10.	Outcome reporting			
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol			

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

6.3 Appendix 3: Freshwater and Marine Studies Excluded from Assessment after Full-text Review.

Table A3-1: Freshwater studies excluded from further assessment after full-text review.

Title	First Author	Year	Journal	Explanation for exclusion
Cyanobacterial harmful algal blooms (CyanoHABs): developing a public health response	Backer	2002	Lake and Reservoir Management	Review of other studies. Nearly all references pre-2000.
Canine cyanotoxin poisonings in the United States (1920s-2012): review of suspected and confirmed cases from three data sources	Backer	2013	Toxins	Review of other studies. Majority of references are newspaper articles of incidences.
Cyanobacteria and algae blooms: review of health and environmental data from the harmful algal bloom-related illness surveillance system (HABISS) 2007–2011	Backer	2015	Toxins	Review of other studies.
Sentinel animals in a one health approach to harmful cyanobacterial and algal blooms	Backer	2016	Veterinary Sciences	Compilation and review of other studies
Virulence genes of *Aeromonas* isolates, bacterial endotoxins and cyanobacterial toxins from recreational water samples associated with human health symptoms	Berg	2011	Journal of Water and Health	Not a recreational exposure health study.
Cyanobacteria: an unrecognized ubiquitous sensitizing allergen?	Bernstein	2011	Allergy Asthma Proc	Laboratory study. Not a recreational exposure health study.
Cylindrospermopsin Accumulation and Release by the Benthic Cyanobacterium *Oscillatoria* sp. PCC 6506 under Different Light Conditions and Growth Phases	Bormans	2014	Bull Environ Contam Toxicol	Study of cylindrospermopsin concentrations. Not a recreational exposure health study.
Widespread anatoxin-a detection in benthic cyanobacterial mats throughout a river network	Bouma-Gregson	2018	Plos One	Detection and distribution field study. Not a recreational exposure health study.
Harmful algae: effects of alkaloid cyanotoxins on animal and human health	Bownik	2010	Toxin Reviews	Review of other studies.

Table A3-1: (continued) **Freshwater studies excluded from further assessment after full-text review.**

Title	**First Author**	**Year**	**Journal**	**Explanation for exclusion**
Cyanotoxins: producing organisms, occurrence, toxicity, mechanism of action and human health toxicological risk evaluation	Buratti	2017	Arch Toxicol	Review of other studies.
Perspective: Advancing the research agenda for improving understanding of cyanobacteria in a future of global change	Burford	2020	Harmful Algae	Review of other studies.
Different Genotypes of Anatoxin-Producing Cyanobacteria Coexist in the Tarn River, France	Cadel-Six	2007	Applied and Environmental Microbiology	Detection and distribution field study. Not a recreational exposure health study.
Health impacts from cyanobacteria harmful algae blooms: Implications for the North American Great Lakes	Carmichael	2016	Harmful Algae	Review of other studies.
First identification of the hepatotoxic microcystins in the serum of a chronically exposed human population together with indication of hepatocellular damage	Chen	2009	Toxicol Sci	Analytical paper for detecting microcystins.
Freshwater harmful algal blooms and cyanotoxin poisoning in domestic dogs	Cherry	2015	JAVMA	General letter to the Editor.
Association of Toxin-Producing Clostridium botulinum with the Macroalga Cladophora in the Great Lakes	Chun	2013	Environ Sci Technol	Study on *Clostridium botulinum*. Not a recreational exposure health study.
Human exposure to endotoxins and fecal indicators originating from water features	de Man	2014	Water Research	Analysis of endotoxins in air and water but no direct association with human exposure.
Human exposure to cyanotoxins and their effects on health	Drobac	2013	Arh Hig Rada Toksikol	Review of other studies.

Table A3-1: (continued) **Freshwater studies excluded from further assessment after full-text review.**

Title	First Author	Year	Journal	Explanation for exclusion
Surveillance for Waterborne Disease and Outbreaks Associated with Recreational Water — United States, 2003–2004	Dziuban	2006	CDC Morbidity and Mortality Weekly Report: Surveillance Summaries	Compilation of waterborne disease outbreaks but limited information about cyanotoxins.
Identifying aerosolized cyanobacteria in the human respiratory tract: A proposed mechanism for cyanotoxin-associated diseases	Facciponte	2018	Science of the Tot Environ	Study on the detection of cyanobacteria in the human respiratory tract but no direct relationship with recreational exposure.
Health-based cyanotoxin guideline values allow for cyanotoxin-based monitoring and efficient public health response to cyanobacterial blooms	Farrer	2015	Toxins	Discusses development of guideline values but does not provide details of case studies.
Human Health Risk Assessment Related to Cyanotoxins Exposure	Funari	2008	Critical Reviews in Toxicology	Review of other studies.
Cyanobacteria blooms in water: Italian guidelines to assess and manage the risk associated to bathing and recreational activities	Funari	2017	Sci Tot Environ	Discusses development of Italian guideline values but does not provide details of case studies.
Benthic cyanobacteria: A source of cylindrospermopsin and microcystin in Australian drinking water reservoirs	Gaget	2017	Water Research	Study in reservoirs. Not recreational exposure.
Bad tastes, odours and toxins in our drinking water reservoirs: are benthic cyanobacteria the culprits?	Gaget	2018	Water Research Australia report	Study in reservoirs. Not recreational exposure.
Simultaneous quantification of microcystins and nodularin in aerosol samples using high-performance liquid chromatography/negative electrospray ionization tandem mass spectrometry	Gambaro	2012	Rapid Commun Mass Spectrom	Analytical techniques paper.
Sensitization of a child to Cyanobacteria after recreational swimming in a lake	Geh	2016	J Allergy and Clinical Immunology	Very limited information provided. Short paragraph conference abstract.

Table A3-1: (continued) **Freshwater studies excluded from further assessment after full-text review.**

Title	First Author	Year	Journal	Explanation for exclusion
Identification of *Microcystis aeruginosa* peptides responsible for allergic sensitization and characterization of functional interactions between cyanobacterial toxins and immunogenic peptides	Geh	2015	Environ Health Persp	Clinical study. Not recreational exposure.
Outbreaks associated with untreated recreational water- United States 2000-2014	Graciaa	2018	CDC Morbidity and Mortality Weekly Report: Surveillance Summaries	Compilation of waterborne disease outbreaks but limited information about cyanotoxins.
One Health and Cyanobacteria in Freshwater Systems: Animal Illnesses and Deaths Are Sentinel Events for Human Health Risks	Hilborn	2015	Toxins	Compilation and review of other studies
Recreational water - associated disease outbreaks - United States 2009-2010	Hlavsa	2014	CDC Morbidity and Mortality Weekly Report: Surveillance Summaries	Compilation of waterborne disease outbreaks but limited information about cyanotoxins.
Associations between chlorophyll a and various microcystin health advisory concentrations	Hollister	2016	F1000Research	Analytical techniques paper.
Chronic biotoxin-associated illness: Multiple-system symptoms, a vision deficit, and effective treatment	Hudnell	2005	Neurotoxicology and Teratology	Clinical study. Not recreational exposure.
Increasing Occurrence of the Benthic Filamentous Cyanobacterium *Lyngbya wollei*: A Symptom of Freshwater Ecosystem Degradation	Hudon	2014	Freshwater Science	Ecological study. Not recreational exposure.
Current approaches to cyanotoxin risk assessment and risk management around the globe	Ibelings	2014	Harmful Algae	Discusses development of guideline values but does not provide details of case studies.

Table A3-1: (continued) **Freshwater studies excluded from further assessment after full-text review.**

Title	First Author	Year	Journal	Explanation for exclusion
First report of anatoxin-a producing cyanobacteria in Australia illustrates need to regularly up-date monitoring strategies in a shifting global distribution	John	2019	Scientific Reports	Analytical paper.
Cyanotoxin management and human health risk mitigation in recreational waters	Koreiviene	2014	Environ Monit Assess	Review of other studies.
Detection and confirmation of saxitoxin analogues in freshwater benthic *Lyngbya wollei* algae collected in the St. Lawrence River (Canada) by liquid chromatography–tandem mass spectrometry	Lajeunesse	2012	Journal of Chromatography A	Analytical paper.
Fresh water, marine and terrestrial cyanobacteria display distinct allergen characteristics	Lang-Yona	2018	Sci Tot Environ	Clinical study. Not recreational exposure.
Exposure to cyanobacteria: acute health effects associated with endotoxins	Levesque	2016	Public Health	Appears to be a short summary of Levesque (2014) Prospective study of acute health effects in relation to exposure to cyanobacteria. Sci Tot Environ
Spatial and temporal variation in microcystin occurrence in wadeable streams in the southeastern United States	Loftin	2016	Environmental Toxicology and Chemistry	Field occurrence and distribution study. Not recreational exposure.
First Report of a Toxic *Nodularia spumigena* (Nostocales/ Cyanobacteria) Bloom in Sub-Tropical Australia. I. Phycological and Public Health Investigations	McGregor	2012	Int Jour Environ Res Public Health	Field identification study. Not recreational exposure.
Microcystin production in benthic mats of cyanobacteria in the Nile River and irrigation canals, Egypt	Mohamed	2006	Toxicon	Field identification study. Not recreational exposure.
Can cyanotoxins penetrate human skin during water recreation to cause negative health effects?	Nielsen	2020	Harmful Algae	Review of other studies.

Table A3-1: (continued) **Freshwater studies excluded from further assessment after full-text review.**

Title	First Author	Year	Journal	Explanation for exclusion
Microbial Communities and Fecal Indicator Bacteria Associated with *Cladophora* Mats on Beach Sites along Lake Michigan Shores	Olapade	2006	Applied and Environmental Microbiology	Field occurrence and distribution study. Not recreational exposure.
Recreational waterborne illnesses: recognition, treatment and prevention	Perkins	2017	American Family Physician	Very general overview.
A review of current knowledge on toxic benthic freshwater cyanobacteria – Ecology, toxin production and risk management	Quiblier	2013	Water Research	Review of other studies.
Primary irritant and delayed-contact hypersensitivity reactions to the freshwater cyanobacterium *Cylindrospermopsis raciborskii* and its associated toxin cylindrospermopsin	Stewart	2006	BMC Dermatol	Laboratory study. Not recreational exposure.
Recreational and occupational field exposure to freshwater cyanobacteria–a review of anecdotal and case reports, epidemiological studies and the challenges for epidemiologic assessment	Stewart	2006	Environ Health	Review of other studies.
Cyanobacterial poisoning in livestock, wild mammals and birds – an overview	Stewart	2008	Advances in Experimental Medicine and Biology	Compilation and review of other studies.
Cyanobacterial lipopolysaccharides and human health - a review	Stewart	2006	Environmental health: a global access science source	Review of other studies.
Cutaneous hypersensitivity reactions to freshwater cyanobacteria–human volunteer studies	Stewart	2006	BMC Dermatol	Laboratory study. Not recreational exposure.

Table A3-1: (continued) **Freshwater studies excluded from further assessment after full-text review.**

Title	First Author	Year	Journal	Explanation for exclusion
Occupational and environmental hazard assessments for the isolation, purification and toxicity testing of cyanobacterial toxins	Stewart	2009	Environ Health	Not recreational exposure.
Addressing Public Health Risks for Cyanobacteria in Recreational Freshwaters: The Oregon and Vermont Framework	Stone	2007	Integrated Environmental Assessment and Management	Approaches to address public health risk. Not specific recreational exposure studies.
Strategies for monitoring and managing mass populations of toxic cyanobacteria in recreational waters: a multi-interdisciplinary approach	Tyler	2009	Environ Health	Approaches for identification, monitoring and management. Not specific recreational exposure studies.
Community volunteer assessment of recreational water quality in the Hutt River, Wellington	Valois	2020	New Zealand Journal of Marine and Freshwater Research	Approaches for increasing public involvement in monitoring studies. Not specific recreational exposure studies.
Managing cyanobacterial toxin risks to recreational users: a case study of inland lakes in South East Queensland	Veal	2018	Water Science and Technology	Study into using cyanotoxin surrogates for management. Not specific recreational exposure studies.
Nebraska experience	Walker	2008	Adv Exp Med Biol	Compilation and review of other studies
Acute animal and human poisonings from cyanotoxin exposure — A review of the literature	Wood	2016	Environmental International	Very comprehensive review of other studies. Useful references.
Quantitative assessment of aerosolized cyanobacterial toxins at two New Zealand lakes	Wood	2011	J Environ Monitor	Environmental monitoring study. Not specific recreational exposure studies.
The Abundance of Toxic Genotypes Is a Key Contributor to Anatoxin Variability in Phormidium-Dominated Benthic Mats	Wood	2017	Marine Drugs	Analytical study comparing toxins per cell versus toxins per dry weight of benthic mat.

Table A3-2: Marine studies excluded from further assessment after full-text review.

Title	First Author	Year	Journal	Explanation for exclusion
Aerosolized Florida red tide toxins and human health effects	Abraham	2006	Oceanography	General overview with no primary exposure and health outcome information.
Harmful algal blooms at the interface between coastal oceanography and human health	Backer	2006	Oceanography	General overview with no primary health outcome information. Shellfish and fish poisoning but not direct studies.
Impacts of Florida red tides on coastal communities	Backer	2009	Harmful Algae	Review article. Overview and collation of other studies.
Prominent human health impacts from several marine microbes: history, ecology and public health implications	Bienfang	2011	International Journal of Microbiology	Review article. Overview and collation of other studies.
Dermatitis caused by algae and bryozoans	Bonamonte	2016	Aquatic Dermatology	Review article. References generally pre-2000.
Characterization of marine aerosol for assessment of human exposure to brevetoxins	Cheng	2005	Environmental Health Perspectives	Related to Backer et al. 2005; human health impact not detailed; outlines characterization of the aerosol.
Characterization of aerosols containing microcystin	Cheng	2007	Marine Drugs	Human health impact not detailed; outlines characterization of the aerosol.
Human risk associated with palytoxin exposure	Deeds	2010	Toxicon	Review article. Overview and collation of other studies.
An epidemiologic approach to the study of aerosolized Florida red tides	Fleming	2002	Harmful Algae	General overview with no specific primary health outcome information.
Overview of Aerosolized Florida Red Tide Toxins: Exposures and Effects	Fleming	2005	Environmental Health Perspectives	General overview with no specific primary health outcome information.
Oceans and human health: Emerging public health risks in the marine environment	Fleming	2006	Marine Poll Bull	General overview with no specific primary health outcome information.
Review of Florida red tide and human health effects	Fleming	2011	Harmful Algae	Review article. Overview and collation of other studies.

Table A3-2: (continued) **Marine studies excluded from further assessment after full-text review.**

Title	**First Author**	**Year**	**Journal**	**Explanation for exclusion**
Ostreopsis cf. *ovata* blooms in coastal water: Italian guidelines to assess and manage the risk associated to bathing waters and recreational activities	Funari	2015	Harmful Algae	Collation of other studies on human health effects and rationale for Italian guidelines. *Ostreopsis* not found in Australian waters.
Harmful algal blooms and public health	Grattan	2016	Harmful Algae	Related to shellfish poisoning
Monitoring, management and mitigation of Karenia blooms in the eastern Gulf of Mexico	Heil	2009	Harmful Algae	No details of human or animal health studies.
The human health effects of Florida red tide (FRT) blooms: an expanded analysis	Hoagland	2014	Environment International	Economic analysis; not health study.
Chronic biotoxin-associated illness: Multiple-system symptoms, a vision deficit and effective treatment	Hudnell	2005	Neurotoxicology and Teratology	Review article. Overview and collation of other studies.
Literature review of Florida red tide: implications for human health effects	Kirkpatrick	2004	Harmful Algae	Review article. Overview and collation of other studies.
Florida red tide and human health: a pilot beach conditions reporting system to minimize human exposure	Kirkpatrick	2008	Science of the total Environment	Outlines the US Integrated Ocean Observing System. No details of human or animal health studies.
Gastrointestinal emergency room admissions and Florida red tide blooms	Kirkpatrick	2010	Harmful Algae	Collation of admissions to hospital. No direct studies of exposure and health outcomes.
Cyanobacteria biennal dynamic in a volcanic mesotrophic lake in central Italy: Strategies to prevent dangerous human exposures to cyanotoxins	Manganelli	2016	Toxicon	Not a health study.
Harmful microalgae blooms (HAB); problematic and conditions that induce them	Maso	2006	Marine Pollution Bulletin	Shellfish poisoning; not a health study.

Table A3-2: (continued) **Marine studies excluded from further assessment after full-text review.**

Title	**First Author**	**Year**	**Journal**	**Explanation for exclusion**
The toxins of *Lyngbya majuscula* and their human and ecological health effects	Osborne	2001	Environment International	Review article. Overview and collation of other studies.
Dermal toxicology of *Lyngbya majuscula*, from Moreton Bay, Queensland, Australia	Osborne	2008	Harmful Algae	Mouse ear swelling test; not recreational exposure study.
Brevetoxin Concentrations in Marine Aerosol: Human Exposure Levels During a *Karenia brevis* Harmful Algal Bloom	Pierce	2003	Bulletin of Environmental Contamination and Toxicology	Other papers (Backer et al. 2003; Fleming et al., 2005; Kirkpatrick et al., 2004) have details on effects of aerosolized red tide toxins on respiratory function.
Dermatotoxins synthesized by blue-green algae (Cyanobacteria)	Rzymski	2012	Postepy Dermatologii I Alergologii	General overview; not health study.
Evaluation of the proinflammatory effects of contaminated bathing water	Sattar	2019	Journal of Toxicology and Environmental Health Part A	Cell-based bioassay; not health study.
Risk management of *Ostreopsis* spp. Blooms along Italian coasts	Scardala	2011	BioOne Complete	Details Italian guidelines but not the health studies underlying the derivations.
Toxic alkaloids in *Lyngbya majuscula* and related tropical marine cyanobacteria	Taylor	2014	Harmful Algae	Review article. Overview and collation of other studies.
Case definitions for human poisonings postulated to palytoxins exposure	Tubaro	2011	Toxicon	Review article. Overview and collation of other studies.
Toxicity of sea algal toxins to humans and animals	Zaccaroni	2008	Algal Toxins: Nature, Occurrence, Effect and Detection	Review article. Overview and collation of other studies. Primary focus is shellfish poisoning.

6.4 Appendix 4: Primary Freshwater and Marine Studies Excluded from Risk of Bias Assessment.

The risk of bias assessment included human studies only and the freshwater and marine studies that were excluded are listed in Table A3-1.

Table A4-1: Primary studies excluded from risk of bias assessment.

Title	First Author	Publication Year	Journal	Explanation for exclusion
FRESHWATER				
First report of (homo)anatoxin-a and dog neurotoxicosis after ingestion of benthic cyanobacteria in The Netherlands.	Fassen	2012	Toxicon	Animal study.
Fatal neurotoxicosis in dogs associated with tychoplanktic, anatoxin-a producing *Tychonema* sp. in mesotrophic Lake Tegel, Berlin.	Fastner	2018	Toxins	Animal study.
First report in a river in France of the benthic cyanobacterium *Phormidium favosum* producing anatoxin-a associated with dog neurotoxicosis.	Gugger.	2005	Toxicon	Animal study.
Neurotoxic cyanobacterium (blue-green alga) toxicosis in Ontario.	Hoff	2007	Canadian Veterinary Journal	Animal study.
Dog Poisonings Associated with a *Microcystis aeruginosa* Bloom in the Netherlands.	Lurling	2013	Toxins	Animal study.
Bloom announcement: first reports of dog mortalities associated with neurotoxic filamentous cyanobacterial mats at recreational sites in Lady Bird Lake, Austin, Texas.	Manning	2020	Data in Brief	Animal study.
Identification of a microcystin in benthic cyanobacteria linked to cattle deaths on alpine pastures in Switzerland.	Mez	1997	European Journal of Phycology	Animal study.
Diagnosis of anatoxin-a poisoning in dogs from North America.	Puschner	2008	Journal of Veterinary Diagnostics and Investigation	Animal study.
Debromoaplysiatoxin as the Causative Agent of Dermatitis in a Dog after Exposure to Freshwater in California.	Puschner	2017	Frontiers in Veterinary Science	Animal study.

Table A4-1: (continued)

Title	First Author	Publication Year	Journal	Explanation for exclusion
FRESHWATER (continued)				
Treatment and diagnosis of a dog with fulminant neurological deterioration due to anatoxin-a intoxication.	Puschner	2010	Journal of Veterinary Emergency and Critical Care	Animal study.
Treatment of cyanobacterial (microcystin) toxicosis using oral cholestyramine: Case report of a dog from Montana.	Rankin	2013	Toxins	Animal study.
Liver failure in a dog following suspected ingestion of blue-green algae (*Microcystis* spp.): a case report and review of the toxin.	Sebbag	2013	Journal of American Animal Hospital Association	Animal study.
Recreational exposure to cyanobacteria.	Stewart	2011	Encyclopedia of Environ Health	Animal study.
Investigation of a *Microcystis aeruginosa* cyanobacterial freshwater harmful algal bloom associated with acute microcystin toxicosis in a dog.	Van der Merwe	2012	Journal of Veterinary Diagnostic Investigation	Animal study.
First report of homoanatoxin-a and associated dog neurotoxicosis in New Zealand.	Wood	2007	Toxicon	Animal study.
Identification of a benthic microcystin-producing filamentous cyanobacterium (Oscillatoriales) associated with a dog poisoning in New Zealand.	Wood	2010	Toxicon	Animal study.
Detection of anatoxin-producing *Phormidium* in a New Zealand farm pond and an associated dog death.	Wood	2017	New Zealand Journal of Botany	Animal study.
MARINE				
Pathologic findings ad toxin identification in cyanobacterial (*Nodularia spumigena*) intoxication in a dog.	Simola	2012	Veterinary Pathology	Animal study.

6.5 Appendix 5: Risk of Bias Assessment of Individual Primary Studies

The methodological quality of individual studies was assessed using an adaptation of the OHAT risk of bias tool (OHAT, 2019). Only human studies were evaluated on applicable risk of bias questions based upon study design. The rating or answer to each risk of bias question was selected on an outcome basis from four options:

- definitely low risk of bias (++)
- probably low risk of bias (+)
- probably high risk of bias (-)
- definitely high risk of bias (--).

Data used to assess risk of bias was extracted using existing approaches/templates such as those available in the *OHAT Handbook* (OHAT, 2019). Study types that did not have an existing template (such as monitoring studies) were assessed against the usual risk of bias domains using questions such as those outlined in the OHAT framework: Table 4 (OHAT, 2019) where applicable. Studies that were determined to have a high risk of bias or serious concerns with study quality were excluded from the review.

Assessments for each individual primary study are given below.

Freshwater Human Studies

Table A5-1: Risk of bias assessments for freshwater primary studies (Format adapted from OHAT risk of bias tool: Table 5, OHAT Handbook; OHAT, 2019).

Study ID: 1 Backer *et al.*, 2008 Study Type: Cohort Study		Risk of bias: Yes/No Unknown N/A	Notes	Risk of bias rating (++/+/-/--)
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	96 exposed: 7 not exposed; The seven participants went to a nearby lake with no bloom, which was regarded as a suitable control site. Of those 7, only 6 reported only swimming during the study period and they also reported that they had participated in activities at the exposed site in 7 days prior to the study.	--
	Cofounding bias			
4.	Confounding (design/analysis)	**Yes; NR**	Confounders assessed: adenoviruses, enteroviruses, faecal coliforms. Insufficient information was provided about the distribution of known confounders.	-
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**	There was no loss of subjects.	++

Backer *et al.*, 2008 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	Environmental data was not provided for the unexposed site. It was not stated whether it was collected. The absence of environmental (sampling, etc.) at the un-exposed site decreases the confidence in the exposure assessment for the study, otherwise exposure was systematically well-designed and performed. 1. Yes. Sample sites were close to the exposure zone. 2. Yes. Replication involved 4 samples sites collected morning and afternoon on the 3 study days. 3. Yes. Sampling covered 4 sample sites across the exposure zone. 4. Yes. Cyanobacteria were identified to species level. 5. Yes. Microcystins were analysed by ELISA. 6. No. Sampling occurred at the same time as exposure. However, the exposure of subjects (type and duration) was not documented. Blood and nasal swab analyses for microcystins was by an experimental assay developed for the project i.e., not a validated and accredited pathology test.	--
9.	Outcome assessment	**Yes**	Outcome assessment was by self-reporting.	--
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol	**Yes**	As per 8, above: the study does not provide exposure information for the un-exposed site, which was deemed to be an appropriate control (comparator) for the exposed site. As per 3, above: Unintended co-exposure occurred because 6 of the un-exposed group reported swimming at the exposed lake site during 7 days before the study.	--

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 2 **Backer *et al.*, 2010** **Study Type: Cohort Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	7 subjects in unexposed group; 81 in exposed group. Unexposed group were only at control lake (no bloom) on one of the three study days and there were different numbers of subjects in exposed group on each of the three days of the study (18, 59, 4)	--
4.	Confounding (design/analysis)	**Yes**	Only adenoviruses and enteroviruses were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**	No loss of subjects.	++

Backer *et al.*, 2010 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	Environmental data was provided for both the exposed and unexposed lakes. 1. No. Water sampling sites were close to the exposure zone. The number of water sampling sites was low, and no information is given about the size of the lakes. There was no air sampling for the unexposed group and not every individual in the exposed group was provided with a personal air sampler. 2. Yes. Replication involved 4 samples at the exposed and 2 at the unexposed sites. Water samples were collected in the morning and evening on the 3 study days (exposed) and 1 study day only (unexposed). 3. Yes. See question 1 response. 4. Yes. Cyanobacteria were identified to species level. 5. Yes. Microcystins were analysed by ELISA and quantified by LC-MS. 6. No. Sampling occurred at the same time as exposure. However, the exposure of subjects (type and duration) was not documented. Blood and nasal swab analyses for microcystins were by an experimental assay developed by the project, i.e. not a validated and accredited pathology test.	--
9.	Outcome assessment	**Yes**	Outcome assessment was by self-reporting.	--
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 3 **Levesque *et al.*, 2014** **Study Type: Cohort Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	There was no comparator group. Residents living adjacent to one of the lakes were considered "less" exposed.	--
4.	Confounding (design/analysis)	**Yes**	Limited accounting for confounders. Only *E. coli* considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**Yes**	Thirty-five subjects out of a total of 501 did not complete symptom journals so were excluded. Also, some subjects did not complete questionnaires correctly or withdrew.	--

Levesque *et al.*, 2014 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	1. Unknown because the exposure areas at lakes was not defined. 2. Duplicate water samples collected daily. 3. Yes. Replication involved 5 sampling stations at two lakes and 4 at the third lake. Water samples were collected once daily. 4. No. Cyanobacterial types were not reported, and counts are given as cell totals only. 5. Yes. Microcystins were analysed by ELISA. 6. No. Relationship between sampling stations and exposure locations and time was not recorded. The exposure of subjects (type and duration) was not documented.	--
9.	Outcome assessment	**Yes**	Outcome assessment was by self-reporting.	--
	Selective Reporting Bias			
10.	Outcome reporting	**Yes**	Unknown because details of excluded families were not provided.	-
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol	**Yes**	Authors comment that people in better health had more frequent contact with the lakes (uncorrected selection bias).	-

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 4 **Stewart *et al*., 2006** **Study Type: Cohort Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	"Reference sites" (controls) had low cyanobacterial numbers but no comparator group with no exposure.	--
4.	Confounding (design/analysis)	**Yes**	Confounding variables were limited to faecal coliform analysis, but these samples were taken only when an exposure day was followed by a routine working day (39% of exposure events).	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**Yes**	A high (>50%) of questionnaires were not returned.	--

Stewart *et al.*, 2006 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	1. Unknown because the exposure areas were not defined. 2. No information about replication (no duplicate samples). Water samples were collected twice daily (morning and afternoon). 3. Yes. There were 1 to 4 sampling stations depending upon size of site. 4. Yes. Cyanobacterial types were reported. Types and cell number data were not provided, and the information was converted to cyanobacterial cell surface area as the exposure variable of interest which was not done by any other study. 5. Yes. Cyanotoxins were analysed by accredited laboratories. 6. No. Relationship between sampling stations and subject exposure locations and time was not recorded. The exposure of subjects (type and duration) was not documented.	--
9.	Outcome assessment	**Yes**	Outcome assessment was by self-reporting.	--
	Selective Reporting Bias			
10.	Outcome reporting	**Yes**	A high (>50%) of questionnaires were not returned.	--
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 5 **Pilotto *et al.*, 1997** **Study Type: Cohort Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**No**	Exposed (777) and unexposed (75). Unexposed subjects did not have contact with water.	**++**
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**Yes**	Of the original participants only 93% participated in the 7-day follow up.	--

Pilotto *et al*., 1997 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	1. Yes. Water sampling was in close proximity to exposure zone. 2. Yes. 10 replicate samples were collected across the exposure zone and pooled to form a single composite sample. 3. Yes. Water sampling was evenly spaced in a regular pattern across the exposure zone to account for spatial variability. 4. Yes. Cyanobacterial cell counts of the dominant types were determined at one accredited laboratory using a technique to achieve a specified level of precision. 5. No. No toxin identification or quantification was done by a chemical analytical technique. Potential cyanobacterial toxicity was measured on a specific concentrated sample using mouse bioassay. Hepatotoxicity was identified in the concentrated samples at one site on two separate interview days, and also at three other sites on one day only. 6. No. The exposure of subjects (type and duration) was not documented.	-
9.	Outcome assessment	**Yes**	Outcome assessment was by self-reporting.	--
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**No**		+

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 6 **Hilborn *et al*., 2014** **Study Type: Observational Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	No comparator group.	--
4.	Confounding (design/analysis)	**Yes**	The report provides water quality indicator data where it was available including the presence of cyanobacteria, *E. coli* and a range of toxin types and concentrations. The data was limited and varied in the time period after exposure associated with the disease reports.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**N/A**		--

Hilborn *et al.*, 2014 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	1. Unknown because sampling details not provided. 2. Unknown because sampling details not provided. 3. Unknown because sampling details not provided. 4. Cyanobacteria identified but no details of identification and quantitation methods. 5. Some cyanotoxin information but no details of identification and quantitation methods. 6. No. Information not provided about exposure.	--
9.	Outcome assessment	**Yes**	Outcome assessment was a mixture of medically diagnosed and unspecified diagnosis.	--
	Selective Reporting Bias			
10.	Outcome reporting	**N/A**		
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 7 **Schaefer *et al*., 2020** **Study Type: Observational Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**No**	Unexposed group (no contact with water): 61 and exposed: 60.	++
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**Yes**	No health outcome data provided.	--

Schaefer *et al.*, 2020 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	1. No. Insufficient for the duration of the study. 47 water samples collected bi-weekly over 2 months. 2. No information was provided about replication. 3. No. Five sampling stations but no spatial sampling at each location. 4. No. No cyanobacterial identification or quantification provided. 5. No. Microcystins were determined by ELISA by the authors. 6. No. No health outcome data was provided.	--
9.	Outcome assessment	**Yes**	No health effects data were provided.	--
	Selective Reporting Bias			
10.	Outcome reporting	**N/A**	The study reports exposure data only via nasal route.	
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 8 **Vidal *et al.*, 2017** **Study Type:** **Observational Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	No comparator group.	--
4.	Confounding (design/analysis)	**Yes**	Only faecal coliforms were considered as confounders.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**		++

Vidal *et al.*, 2017 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	1. Water sampling occurred once a week as part of a monitoring program by the Montevideo authorities. During the exposure period blooms of mainly *Microcystis* with the presence of “foam” (scum) being were observed. 2. No sample replication. 3. No. 4. Yes. Cyanobacteria identification and quantification was part of the monitoring program. 5. Yes. Cyanotoxins were identified and quantified as part of the monitoring program. 6. Yes. Despite the water sampling potentially not being at the exact location as exposure, the detection of microcystins in the explanted liver provided sound evidence of exposure.	--
9.	Outcome assessment	**No**	The extensive hospital serology tests for hepatitis A, B, and C, Epstein-Barr virus, and cytomegalovirus were negative. Histological studies and microcystin determination were performed on the explanted liver. The analysis of MCs revealed the presence of two microcystin toxins: Microsytin-LR (MC-LR) and [D-Leu^1]MC-LR, which was considered to confirm the role of microcystins in the development of hepatitis in this child.	++
	Selective Reporting Bias			
10.	Outcome reporting	**N/A**		
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 9 **Giannuzzi *et al.*, 2011** **Study Type: Case Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	N/A	Comparison groups: not applicable to Case studies and Observational studies	
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	N/A	Attrition/Exclusion: not applicable to Case studies and Observational studies	

Giannuzzi *et al.*, 2011 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**No**	1. Yes. Water samples were collected for a quantitative phytoplankton and toxin analysis on the same day and at the same place where the patient was immersed within 4 h of the incident. 2. Yes. Replicate samples were taken. 3. Not applicable since sampling was targeted to where the patient was immersed. 4. Yes. Cyanobacterial types were reported. 5. Yes. Cyanotoxins were analysed by accredited laboratories. 6. Yes. Water samples were collected for a quantitative phytoplankton and toxin analysis on the same day and at the same place where the patient was immersed within 4 h of the incident. The patient was immersed in an intense *Microcystis* bloom but the volume of water consumed is unknown.	+
9.	Outcome assessment	**No**	Medically diagnosed: The subject was immersed in algal scum and swam back to shore and a few hours later. He began to experience GI symptoms, malaise, nausea, vomiting and muscle weakness. His condition worsened and he was hospitalized and diagnosed with a liver disorder. He was discharged from intensive care after 8 d.	++
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**No**		++

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 10 Slavin, 2008 Study Type: Case Study		Risk of bias: Yes/No Unknown N/A	Notes	Risk of bias rating (++/+/-/--)
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	N/A	Comparison groups: not applicable to Case studies and Observational studies	
4.	Confounding (design/analysis)	Yes	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	N/A	Attrition/Exclusion: not applicable to Case studies and Observational studies	

Slavin, 2008 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	This report provides no significant environmental data to confirm any sort of significant exposure and limited details of outcome assessment.	--
9.	Outcome assessment	**Yes**	While the outcome was medically diagnosed the author makes an association between a range of possible environmental causes including algae infestation in the lakes.	--
	Selective Reporting Bias			
10.	Outcome reporting	**N/A**		
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 11 Trevino-Garrison *et al.*, 2015 **Study Type: Case Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	N/A	Comparison groups: not applicable to Case studies and Observational studies	
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	N/A	Attrition/Exclusion: not applicable to Case studies and Observational studies	

Trevino-Garrison *et al.*, 2015 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high-level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	The study provides limited environmental data to accompany the reports and determine exposure characterisation. Environmental data is provided for only two cases – in one case, water analyses on the same day as exposure confirmed cyanobacterial cell concentrations and microcystin toxin levels at a public health Warning level; in the second case the subject fell in the lake that was under a public health Warning also due to the presence of high cyanobacterial cell concentrations and microcystin levels.	--
9.	Outcome assessment	**Yes**	The authors note a healthcare provider may find it difficult to confirm cyanobacterial toxins are the cause of the illness based on symptoms alone. Hence under-reporting may have occurred.	--
	Selective Reporting Bias			
10.	Outcome reporting	**N/A**		
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Marine Human Studies

Table A5-2: Risk of bias assessments for included marine primary studies (Format adapted from OHAT risk of bias tool: Table 5, OHAT Handbook; OHAT, 2019).

Study ID: 1 **Backer *et al.*, 2003** **Study Type: Cohort or Prospective Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	The two groups were exposed at different times and different locations – the "Offshore" event at Sarasota in February, 1999 (non-exposure, i.e. "control"); and the "Onshore" red tide event (exposure) in October, 1999 at Jacksonville. The events were therefore separated both in location and in time by 8-months.	-
	Cofounding bias			
4.	Confounding (design/analysis)	**Yes**	No confounders considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**		++

Backer *et al*., 2003 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	In all marine studies on aerosolised brevetoxins there is a major influence of weather conditions (e.g. wind speed and direction) that determines the variability and characterisation of exposure. Seawater samples (11) were collected twice daily to determine *K. brevis* cells and brevetoxins. Six air samplers were placed 65m apart in the study area to capture airborne particles for brevetoxin analyses in a grid sample matrix. 1. Yes. 2. No details given about replication. 3. No details given about spatial distribution of water sampling. Six air samplers were placed 65m apart in the study area. 4. Limited information about identification and quantitation of *K. brevis* cells. 5. Brevetoxins measured by HPLC. 6. The exposure time varies widely (10 min – 8h). No information about volumes of water ingested and the air samplers were fixed so may not directly relate to the subjects' exposure.	--
9.	Outcome assessment	**Yes**	Health outcomes were self-reported. All marine studies on aerosolised brevetoxin exposure are complicated by the circumstances of study participants often residing in the region which had a history of red tide exposure. These residents may have adapted to chronic red tide aerosol exposure and this may have influenced their self-reported health outcome responses.	--
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol	**Yes**	An issue was raised about whether the symptoms reported by Jacksonville were result of acute exposure on day of study or result of previous periodic exposures since a red tide had been offshore for a week before study commenced.	--

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 2 Bean *et al.*, 2011 Study Type: Cohort or Prospective Study		Risk of bias: Yes/No Unknown N/A	Notes	Risk of bias rating (++/+/-/--)
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	No comparator group.	--
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**		++

Bean *et al.*, 2011 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	In all marine studies on aerosolised brevetoxins there is a major influence of weather conditions (e.g. wind speed and direction) that determines the variability and characterisation of exposure. From Cheng *et al*. (2005): 1. Air samplers were set up along 2 beaches. No distance details given. Personal air samplers on lapel near breathing zone of all subjects. Sea water samples collected 3x each day from surf zone adjacent to each air sampler location. No details given about spatial dimensions of the exposure zone. 2. No details given about sample replication. 3. No details given about spatial dimensions of the exposure zone. 4. Yes. 5. Yes. Brevetoxin were analysed by ELISA and quantified by LC-MS. 6. No. Sampling occurred at the same time as exposure. However, the exposure of subjects (type and duration) was not documented.	--
9.	Outcome assessment	**Yes**	Outcomes were self-reported. All marine studies on aerosolised brevetoxin exposure are complicated by the circumstances of study participants often residing in the region which had a history of red tide exposure. These residents may have adapted to chronic red tide aerosol exposure and this may have influenced their self-reported health outcome responses.	--
	Selective Reporting Bias			
10.	Outcome reporting	**Yes**	As this paper is a compilation of multiple studies it was not possible to assess selective reporting.	-
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol	**Yes**	As this paper is a compilation of multiple studies it was not possible to assess selective reporting.	-

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 3 **Cheng *et al.*, 2010** **Study Type: Cohort or Prospective Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	No comparator group. Subjects had a pre- and post-beach nasal swab.	--
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**N/A**	No health outcome data reported.	

Cheng *et al.*, 2010 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	Focus of the paper is on the suitability of using personal air samplers to monitor exposure of study participants to aerosolised brevetoxins and the correlation in concentrations measured with the personal air samplers and those measured by high-volume air samplers. 1. Air sampling only. No water sampling reported. 2. Three high volume air samplers but all located in close proximity to one another. 3. Personal air samplers were placed on lapel breathing zone which accounted for spatial variance. 4. Refer to other studies for K. brevis identification and quantitation. 5. Yes. Only air sample measurements. Brevetoxins analysed by ELISA. 6. Yes, since personal air samplers were used. However, these measurements are experimental, non-validated tests.	-
9.	Outcome assessment	**N/A**	Health outcomes were reported in Fleming *et al.* (2005; 2007).	
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol	**Yes**	Due to prevalence of aerosolised brevetoxins in the study environment it is possible subjects may have been exposed to brevetoxins prior to the study period.	--

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 4 **Fleming *et al.*, 2005** **Study Type: Cohort or Prospective Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	This study involved the same cohort being studied during a non-exposure and an exposure period. However, *K. brevis* cells were in the waters at the beach study site even during the "non-exposure" period.	--
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**		++

Fleming *et al.*, 2005 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	Cell counts were done in water samples and brevetoxins were measured in water and air samples. From Cheng *et al.* (2005): 1. Air samplers were set up along 2 beaches. No details of the distances between sites were given. Personal air samplers were located on the lapel near the breathing zone of all subjects. Sea water samples collected 3x each day from surf zone adjacent to each air sampler location. No details given about spatial dimensions of the exposure zone. 2. No details given about sample replication. 3. No details given about spatial dimensions of the exposure zone. 4. Yes. 5. Yes. Brevetoxin were analysed by ELISA and quantified by LC-MS. 6. No. Sampling occurred at the same time as exposure. However, the exposure of subjects (type and duration) was not documented. Participants were asked to spend a minimum of 1 h at the beach in areas where environmental monitoring was on-going but no information is given about their activities.	--
9.	Outcome assessment	**Yes**	Health outcomes self-reported. Spirometer assessments have been reported to have limitations.	--
	Selective Reporting Bias			
10.	Outcome reporting	**Yes**	130 subjects enrolled in study and 59 asthmatics participated in study activities.	--
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**Yes**	Due to prevalence of aerosolised brevetoxins in the study environment it is possible subjects may have been exposed to brevetoxins prior to the study period.	--

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 5 **Fleming *et al*., 2007** **Study Type: Cohort or Prospective Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	This study involved the same cohort being studied during a non-exposure and an exposure period. However, *K. brevis* cells were in the waters at the beach study site even during the "non-exposure" period.	--
4.	Confounding (design/analysis)	**Yes**	No confounders considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**		++

This study includes environmental data from Jan 2003 (unexposed) and Mar 2003 (exposed) which is reported in Fleming *et al* (2005). It is considered that this study may not be a "new" group of 97 but include data for the 59 asthmatics previously reported in Fleming *et al* (2005).

Fleming *et al.*, 2007 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	Cell counts were made in water samples and brevetoxins were measured in water and air samples. From Cheng *et al*. (2005): 1. Air samplers were set up along 2 beaches. No details of the distances between sites were given. Personal air samplers were located on the lapel near the breathing zone of all subjects. Sea water samples collected 3x each day from surf zone adjacent to each air sampler location. No details given about spatial dimensions of the exposure zone. 2. No details given about sample replication. 3. No details given about spatial dimensions of the exposure zone. 4. Yes. 5. Yes. Brevetoxin were analysed by ELISA and quantified by LC-MS. 6. No. Sampling occurred at the same time as exposure. However, the exposure of subjects (type and duration) was not documented. Participants were asked to spend a minimum of 1 h at the beach in areas where environmental monitoring was on-going but no information is given about their activities.	--
9.	Outcome assessment	**Yes**	Health outcomes self-reported. Spirometer assessments have been reported to have limitations.	--
	Selective Reporting Bias			
10.	Outcome reporting	**Yes**	Unknown	-
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**Yes**	Due to prevalence of aerosolised brevetoxins in the study environment it is possible subjects may have been exposed to brevetoxins prior to the study period.	--

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 6 Fleming *et al.*, 2009 **Study Type: Cohort or Prospective Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	This study involved the same cohort being studied during a non-exposure and an exposure period. However, *K. brevis* cells were in the waters at the beach study site even during the "non-exposure" period.	--
4.	Confounding (design/analysis)	**Yes**	No confounders considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**		++

Includes environmental data from Mar 2005 (exposed) which is reported in Fleming *et al* (2007).

Fleming *et al.*, 2009 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	From Cheng *et al*. (2005) air sampling details. 1. Air samplers were set up along 2 beaches. No details of the distance between sites is given. Personal air samplers were placed on the lapel near breathing zone of all subjects. Sea water samples collected 2x each day from surf zone adjacent to each air sampler location. No details given about spatial dimensions of the exposure zone. 2. No details given about sample replication. 3. No details given about spatial dimensions of the exposure zone. 4. Yes. 5. Yes. Brevetoxin were analysed by ELISA and quantified by LC-MS. 6. No. Sampling occurred at the same time as exposure. However, the exposure of subjects (type and duration) was not documented. Participants were asked to spend a minimum of 1 h at the beach in areas where environmental monitoring was on-going but no information is given about their activities.	--
9.	Outcome assessment	**Yes**	Health outcomes self-reported. Spirometer assessments have been reported to have limitations.	--
	Selective Reporting Bias			
10.	Outcome reporting	**Yes**	Unknown	-
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**Yes**	Due to prevalence of aerosolised brevetoxins in the study environment it is possible subjects may have been exposed to brevetoxins prior to the study period.	--

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 7 Kirkpatrick *et al.*, 2011 Study Type: Cohort or Prospective Study		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	This study involved the same cohort being studied during a non-exposure and an exposure period. Due to prevalence of aerosolised brevetoxins in the study environment it is possible subjects may have been exposed to brevetoxins prior to the study period.	--
4.	Confounding (design/analysis)	**Yes**	No other confounders considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**		++

Kirkpatrick *et al.*, 2011 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	Authors refer to Fleming *et al.* (2005; 2007) and Cheng *et al.* (2005). From Cheng *et al*. (2005): 1. Air samplers were set up along 2 beaches. No details of the distances between sites were given. Personal air samplers were located on the lapel near the breathing zone of all subjects. Sea water samples collected 3x each day from surf zone adjacent to each air sampler location. 2. No details given about spatial dimensions of the exposure zone. 3. No details given about sample replication. 4. No details given about spatial dimensions of the exposure zone. 5. Yes. 6. Yes. Brevetoxin were analysed by ELISA and quantified by LC-MS. 7. No. Sampling occurred at the same time as exposure. However, the exposure of subjects (type and duration) was not documented. Participants were asked to spend a minimum of 1 h at the beach in areas where environmental monitoring was on-going but no information is given about their activities.	--
9.	Outcome assessment	**Yes**	Health outcomes self-reported. Authors report the handheld peak flow meters used to assess respiratory function are relatively inaccurate. These meters were only used to measure peak flow post 1 h exposure and not prior to exposure.	--
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**Yes**	Due to prevalence of aerosolised brevetoxins in the study environment it is possible subjects may have been exposed to brevetoxins prior to the study period.	--

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 8 **Lin *et al.*, 2016** **Study Type: Cohort or Prospective Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	23% of participants did not immerse themselves in the water and were not included in the study. No health outcome data was collected/provided for those that did not immerse themselves in the water.	--
4.	Confounding (design/analysis)	**Yes**	Authors acknowledge that since the phytoplankton cell counts were low, they could not be confident that health outcomes were the result of phytoplankton exposure alone.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**Unknown**	To focus on those with recreational water contact only participants who reported body immersion were included in models of the association between phytoplankton concentration and illness.	-

Lin *et al.*, 2016 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	Water sampling was systematic at multiple sites at the beach. Phytoplankton cell counts were performed on a daily composite sample and were quantitatively assayed for both totals and major phytoplankton group counts resulting in a low level of discrimination of potentially toxic or problematic organisms in the analysis. The high level taxonomic groups used were Cyanobacteria; Dinophyta (dinoflagellates); Bacillariophyta (diatoms); and miscellaneous other groups. The counting protocol involved comprehensive identification of all genera and types, however this data was not used in the logistic regression models. The data was however used to determine associations between major groups and major symptom classes. Also, although water samples were analysed for two different cyanotoxins (Debromoaplysiatoxin and lyngbyatoxin-a), there were no detections and concentrations were reported as all <LOD.	--
9.	Outcome assessment	**Yes**	Outcomes self-reported. The authors identified a possibility for responder bias since one adult was allowed to answer questions for all household members.	--
	Selective Reporting Bias			
10.	Outcome reporting	**Unknown**	To focus on those with recreational water contact only participants who reported body immersion were included in models of the association between phytoplankton concentration and illness.	-
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**No**		++

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 9 **Milian *et al.*, 2007** **Study Type: Cohort or Prospective Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	This study involved the same cohort being studied during a non-exposure and an exposure period. The study reported that both *K brevis* cells and brevetoxins were also present during what was defined as the non-exposure study periods.	--
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**		**++**

Milian *et al.*, 2007 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	From Cheng *et al.* (2005): 1. Air samplers (6) were set up along the beach. No details of the distances between sites were given. Personal air samplers were located on the lapel near the breathing zone of all subjects. Sea water samples collected 3x each day from surf zone adjacent to each air sampler location. 2. No details given about spatial dimensions of the exposure zone. 3. No details given about sample replication. 4. No details given about spatial dimensions of the exposure zone. 5. Yes. 6. Yes. Brevetoxin were analysed by ELISA and HPLC. 7. Yes. Sampling occurred at the same time as exposure. Personal air samplers on lapel near breathing zone of all subjects.	**-**
9.	Outcome assessment	**Yes**	Outcomes self-reported.	**--**
	Selective Reporting Bias			
10.	Outcome reporting	**No**		**++**
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**Yes**	Due to prevalence of aerosolised brevetoxins in the study environment it is possible subjects may have been exposed to brevetoxins prior to the study period.	**--**

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 10 **Morris Jr. *et al.*, 2006** **Study Type: Cohort or Prospective Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**No**	The study involved 107 "watermen" as participants; 29 controls i.e. participants who had minimal contact with estuarine waters.	**++**
4.	Confounding (design/analysis)	**Yes**	No confounders were reported.	**--**
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**		**++**

Morris Jr. *et al*., 2006 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	The exposure data to *Pfiesteria* in this study was not quantitative and was only recorded as positive or negative. In addition, the exposure assessment was based around a routine ongoing monitoring program by the Maryland Department of Natural Resources during 1999 – 2002 where samples were obtained from the tributaries where the enrolled watermen worked. The overlapping study participant work area grids and water monitoring grids did not provide certainty regarding the temporal overlap of work exposure and *Pfiesteria* detection. Participants self-reported exposure to any type of known chemical toxicants and selected symptoms provided to them based on "possible estuary-associated syndrome".	--
9.	Outcome assessment	**Yes**	Participants self-reported symptoms.	--
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)			

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 11 **O'Halloran *et al.*, 2017** **Study Type: Cohort or Prospective Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	No comparator group. All subjects were surfers.	--
4.	Confounding (design/analysis)	**Yes**	Only *Enterococcus* was considered. Authors note that confounding factors that may have been responsible for the adverse health outcome, such as local wildfires and aerial pesticide spraying which were not considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**		++

O'Halloran *et al.*, 2017 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	Exposure assessment was based around a sampling program from weekly samples from the end of a wharf over the 8 months of the study to determine chlorophyll *a,* phytoplankton cell concentrations of *Pseudo-nitzschia australis* and *Alexandrium catenella* and domoic acid toxin (DA produced by *P. australis*). While these samples were in Monterey Bay area, they were not necessarily representative of the surfers' exposure zone.	--
9.	Outcome assessment	**Yes**	Outcomes were self-reported via the surveys.	--
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)			

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 12 **Backer *et al.*, 2005** **Study Type: Cohort or Prospective Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	The same cohort was studied during a non-exposure and an exposure period. The comparison was therefore the same group at different times.	**-**
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	**--**
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**		**++**

Backer *et al.*, 2005 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	A limitation was associated with characterising aerosol exposure measurement. This is covered in the authors' statement that: "the traditional approach to individual occupational exposure assessment would be to have the lifeguards wear the personal samplers. However, there was concern that the personal samplers would interfere with emergency response activities or be destroyed by immersion in seawater. Instead, personal exposure was measured by placing samplers on the lifeguard towers near the lifeguards' breathing zones".	--
9.	Outcome assessment	**Yes**	Health outcomes self-reported. Spirometer assessments have been reported to have limitations.	--
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**Yes**	Due to prevalence of aerosolised brevetoxins in the study environment it is possible subjects may have been exposed to brevetoxins prior to the study period.	--

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 13 **Galliteli *et al.*, 2005** **Study Type:** **Observational Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	No comparator group.	--
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**No**		++

Gallitelli *et al.*, 2005 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	Exposure characterisation was limited as phytoplankton presence/abundance was measured at three days after the onset of symptoms during both summers. Results are reported only as: "an unusual proliferation of the tropical microalga *Ostreopsis* genus (more than 1 million cells/L) during both episodes."	--
9.	Outcome assessment	**No**		+
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)			

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 14 **Osborne *et al.*, 2007** **Study Type:** **Observational Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**No**	There was a control group of 367 postal survey respondents who reported no water exposure	++
4.	Confounding (design/analysis)	**Yes**	Confounders to eliminate dermatosis associated with marine organisms were considered. However, there were no environmental measurements of possible confounders.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**Yes**	Persons with wheals, which are often associated with cnidarian stinging episodes but not exposure to toxic *Lyngbya majuscula*, were excluded.	--

Osborne *et al.*, 2007 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?		There was no concurrent or reported exposure characterisation associated with the survey period. This was even though the survey covered 7 months (January to July) since this was when blooms of *L. majuscula* had occurred.	--
9.	Outcome assessment	**Yes**	Health outcomes self-reported.	--
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**Yes**	Authors note the possibility of non-respondent bias was potentially high. This is because postal survey was mailed to 5,000 residents with a response rate of 27%. High numbers of people (78%) responding to the survey reported recreational water activity in Moreton Bay, QLD. However, the demographics of the respondents generally resembled the Australian Bureau of Statistics population data for Bribie Island.	--

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 15 Osborne and Shaw, 2008 **Study Type: Observational Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	No comparator group.	--
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**Yes**	Cases of *Lyngbya*-like symptoms were identified subjectively based on reporting of symptoms in first aid reports. Therefore, some outcomes could have been missed or excluded.	--

Osborne and Shaw, 2008 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	Exposure characterisation and assessment was based solely on National Parks staff reporting *Lyngbya* being present in early 1998 and not afterwards. Signs had been erected warning of 'harmful algae' at a location where *Lyngbya*-like symptoms were reported.	--
9.	Outcome assessment	**Yes**	Outcome assessment on the first aid report symptoms by first-aiders with unspecified qualifications.	--
	Selective Reporting Bias			
10.	Outcome reporting	**Yes**	See question 7.	-
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)			

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 16 Tichadou *et al.*, 2010 **Study Type: Observational Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	**Yes**	No comparator group.	--
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	**Yes**	Only cases in which *Ostreopsis* was considered a plausible cause were included based on the identification of compatible clinical features in at least 2 persons in a location where a bloom was demonstrated.	--

Tichadou *et al.*, 2010 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	Timely exposure characterisation was limited/poor as seawater and/or macrophyte analyses could only be done the day after symptoms are reported and several hours may elapse between occurrence of symptoms and reporting to the poison control centre. *Ostreopsis* blooms can last only a few hours so the delay in sampling may miss a bloom occurrence.	--
9.	Outcome assessment	**Yes**	Authors note the nonspecific nature of clinical manifestations the probably resulted in under-diagnosis and thus under-reporting.	--
	Selective Reporting Bias			
10.	Outcome reporting	**Yes**	See question 7.	--
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)			

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 17 **Honner *et al.*, 2010** **Study Type: Case Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	N/A	Comparison groups: not applicable to Case studies and Observational studies	
4.	Confounding (design/analysis)	**Yes**	As part of the clinical assessment confounders were considered but there was limited environmental assessment of confounders.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	N/A	Attrition/Exclusion: not applicable to Case studies and Observational studies	

Honner *et al.*, 2010 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	The only environmental data to accompany the exposure period and location is from weekly monitoring of ocean levels of total bacteria, faecal bacteria and enterococci. Two days prior to the woman scuba diving the faecal bacteria and enterococci levels exceeded regulatory limits.	--
9.	Outcome assessment	**No**	Medically diagnosed and full clinical assessment.	++
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 18 **Lee *et al.*, 2009** **Study Type: Case Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	N/A	Comparison groups: not applicable to Case studies and Observational studies	
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	N/A	Attrition/Exclusion: not applicable to Case studies and Observational studies	

Lee *et al.*, 2009 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	The study has no environmental data to accompany the exposure period, only observations made by the subject. It is therefore a potential association with red tide only with no exposure characterisation.	--
9.	Outcome assessment	**Yes**	While it was medically reported it is not a full clinical assessment. There was a presumptive diagnosis of red-tide associated asthma.	-
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 19 Namendys-Silva *et al.*, 2018 **Study Type: Case Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	N/A	Comparison groups: not applicable to Case studies and Observational studies	
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	N/A	Attrition/Exclusion: not applicable to Case studies and Observational studies	

Namendys-Silva *et al.*, 2018 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	The report has no environmental exposure data and no identification of the diatom.	--
9.	Outcome assessment	**Yes**	While it was medically reported it is not a full clinical assessment. Presumptive diagnosis based on a microorganism (compatible with a marine diatom) being found in the bronchoalveolar lavage sample.	-
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 20 **Reddy *et al.*, 2019** **Study Type: Case Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	N/A	Comparison groups: not applicable to Case studies and Observational studies	
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	N/A	Attrition/Exclusion: not applicable to Case studies and Observational studies	

Reddy *et al.*, 2019 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	The report has limited environmental data for any suitable exposure characterisation. The study presents state records of *Karenia brevis* cell concentration data integrated for a 1 month period from the Florida Fish and Wildlife Commission monitoring program at the same time as the incident in the study.	--
9.	Outcome assessment	**Yes**	While it was medically reported it was not a full clinical assessment. The presumptive diagnosis was based upon the subject reporting swimming in a red tide.	-
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 21 Steensma, 2007 Study Type: Case Study		Risk of bias: Yes/No Unknown N/A	Notes	Risk of bias rating (++/+/-/--)
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	N/A	Comparison groups: not applicable to Case studies and Observational studies	
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	N/A	Attrition/Exclusion: not applicable to Case studies and Observational studies	

Steensma, 2007 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	Limited environmental data for exposure characterisation. Cell concentrations of *Karenia brevis* in the area of the sailing during the week of the incident and exposure came from data came from the Florida Fish and Wildlife Commission monitoring program.	--
9.	Outcome assessment	**Yes**	While it was medically reported it is not a full clinical assessment. It was therefore a presumptive diagnosis.	-
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

Study ID: 22 **Werner *et al.*, 2011** **Study Type: Case Study**		**Risk of bias: Yes/No Unknown N/A**	**Notes**	**Risk of bias rating (++/+/-/--)**
Q				
	Selection bias			
1.	Randomization	N/A	Randomization: not applicable to Cohort, Case studies and Observational studies	
2.	Allocation concealment	N/A	Allocation concealment: not applicable to Cohort, Case studies and Observational studies	
3.	Comparison groups appropriate	N/A	Comparison groups: not applicable to Case studies and Observational studies	
4.	Confounding (design/analysis)	**Yes**	No confounders were considered.	--
	Performance Bias			
5.	Identical experimental conditions	N/A	Identical experimental conditions: not applicable to Cohort, Case studies and Observational studies	
6.	Blinding of researchers during study?	N/A	Blinding of researchers during study?: not applicable to Cohort, Case studies and Observational studies	
	Attrition/Exclusion Bias			
7.	Missing outcome data	N/A	Attrition/Exclusion: not applicable to Case studies and Observational studies	

Werner *et al.*, 2011 (continued)

	Detection Bias			
8.	Exposure characterisation 1. Was the sampling and monitoring sufficiently close to the exposure zone? 2. Was there sufficient sample replication? 3. Was there recognition and accounting for spatial variance? 4. Were the cyanobacteria and/or algal types and numbers confirmed by credible high level taxonomic identification and quantitation methods? 5. Were cyanotoxins identified and quantified by appropriate methods? 6. Is there sufficient confidence in confirmation or matching of exposure with adverse health outcomes/no outcomes (no significant time lags were observed between sampling/monitoring for cyanobacteria/cyanotoxins and exposure/health effects reports)?	**Yes**	The report has no environmental monitoring data to allow for exposure characterisation.	--
9.	Outcome assessment	**Yes**	The case was reported as having the typical histopathological findings of *Lyngbya* dermatitis.	-
	Selective Reporting Bias			
10.	Outcome reporting	**No**		++
	Other Sources of Bias			
11.	Other threats (e.g. statistical methods appropriate; researchers adhered to the study protocol)	**N/A**		

Risk of bias rating:

Definitely low risk of bias (++)	++	Probably low risk of bias (+)	+	Probably high risk of bias (-)	-	Definitely high risk of bias (--)	--

6.6 Appendix 6: Derivations of Freshwater and Marine Recreational Guidelines

The collation of derivations of recreational water guideline values for freshwater cyanotoxins from various countries and Australian states is given in Tables A6-1 and A6-2.

The derivations are based upon TDI or RfD that are determined by:

Tolerable daily intake (TDI) or Reference Dose (RfD)
TDIs are used to determine recreational guideline values for exposure to cyanobacterial toxins.
$\text{TDI or RfD} = \dfrac{\text{NOAEL or LOAEL}}{\text{uncertainty factors}}$

Compilation of the derivations of recreational water guidelines in terms of cyanobacterial cell counts for the countries, jurisdictions, and Australian states where this is provided is given in Table A6-3.

A collation of recreational water guideline values developed for marine algae and cyanobacteria from Australian and international sources is given in Table A6-4.

Table A6-1: Derivation of tolerable daily intake (TDI) or reference dose (RfD) for application in the derivation of recreational guideline values for the range of cyanotoxins for all available countries and jurisdictions.

Country or Jurisdiction	Study	Test Animal	Duration	Material/ Toxin	LOAEL (µg/kg/ day)	NOAEL (µg/kg/ day)	Uncertainty Factors (UF)				Sum of UF	TDI or RfD (µg/kg/ day)
							Intra-species variability	Inter-species variability	LOAEL to NOAEL	Life-time exposure		
Microcystin												
Australia NHMRC 2008	Falconer *et al.* 1994	pig	44 days	Bloom material[1.]	100		10	10	5	10 (carcinogenicity concerns) And 0.32 (study time conversion)	1600	0.0625
Canada Health Canada 2020, Section 7.1	Heinze 1999	rat	28 days	Purified microcystin-LR	50		10	10	3 3 for database deficiencies	Not necessary as types of exposure are short-term	900	0.056
New Zealand 2009	Falconer *et al.* 1994	pig	44 days	Bloom material[1.]	88		10	10	2	5	1000	0.088
	Fawell *et al.* 1999a	mouse	13 weeks	Purified microcystin-LR via gavage		40	10	10	-	5	500	0.08
USEPA 2019a	Heinze 1999	rat	28 days	Purified microcystin-LR	50		10	10	3	3 (database limitations)	900 (but 1000 used)	0.05
WHO 2020	Fawell *et al.*, 1999a	mouse	13 weeks			40	10	10			100	0.4
California 2016 (Alert)	Heinze 1999	rat	28 days	Purified microcystin-LR	50 6.4[2.]		10	10		10 (database limitations)	1000	$6x10^{-3}$
California 2016 (Action Tier 1)	Heinze 1999	rat	28 days	Purified microcystin-LR	50 6.4[2.]		10	10		3 (database limitations)	300	$2x10^{-2}$
Massachusetts 2021	Based on	WHO	2003	No	details	given						

Table A6-1: (continued)

Country or Jurisdiction	Study	Test Animal	Duration	Material/ Toxin	LOAEL (µg/kg/ day)	NOAEL (µg/kg/ day)	Uncertainty Factors (UF)				Sum of UF	TDI or RfD (µg/kg/ day)
							Intra-species variability	**Inter-species variability**	**LOAEL to NOAEL**	**Life-time exposure**		
Microcystin (continued)												
New Jersey 2017 (revised 2020)	Fawell *et al.*, 1999a	mouse	13 weeks		40		10	10	3	10 (database limitations)	3000	0.01
Ohio 2020	Used USEPA	2019a										0.05
Oregon Stone & Bress 2007	Used WHO	2003	TDI	value								0.04
Oregon Farrer *et al.*, 2015	Heinze 1999	rat	28 days	Purified microcystin-LR	50[4.]		10	10	10		1000	0.05
Oregon 2019	Heinze 1999	rat	28 days	Purified microcystin-LR	50[4.]		10	10	10		1000	0.05
Vermont Stone & Bress 2007	Used WHO	(2003)	TDI	value								0.04
Washington 2008	Used WHO	(2003)	TDI	value								0.04
Saxitoxin (Stx-eqiv)[6.]												
WHO 2020	Human	poisoning	data		1.5				3			0.5
Ohio 2020	EFSA 2009	Human	poisoning	data		0.5		10		10 (database limitations)	100	0.005
Oregon 2019	EFSA 2009					0.5				10 (database limitations)	10	0.05
Oregon Farrer *et al.* 2015	EFSA 2009	Human	poisoning	data		0.5				10 (database limitations)	10	0.05
Washington 2011	EFSA 2009					0.5						0.5

Table A6-1: (continued)

Country or Jurisdiction	Study	Test Animal	Duration	Material/ Toxin	LOAEL (µg/kg/ day)	NOAEL (µg/kg/ day)	Uncertainty Factors (UF)				Sum of UF	TDI or RfD (µg/kg/ day)
							Intra-species variability	**Inter-species variability**	**LOAEL to NOAEL**	**Life-time exposure**		
Anatoxin-a												
USEPA 2019a	Available acute oral toxicity data was considered inadequate to support derivation of an acute RfD											
WHO 2020	Fawell *et al.* 1999b	mouse	28 days	Purified anatoxin-a		98	10	10			100	0.98
California 2016 (Tier 1)[3.]	Fawell *et al.* 1999b	mouse	28 days	Purified anatoxin-a		100	10	10		10 (database limitations)	1000	0.1
California 2016 (Tier 2)[3.]	Fawell *et al.* 1999b	mouse	28 days	Purified anatoxin-a		2,500	10	10		10 (database limitations)	1000	2.5
New Jersey 2017 (revised 2020)	Fawell & James 1994; Fawell *et al.* 1999b	mouse	28 days	Purified anatoxin-a		98	10	10	1	3 (database limitations) 3 (modifying factor)	1000	0.1
Ohio 2020	Astrachan & Archer 1981; Astrachan *et al.* 1980	rat	7 weeks			50	10	10		10 (database limitations)	1000	0.05
Oregon 2019	Fawell & James 1994; Fawell *et al.* 1999b	mouse	28 days	Purified anatoxin-a		100	10	10		10 (database limitations)	1000	0.1
Oregon Farrer *et al.* 2015	Fawell *et al.* 1999b	mouse	28 days	Purified anatoxin-a		100	10	10		10 (database limitations)	1000	0.1
Washington 2008	Fawell & James 1994; Fawell *et al.* 1999b	mouse	28 days	Purified anatoxin-a		2,500	10	10		10 (database limitations)	1000	3 (rounded) (short-term value)
	Astrachan & Archer 1981; Astrachan *et al.* 1980	rat	7 weeks		500		10	10		10 (database limitations)	1000	0.5 (sub chronic)

Table A6-1: (continued)

Country or Jurisdiction	Study	Test Animal	Duration	Material/ Toxin	LOAEL (µg/kg/ day)	NOAEL (µg/kg/ day)	Uncertainty Factors (UF)				Sum of UF	TDI or RfD (µg/kg/ day)
							Intra-species variability	**Inter-species variability**	**LOAEL to NOAEL**	**Life-time exposure**		
Cylindrospermopsin												
USEPA 2019a	Humpage & Falconer 2003	mouse	11 weeks	Purified cylindrospermopsin		30	10	10		3 (database limitations)	300	0.1
WHO 2020	Humpage & Falconer 2003	mouse	11 weeks	Purified cylindrospermopsin		30	10	10		3 (database limitations)	300	0.1
California 2016 (Tier 1)	Humpage & Falconer 2003	mouse	11 weeks	Purified cylindrospermopsin		33 BMDL[2.]	10	10		10 (database limitations)	1000	3.3 $x10^{-2}$
California 2016 (Tier 2)	Humpage & Falconer 2003	mouse	11 weeks	Purified cylindrospermopsin		33 BMDL[2.]	10	10		6 (database limitations)	600	5.5 $x10^{-2}$
New Jersey 2018 (revised 2020)	Humpage & Falconer 2003	mouse	11 weeks	Purified cylindrospermopsin		30	10	10		10 (database limitations)	100	0.03
Ohio 2020	Based on	USEPA	2019a									
Oregon 2019	Humpage & Falconer 2003	mouse	11 weeks	Purified cylindrospermopsin		30	10	10		3 (database limitations)	300	0.1
Washington 2011	Based on	USEPA	2006			33 BMDL[2.5.]	10	10		10 (database limitations)	1000	3.3 $x10^{-2}$

[1.] Cyanobacterial bloom material containing nine microcystin congeners but no microcystin-LR

[2.] OEHHA (2012) calculated a 95% lower confidence limit of the Benchmark Dose (BMDL) of 6.4 µg/kg/day to represent the dose of microcystin that serves as the point of departure to estimate a safe dose for humans. In 2016 document this value is termed 'point of departure' (POD) representing the lower end of the observed range of adverse effects.

[3.] California (2016) anatoxin-a NOAEL based on Farrer *et al.* (2015) Oregon Health Authority guideline derivation.

[4.] Oregon did not agree with California using BMDL since USEPA (2012) recommends against using it where there are fewer than 3 dose groups (excluding controls) and Heinze (1999) study only had 2 dose groups.

[5.] Based on USEPA (2006)

[6.] Stx-equiv = saxitoxin equivalents

LOAEL = lowest observed adverse effect level = the lowest does at which adverse health effects are observed.

NOAEL = no observed adverse effect level = the highest dose at which no adverse health effects are observed.

Table A6-2: Derivation of recreational water guideline values for the range of cyanotoxins from tolerable daily intake (TDI) or reference dose (RfD) given in Table A6-1.

Country or Jurisdiction	TDI (µg/kg/day)	RfD (µg/kg/day)	Weight (kg)	Intake-surface water ingestion (L/hour)	Duration (Hours/day)	Ingestion rate (L/day)	Guideline (µg/L)
Microcystin							
Australia NHMRC 2008	0.0625		15 (child) 70 (adult)			0.1	10 (child) 44 (adult)
WHO 2020	0.4		15 (child)			0.25	24
Canada Health Canada 2020	0.056		23 (child 4-8 y)			0.103 (child 6-10 y)	10 (based on an allocation factor of 0.8)
New Zealand 2009	0.08		15 (child) 70 (adult)			0.1	12 (child) – action level; 56 (adult)
USEPA 2019a p72		0.05	31.8 (6-10 y)			0.21 (6-10 y)	8
California 2016 (Alert)		0.006	30.25 (child)	0.05	5	0.25	0.8 (Alert)
California 2016 (Action Tier 1)		0.02	30.25 (child)	0.05	2	0.1	6 (Action Tier 1)
California 2016 (Action Tier 2)							20 (Action Tier 2) based on WHO (1999) and Fawell (1994; 1999) mouse studies
Massachusetts 2021	0.04 (WHO, 2003)		70 (adult) 35 (child)	0.05 (adult) 0.10 (child)	1 (adult) 1 (child)	0.05 0.1	56 (adult) 14 (child) (recommended value)
New Jersey 2018 (revised 2020)		0.01	31.8 (6-<11 y old)	0.12		0.12	2.65 rounded to 3
Ohio 2020		0.05	31.8 (6-<11 y old)			0.21	8
Oregon 2019 Stone& Bress 2007	0.05		20	0.05	2	0.1	8
Oregon Farrer *et al*. 2015	0.05		20 (4-6 y old)			0.1	10
Oregon 2019	0.05		31.8 (6-11 y old)			0.21	8

Table A6-2: (continued)

Country or Jurisdiction	TDI (µg/kg/day)	RfD (µg/kg/day)	Weight (kg)	Intake-surface water ingestion (L/hour)	Duration (Hours/day)	Ingestion rate (L/day)	Guideline (µg/L)
Microcystin (continued)							
Vermont Stone& Bress 2007	0.04		15 (child)	0.05	2	0.1	6
Washington 2011	0.04		15 (child)	0.05	2	0.1	6
Saxitoxin							
WHO 2020	0.5		15 (child)			0.25	30
Ohio 2020		0.005	31.8 (6-11 y old)			0.21	0.8
Oregon Farrer *et al.* 2015	0.05		20 (4-6 y old)	0.05	2	0.1	10
Oregon 2019	0.05		31.8 (6-11 y old)			0.21	8
Washington 2011		0.5 (acute)	15 (child)	0.05	2	0.1	75
Anatoxin-a							
WHO 2020	0.98		15 (child)			0.25	60 (rounded up)
California 2016 (Action Tier 1)		0.1	20 (child)	0.05	2	0.1	20 (Tier 1 based on Oregon Health Authority)
California 2016 (Action Tier 2)		2.5	30.25 (child)	0.05	5	0.25	90
New Jersey 2018 (revised 2020)		0.1	31.8 (6-<11 y old)			0.12	26.5 rounded to 27
Ohio 2020		0.05	31.8 (6-<11 y old)			0.21	8
Oregon Farrer *et al.* 2015	0.1		20 (4-6 y old)	0.05	2	0.1	20
Oregon 2019	0.1		31.8 (6-11 y old)			0.21	15
Washington 2008		3 (short-term) 0.5 (sub-chronic)	15 (child) 15 (child)	0.05 0.05	2 2	0.1 0.1	450 75 1 (final value chosen based on Fawell *et al.* 1999)

Table A6-2: (continued)

Country or Jurisdiction	TDI (µg/kg/day)	RfD (µg/kg/day)	Weight (kg)	Intake-surface water ingestion (L/hour)	Duration (Hours/day)	Ingestion rate (L/day)	Guideline (µg/L)
Cylindrospermopsin							
WHO 2020	0.1		15 (child)			0.25	6
USEPA 2019a p72	0.1		31.8 (6-10 y)			0.21 (6-10 y)	15
California 2016 (Action Tier 1)		0.033	30.25 (child)	0.05	5	0.25	4
California 2016 (Action Tier 2)		0.055	30.25 (child)	0.05	2	0.1	17
New Jersey 2018 (revised 2020)		0.03	31.8 (6-<11 y old)			0.12	7.95 rounded to 8
Ohio 2020		0.1	31.8 (6-<11 y old)			0.21	15
Oregon Farrer *et al.* 2015	0.03 (EPA sub-chronic)		20 (4-6 y old)	0.05	2	0.1	6
Oregon 2019	0.1		31.8 (6-11 y old)			0.21	15
Washington 2011		0.03 (sub-chronic)	15 (child)	0.05	2	0.1	4.5

TDI = tolerable daily intake; RfD = oral reference dose.

Guideline concentration = [weight x TDI]/ [intake x duration] or [weight x RfD]/ [intake x duration].

TDI of 0.04 µg/kg/day is from WHO on the basis of repeated oral administration of microcystin-LR in mice and effects on the liver.

Water ingestion of 0.05 L/h based on USEPA (1991) and Dang (1996) guidance for incidental ingestion of surface waters.

Table A6-3: Compilation of the derivation of recreational water guidelines in terms of cyanobacterial cell counts for the countries and jurisdictions where this is provided.

Country or Jurisdiction	Toxin	Derivation for guideline for cyanobacterial cell counts			
		Relationship between cell count (cells/mL) and toxin level (µg/L)	**Toxin guideline value (µg /L) (from above table)**	**Toxin cell quota for total microcystins per cell µg /cell**	**Guideline (cells/mL)**
Australia					
NHMRC 2008	Microcystin-LR		10 (child) 44 (adult)	2×10^{-7}	50,000 (child) 220,000 (adult)
New Zealand					
NZ 2009			12 (child) – action level 56 (adult)	6.3×10^{-7} Wood *et al.* (2006)	19,000 (child) 90,000 (adult)
Canada					
Health Canada 2020 Section 7.2	Microcystin-LR		10	2×10^{-7}	50,000
	Anatoxin-a	Not given			
	Cylindrospermopsin	Not given			
	Saxitoxin	Not given			

Table A6-3: (continued)

Country or Jurisdiction	Toxin	Derivation for guideline for cyanobacterial cell counts			
		Relationship between cell count (cells/mL) and toxin level (µg/L)	**Toxin guideline value (µg /L) (from above table)**	**Toxin cell quota for total microcystins per cell µg /cell**	**Guideline (cells/mL)**
United States					
Massachusetts 2021	Microcystin	WHO (2003) 20,000 cells/mL = 2-4 µg/L 100,000 cells/mL = 20 µg/L Linearity assumed	Based on conservative (child) toxin concentration 14 µg/L cell count is 70,000 cells/mL		70,000
Washington 2008	Microcystins	Not given			
Washington 2008	Anatoxin-a	Not given			
Washington 2011	Cylindrospermopsin	Not given			
Washington 2011	Saxitoxin	Not given			

Guideline cell count (Canada) = [(toxin guideline value µg /L) x 10^{-3} L/mL]/ toxin cell quota (µg /cell)

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Table A6-4: Collation of recreational water guideline values developed for marine algae and cyanobacteria from Australian and international sources. In no cases were details of the derivation of these guidelines provided.

Reference	Water body grading	Derivation details
NHMRC 2008	Rating very poor – very good	No derivation details
Water NSW 2021		No derivation details
Western Australia 2021		No derivation details
Florida 2021		No derivation details

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6.7 Appendix 7: Compilation of Alert and Action Levels for Freshwater and Marine Recreational Guidelines

The freshwater and marine recreational guideline Alert and Action levels were collated from countries around the world and from every available US state. These are given below:

Table A7-1: Compilation of recreational water guideline values for freshwater cyanobacteria and cyanobacterial toxins from Australian and international sources excluding USA.

Table A7-2: Compilation of recreational water guideline values for freshwater cyanobacteria and cyanobacterial toxins from US Federal and State agencies.

Table A7-3: Collation of recreational water guideline values for marine algae and cyanobacteria from international and Australian sources.

Table A7-1: Compilation of recreational water guideline values for freshwater cyanobacteria and cyanobacterial toxins from Australian and international sources excluding USA. Where the guideline specifies Microcystin-LR this is stated. Otherwise, it is given as total microcystins.

Source	**Toxin**	**Toxin concentration**		**Cell count [1.]**		**Surrogates**		**Presence of scum as an Action level**	**Comment**
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]		
Australia									
NHMRC 2008	microcystin *Microcystis aeruginosa*		≥10 µg/L total microcystins	≥5000 - <50000 cells/mL	≥50000 cells/mL	≥0.4 - <4 mm^3/L of total toxin producing cyanobacteria biovolume OR ≥0.4 - <10 mm^3/L of total cyanobacteria biovolume	≥4 mm^3/L of total toxin producing cyanobacteria biovolume OR ≥10 mm^3/L of total cyanobacteria biovolume	Yes Action mode – scums consistently present	NHMRC, 2008 Table 6.2, Details of derivation provided. 3 levels: Surveillance mode (green) Alert mode (amber) Action mode (red)
	cylindrospermopsin	Not given							
	anatoxin-a	Not given							
	saxitoxin	Not given							
NSW Water NSW 2021	microcystin	Not given		>5000 - <50,000 cells/mL *Microcystis aeruginosa*	>50,000 cells/mL *Microcystis aeruginosa*	≥0.4 - <4 mm^3/L of total toxin producing cyanobacteria biovolume OR ≥0.4 - <10 mm^3/L of total cyanobacteria biovolume	≥4 mm^3/L of total toxin producing cyanobacteria biovolume OR ≥10 mm^3/L of total cyanobacteria biovolume	No	Based upon NHMRC, 2008 3 levels: Green alert Amber alert Red alert
	cylindrospermopsin	Not given							
	anatoxin-a	Not given							
	saxitoxin	Not given							

Table A7-1: (continued)

Source	Toxin	Toxin concentration		Cell count [1.]		Surrogates		Presence of scum used as an Action level	Comment
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]		
Queensland SE Qld 2016 Veal *et al.* 2018	microcystin	≥3 µg/L	≥10 µg/L (Tier 1) ≥25 µg/L (Tier 2)					No	No guideline derivation 4 levels: Low, medium, high, extreme
	cylindrospermopsin	≥3 µg/L	≥10 µg/L (Tier 1) ≥25 µg/L (Tier 2)						
	anatoxin-a	≥3 µg/L	≥10 µg/L (Tier 1) ≥25 µg/L (Tier 2)						
	saxitoxin	≥9 µg/L	≥30 µg/L (Tier 1) ≥75 µg/L (Tier 2)						
	nodularin	≥4 µg/L	≥13 µg/L (Tier 1) ≥30 µg/L (Tier 2)						
ACT 2014	microcystin *Microcystis aeruginosa*			≥5,000 - <50,000 cells/mL	≥50,000-≤125,000 cells/mL (Tier 1) ≥125,000 cells/mL (Tier 2)	≥0.4 - <4 mm^3/L	≥4 - <10 mm^3/L (Tier 1) ≥10 mm^3/L of total toxin producing cyanobacteria biovolume (Tier 2)	Yes For extreme alert level – >125,000 cells/mL (Tier 2) or scums consistently present	≥50,000 M. aeruginosa or >4 mm^3/L for aerosol from jet fountain in Lake Burley Griffin. 4 levels: Low, medium, high, extreme
Victoria 2021	microcystin *Microcystis aeruginosa*			>50,000 cells/mL (one location)	>50,000 cells/mL (many locations)	≥4 mm^3/L of total toxin producing cyanobacteria biovolume OR >10 mm^3/L of total cyanobacteria biovolume (one location)	≥4 mm^3/L of total toxin producing cyanobacteria biovolume OR >10 mm^3/L of total cyanobacteria biovolume (many locations)	No	Alert and action change based on number of locations – not changes in cell count or biovolume 3 levels: Minor, moderate, major

Table A7-1: (continued)

Source	Toxin	Toxin concentration		Cell count [1.]		Surrogates		Presence of scum used as an Action level	Comment
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]		
Tasmania 2011	microcystin		≥10 µg/L total (Tier 1)	>5,000 – 50,000 cells/mL M. aeruginosa	≥50,000 cells/mL toxic M. aeruginosa (Tier 1)	>0.4 - <4 mm^3/L of total cyanobacteria biovolume where known toxin producer is dominant OR >4 - <10 mm^3/L of total cyanobacteria biovolume where known toxin producers are NOT present	≥4 mm^3/L total cyanobacteria (Tier 1) ≥10 mm^3/L of total cyanobacteria biovolume where known toxin producers are NOT present (Tier 2)	Yes Level 2 Action mode: 'where cyanobacterial scum is well established'.	From NHMRC 2008 Tier 1 Action – known toxic producing species dominant; Tier 2 Action- no microcystin or other toxin present 3 levels: Detection/surveillance alert, action
	cylindrospermopsin								
	anatoxin-a								
	saxitoxin								

Table A7-1: (continued)

Source	Toxin	Toxin concentration		Cell count [1.]		Surrogates		Presence of scum used as an Action level	Comment
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]		
New Zealand 2009	microcystin-LR (toxicity equivalents)		≥12 µg/L total microcystins (child – see derivation p52)			0.5 - <1.8 mm^3/L of total toxin producing cyanobacteria biovolume OR 0.5 - <10 mm^3/L of total cyanobacteria biovolume	≥1.8 mm^3/L of total toxin producing cyanobacteria biovolume OR ≥10 mm^3/L of total cyanobacteria biovolume	Yes Action mode – Situation 3 Cyanobacterial scums consistently present	Section 3.2 3 levels: Surveillance – green mode Alert – amber mode Action – red mode
	Benthic					20-50% potentially toxigenic cyanobacteria attached to substrate	>50% potentially toxigenic cyanobacteria attached to substrate OR Up to 50% potentially toxigenic cyanobacteria are visibly detaching and accumulating as scum	Yes Action mode Situation 2 See details under Action.	Section 3.5 3 levels: Surveillance – green mode Alert – amber mode Action – red mode

Table A7-1: (continued)

Source	**Toxin**	**Toxin concentration**		**Cell count** [1.]		**Surrogates**		**Presence of scum used as an Action level**	**Comment**
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]		
Canada 2020	microcystin		10 µg/L		50,000 cells/mL Total cyanobacteria			No	Derivation details provided. No levels given.
	cylindrospermopsin	Not given							
	anatoxin-a	Not given							
	saxitoxin	Not given							
British Columbia 2018	microcystin-LR		>20 µg/L					No	Derivation details not provided. No levels given.
	cylindrospermopsin	Not given							
	anatoxin-a	Not given							
	saxitoxin	Not given							
Czech Republic 2012	microcystin-LR			>20,000 cells/mL	>100,000 cells/mL			No	From Chorus (2012) Table 2 2 levels: 1st warning level, 2nd warning level
	cylindrospermopsin	Not given							
	anatoxin-a	Not given							
	saxitoxin	Not given							
France 2012	microcystin-LR eq		≥25 (± 5%) µg/L	>20,000 - 100,000 (± 20%) cells/mL	>100,000 (± 10%) cells/mL			Yes Appearance in recreational or bathing area	From Chorus (2012) Table 2 Funari *et al.* (2017) Table 1; cyanobacteria total, type not specified. 2 levels - unnamed
	cylindrospermopsin	Not given							
	anatoxin-a	Not given							
	saxitoxin	Not given							

Table A7-1: (continued)

Source	Toxin	Toxin concentration		Cell count [1]		Surrogates		Presence of scum used as an Action level	Comment
		Alert[2]	Action[3]	Alert[2]	Action[3]	Alert[2]	Action[3]		
Italy 2017	microcystin-LR eq	<20 µg/L	>20 µg/L	≥20,000 (± 20%) cells/mL Total cyanobacteria	>100,000 (± 20%) cells/mL potentially toxigenic cyanobacteria			Yes Emergency level – surface scums containing toxic cyanobacteria	Funari *et al.* (2017) Table 2 3 levels: routine, alert, emergency
	cylindrospermopsin		>20 µg/L						
	anatoxin-a		>20 µg/L						
	saxitoxin		Not given						
Netherlands 2017	microcystin-LR eq	Not given				12.5-75 µg/L cyanobacterial chlorophyll-a Or 2.5-15 mm^3/L of total cyanobacteria biovolume	>75 µg/L cyanobacterial chlorophyll-a Or >15 mm^3/L of total cyanobacteria biovolume	Yes Alert level 1 - cells form scum layers; Alert level 2 – scums are persistent	From Chorus (2012) Funari *et al.* (2017) Table 1 3 levels: Surveillance, alert level 1, alert level 2
	cylindrospermopsin	Not given							
	anatoxin-a	Not given							
	saxitoxin	Not given							
Turkey 2017	microcystin-LR eq		>25 µg/L		20,000 – 100,000 cells/mL (Tier 1) Scum observed (Tier 2)	<10 µg/L Chlorophyll-a		Yes Level 3 Scums in bathing area	From Chorus (2012) Funari *et al.* (2017) Table 1 3 levels: Level 1, Level 2, Level 3
	cylindrospermopsin	Not given							
	anatoxin-a	Not given							
	saxitoxin	Not given							

Table A7-1: (continued)

Source	**Toxin**	**Toxin concentration**		**Cell count** [1.]		**Surrogates**		**Presence of scum used as an Action level**	**Comment**
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]		
Scotland 2012	microcystin-LR eq			≥20,000 cells/mL	≥100,000 cells/mL	≥10 µg/L Chlorophyll-a With dominance of cyanobacteria	≥50 µg/L Chlorophyll-a With dominance of cyanobacteria	Yes High probability level- Cyanobacterial scum formation	Annex G, Table 8.3 3 levels: Relatively low probability of adverse health effects; Moderate probability of adverse health effects; High probability of adverse health effects;
	cylindrospermopsin	Not given							
	anatoxin-a	Not given							
	saxitoxin	Not given							
WHO 2003	microcystin	(2-4) - 20 µg/L	≥20 µg/L	>20,000 – 100,000 cells/mL	≥100,000 cells/mL	>10 - 50 µg/L Chlorophyll-a	≥50 µg/L Chlorophyll-a		
	cylindrospermopsin								
	anatoxin-a								
	saxitoxin								
WHO 2020	microcystin		≥24 µg/L					No	No action levels
	cylindrospermopsin		≥6 µg/L						
	anatoxin-a		≥59 µg/L						
	saxitoxin		≥30 µg/L						

Table A7-1: (continued)

Source	Toxin	Toxin concentration		Cell count [1.]		Surrogates		Presence of scum used as an Action level	Comment
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]		
Chorus and Testai 2021	microcystin	≤24 μg/L	>24 μg/L			Up to 4-8 mm^3/L cyanobacterial biovolume OR Up to12-24 μg/L Chlorophyll-a with dominance of cyanobacteria		Yes Alert level 2: Visible, thick cyanobacterial scums covering most of water surface	Chapter 5.2 Section 5.2.3.2 3 levels: Vigilance, Alert level 1, Alert level 2
	cylindrospermopsin	≤6 μg/L	>6 μg/L						
	anatoxin-a	≤60 μg/L	>60 μg/L						
	saxitoxin	≤30 μg/L	>30 μg/L						

[1.] Cell count based on all total potentially toxic cyanobacteria unless specified

[2.] Alert = health advisory;

[3.] Action = health warning/guideline/health advisory; where sources did not distinguish between Alert and Action values the value was listed as Action

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Australia

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Table A7-2: Compilation of recreational water guideline values for freshwater cyanobacteria and cyanobacterial toxins from US Federal and State agencies. Where the guideline specifies Microcystin-LR this is stated. Otherwise, it is given as total microcystins.

Source	Toxin	Toxin concentration		Cell count [1.]		Surrogates		Scum as Action Level	Comment
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]		
USEPA 2019a	microcystins		8 µg/L					No	2019 document Table 6.1
	cylindrospermopsin		15 µg/L						One level only
	anatoxin-a		Not given						
	saxitoxin		Not given						
Congressional Research Service 2019									2019 document, lists USEPA 2019a, WHO 2003 and range of US state guidelines
Arkansas 2019	microcystins		8 µg/L					No	Based on USEPA 2019a One level only
	cylindrospermopsin		15 µg/L						Based on USEPA 2019a WHO 2003 cell count and chlorophyll-a values used.
	anatoxin-a		Not given						
	saxitoxin		Not given						
California 2016	microcystins	0.8 µg/L	6 µg/L (Tier 1) 20 µg/L (Tier 2)	4,000 cells/mL (potential toxin producers)				No	Appendix A 2016 outlines details of derivation of values and references Tier 1 – Warning Tier 2 - Danger
	cylindrospermopsin	1 µg/L	4 µg/L (Tier 1) 17 µg/L (Tier 2)						
	anatoxin-a	Detect (<u><</u>1 µg/L)	20 µg/L (Tier 1) 90 µg/L (Tier 2)						
	saxitoxin	Not given	Not given						

Table A7-2: (continued)

Source	Toxin	Toxin concentration		Cell count [1.]		Surrogates		Scum as Action Level	Comment
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]		
Colorado 2020	microcystin		8 µg/L					Caution sign to be posted	Toolkit 2020 p6
	cylindrospermopsin		15 µg/L					when potentially toxic algae are visible	Only one level No direct guidelines given
	anatoxin		15 µg/L						
	saxitoxin		8 µg/L						
Connecticut 2019			Not given	>20,000 - <100,000 cells/mL	>100,000 cells/mL			No	2019 BGA Management Document No reference to toxins. Two levels – Alert and Action
Idaho 2015			Not given		≥100,000 cells/mL potentially toxigenic taxa (Tier 1) >40,000 cells/mL (*Microcystis* or *Planktothrix*) (Tier 2)			Yes Is surface scum visible and associated with toxigenic species?	Table 3 p7 Adapted from Oregon Department of Human Services 2015 Two levels – Tier 1 and 2
Illinois 2019	microcystin		8 µg/L					No	Based on USEPA 2019a
	cylindrospermopsin		15 µg/L						Based on USEPA 2019a
	anatoxin-a		Not given						
	saxitoxin		Not given						

Table A7-2: (continued)

Source	Toxin	Toxin concentration		Cell count [1]		Surrogates		Scum as Action Level	Comment
		Alert[2]	Action[3]	Alert[2]	Action[3]	Alert[2]	Action[3]		
Indiana 2020	microcystin	8 µg/L	20 µg/L 0.8 µg/L (dog)		100,000 cells/mL			No	Taken from June 20, 2020 Lake sampling update Two levels – advisory and prohibited
	cylindrospermopsin	15 µg/L	20 µg/L 1 µg/L (dog)						Refer to WHO 2003, USEPA 2019a and Ohio guidelines
	anatoxin-a	80 µg/L	300 µg/L 0.4 µg/L (dog)						
	saxitoxin	8 µg/L (0.8 µg/L in Ohio River doc)	3 µg/L 0.05 µg/L (dog)						Error for Action value??? Lower than Alert value.
Iowa 2017	microcystin		20 µg/L					No	Taken from fact sheet 2p. No details of derivation.
	cylindrospermopsin		Not given						Only one level
	anatoxin-a		Not given						
	saxitoxin		Not given						
Kansas 2020	microcystin	>4 µg/L – ≤ 8 µg/L	>8 µg/L – ≤ 2,000 µg/L (Tier 1) >2,000 µg/L (Tier 2)	>80,000 cells/mL – ≤ 250,000 cells/mL	>250,000 cells/mL – <10,000,000 cells/mL(Tier 1) >10,000,000 cells/mL(Tier 2)			Yes Warning – if there is verification of significant cyanobacterial scum present a warning may be issued	Alert = Watch Tier 1 Action = Warning Tier 2 Action = Hazard
	cylindrospermopsin	Not given							
	anatoxin-a	Not given							
	saxitoxin	Not given							
Massa-chusetts 2021	microcystin	<14 µg/L	≥14 µg/L	>50,000 - <70,000 cells/mL	≥70,000 cells/mL			Yes If a visible cyanobacteria scum or mat is evident MDPH	Derivation details outlined. Use conservative value based on child.
	cylindrospermopsin		Not given					recommends an immediate posting to	
	anatoxin-a		Not given					advise against contact	
	saxitoxin		Not given						

Table A7-2: (continued)

Source	**Toxin**	**Toxin concentration**		**Cell count** [1.]		**Surrogates**		**Scum as Action Level**	**Comment**
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]		
Montana 2019	microcystin	8 -20 µg/L	>20 µg/L	20,000 – 100,000 cells/mL	>100,000 cells/mL			No	Three tier approach based on WHO 2003, USEPA 2019a and California 2016
	cylindrospermopsin		Not given						Tier 1 and 2 – Caution Tier 3 -Consider Closure
	anatoxin-a	Detect – 20 µg/L	>20 µg/L						
	saxitoxin		Not given						
New Jersey 2020	microcystin		3 µg/L (Advisory) >20-<2,000 µg/L (Warning) >2,000 µg/L (Danger)	≥40,000 - 80,000 cells/mL	≥80,000 cells/mL (Advisory)			No	Cell count based on WHO 2003 and from proposed 2020 Strategy
	cylindrospermopsin		8 µg/L						Five levels – Watch, Alert, Advisory, Warning, Danger
	anatoxin		27 µg/L						
	saxitoxin		Not given						
New York 2021	microcystin		≥10 µg/L (open water) ≥20 µg/L (shoreline)				>25 µg/L chlorophyll-a	No	Reopen if 1d after dissipation <10 µg/L or <4 µg/L (USEPA, 2016) Table 5 p 46
	cylindrospermopsin		Not given						
	anatoxin-a		Not given						
	saxitoxin		Not given						

Table A7-2: (continued)

Source	Toxin	Toxin concentration		Cell count [1]		Surrogates		Scum as Action Level	Comment
		Alert[2]	Action[3]	Alert[2]	Action[3]	Alert[2]	Action[3]		
Ohio 2020 and Ohio River 2021	microcystin		8 µg/L	≥20,000 - <100,000 cells/mL	≥100,000 cells/mL	10 - <50 µg/L chlorophyll-a (cyanobacteria dominant)	≥50 µg/L chlorophyll-a (cyanobacteria dominant)	No	Cell count and chlorophyll-a based on WHO 2003. Ohio EPA link broken. Table 6 Ohio and WV Table 7 WV – different values
	cylindrospermopsin		15 µg/L						
	anatoxin-a		8 µg/L						
	saxitoxin		0.8 µg/L						
Oregon 2019	microcystin		8 µg/L 0.2 µg/L (dog)					Yes Advisory – visible scum	Appendix B has detailed derivation.
	cylindrospermopsin		15 µg/L 0.4 µg/L (dog)					with documentation	
	anatoxin-a		15 µg/L 0.4 µg/L (dog)					and sampling	
	saxitoxin-eq		8 µg/L 0.02 µg/L (dog)						
Pennsylvania 2014	microcystin	6 µg/L	20 µg/L					Yes Avoid contact	Based on Ohio
	cylindrospermopsin	5 µg/L	20 µg/L					Advisory where there is a visible	
	anatoxin-a	80 µg/L	300 µg/L					blue-green algal	
	saxitoxin-eq	0.8 µg/L	3 µg/L					bloom	

Table A7-2: (continued)

Source	**Toxin**	**Toxin concentration**		**Cell count** [1.]		**Surrogates**		**Scum as Action Level**	**Comment**
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]		
Rhode Island 2020	microcystin-LR (eq)		4 µg/L		>70,000 cells/mL			Yes- Issue health advisory if visible cyanobacteria	
	cylindrospermopsin	Not given						scum or mat	
	anatoxin-a	Not given							
	saxitoxin	Not given							
Utah 2017	microcystin	4-2,000 µg/L	>2,000 µg/L	20,000-10,000,000 cells/mL	>10,000,000 cells/mL			No	Based on WHO (2003), USEPA (2016) and California (2016)
	cylindrospermopsin		>8 µg/L						3 levels – Tiers 1, 2 and 3
	anatoxin-a	Detection-90 µg/L	>90 µg/L						
	saxitoxin		Not given						
Vermont 2015	microcystin-LR (eq)		≥6 µg/L					Yes – Close beach if visible	Appendix D Guidance Doc
	cylindrospermopsin		≥10 µg/L					blue-green	
	anatoxin-a		≥10 µg/L					algae bloom/scum	
	saxitoxin		Not given						
Virginia 2019	microcystin		8 µg/L		40,000 cells/mL (*Microcystis* sp) 100,000 cells/mL (total toxigenic sp)			No	Based on USEPA 2016 3 levels – Tiers 1, 2 and 3
	cylindrospermopsin		15 µg/L						
	anatoxin-a		Not given						
	saxitoxin		Not given						

Table A7-2: (continued)

Source	Toxin	Toxin concentration		Cell count [1.]		Surrogates		Scum as Action Level	Comment
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]		
Washing-ton 2008; 2011	microcystin		6 µg/L					No	Derivation details outlined.
	cylindrospermopsin		4.5 ug/L						
	anatoxin-a		1 ug/L						Anatoxin-a value based on Fawell (1999)
	saxitoxin		75 ug/L						
West Virginia 2018	microcystin	6 µg/L	20 µg/L					No	
	cylindrospermopsin	5 µg/L	20 µg/L						
	anatoxin-a	80 µg/L	300 µg/L						
	saxitoxin	0.8 µg/L	3 µg/L						
Wisconsin 2019	microcystin-LR	10-20 µg/L	20-2000 µg/L (Tier 1) >2000 µg/L (Tier 2)	20,000-100,000 cells/mL	100,000-10,000,000 (cells/mL) (Tier 1) >10,000,000 (cells/mL) (Tier 2)			Yes There is an advisory level (Tier 1 Action = High) if a	Based on WHO 2003 guidelines Four levels – Low, moderate, high and very high
	cylindrospermopsin	Not given						scum layer	
	anatoxin-a	Not given						is visible	
	saxitoxin	Not given							

[1.] Cell count based on all total potentially toxic cyanobacteria unless specified;

[2.] Alert = health advisory;

[3.] Action = health warning/guideline/health advisory; where sources did not distinguish between Alert and Action values the value was listed as Action

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Table A7-3: Collation of recreational water guideline values for marine algae and cyanobacteria from international and Australian sources. Note that the only published guidelines values for the marine situation are for cell numbers of a range of specific toxic organisms. No jurisdiction has developed or published a guideline for individual toxins or surrogates other than cell numbers. The Table includes columns for these to be consistent with Tables A7-1 and A7-2.

Country or Jurisdiction	**Organism**	**Toxin concentration**		**Cell count** [1.]		**Surrogates**		**Comment**
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	
UNITED STATES								
Florida Fish and Wildlife Research Institute 2021	*Karenia brevis*			>10,000 cells/L – 100,000 cells/L (LOW)	>100,000 cells/L – 1,000,000 cells/L (MED) >1,000,000 cells/L (HIGH)			LOW, MED and HIGH- respiratory irritation No information about derivation of levels
AUSTRALIA								
National NHMRC 2008	*Karenia brevis*			<u><</u>1 cell/mL	>1 - <10 cells/mL (Tier 1) <u>></u>10 cells/mL (Tier 2)			NHMRC 2008 Table 7.3
	Lyngbya majuscula *Pfiesteria* sp.				Present in: Low numbers (Tier 1) High numbers (Tier 2)			'low' and 'high' not defined

Table A7-3: (continued)

Country or Jurisdiction	Organism	Toxin concentration		Cell count [1.]		Surrogates		Comment
		Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	Alert[2.]	Action[3.]	
Water NSW 2021.	*Karenia brevis*				10 cells/mL			
	Lyngbya *Pfiesteria*				High numbers			'High' not defined
Western Australia Department of Health, Public Health and Clinical Services 2021.	*Lyngbya majuscula*			Detected	Relative widespread visible presence of algal filaments			NHMRC 2008
	Trichodesmium				Presence of algal scums			NHMRC 2008
	Other cyanobacteria			≥5,000 cells/L	≥15,000 cells/L			
	Karenia brevis			≥5,000 cells/L	≥10,000 cells/L			
	Karenia sp.			≥50,000 cells/L	≥100,000 cells/L			
	Pfiesteria			Detected	Presence of algal scums			NHMRC 2008

1. Cell count based on all total potentially toxic cyanobacteria unless otherwise specified

2. Alert = health advisory;

3. Action = health warning/guideline/health advisory; where sources did not distinguish between Alert and Action values the value was listed as Action

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6.8 Appendix 8: Administrative and Technical Assessment of Selected Existing Recreational Water Guidelines

An assessment was made of selected existing recreational water guidelines (New Zealand, Canada, U.S. EPA, WHO, California, Massachusetts, Oregon, and Washington) based on administrative and technical criteria developed by NHMRC outlined in the AGREE Reporting Checklist (citation https://www.bmj.com/content/352/bmj.i1152). This assessment was made only for those guidelines that provided comprehensive documentation. Criteria have been colour-coded to assess minimum requirements as follows: 'Must have', 'Should have' or 'May have'

Table A8-1: Assessment of selected existing recreational water guidelines based on administrative and technical criteria

New Zealand guidelines for cyanobacteria in recreational fresh waters: Interim Guideline 2009 and 2018 Review

	Criteria	Y/N/NA	Response
	Overall guidance/advice development process		
	Are the key stages of the organisation's advice development processes compatible with Australian processes?		NHMRC to review and complete
	Are the administrative processes documented and publicly available?	Y	See listed website
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?	Y	2009 Guidelines prepared by: Susanna A Wood: Cawthron Institute David P Hamilton, Wendy J Paul: University of Waikato Karl A Safi: National Institute of Water and Atmospheric Research Wendy M Williamson: Environmental Science and Research Ltd Review of guidelines prepared by scientists at Cawthron Institute, Nelson, NZ Conflict of interest not declared in Guidelines or Review.
	Are funding sources declared?	Y	Guidelines and Review prepared for NZ Ministry of Environment and Ministry of Health.
	Was there public consultation on this work? If so, provide details.	Y	Review reports an end-user workshop Section 2.
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?		2009 Guidelines and Review do not report peer review
	Was the guidance/advice developed or updated recently? Provide details.	N	Available at: https://www.mfe.govt.nz/publications/fresh-water-environmental-reporting/guidelines-cyanobacteria [Accessed February 2021] In 2018, the Ministry for the Environment commissioned a report that summarises literature and data published since 2009, and outlines recommended changes to the guidelines. Further research and updates are needed to finalise the guidelines. Until the changes are finalised it is recommended that users continue to use the existing 2009 guidelines.

Table A8-1: (continued)

New Zealand guidelines for cyanobacteria in recreational fresh waters: Interim Guideline 2009 and 2018 Review

	Criteria	Y/N/NA	Response
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?	Y	2009 Guidelines Section 1. Introduction provides an overview of the purpose and status of the document as well as advice on who should use it. Section 2. Framework provides a background to the overall guidelines approach, recommendations on agency roles and responsibilities, and information on the condition of use of this document
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?	Y	Review used a mixture of peer-reviewed research articles and review articles, technical reports, student theses and book chapters were identified during the search.
	Does the organisation use or undertake systematic literature review methods to identify and select data underpinning the advice? Are the methods used documented clearly?		Stage 2 of the guidelines review project involved a review of new literature on toxic cyanobacteria in New Zealand published during 2009-2017. Appendix 1 of Review.
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?		Unknown
	Are inclusion/exclusion criteria used to select or exclude certain studies from the review? If so, is justification provided?	Y	p. 4 Review Only studies that related to aquatic freshwater cyanobacteria were retained, so several studies on marine and terrestrial cyanobacteria were not included. Studies that focussed on the ecology of cyanobacteria not known to produce toxins were not included.
	Does the organisation use or adopt review findings or risk assessments from other organisations? What process was used to critically assess these external findings?		Unknown
	Can grey literature such as government reports and policy documents be included?		Unknown
	Is there documentation and justification on the selection of a toxicological endpoint for use as point of departure for health-based guideline derivation?	Y	Appendix 2 Review Updated microcystin toxicity calculations to derive the Action Level Threshold for planktonic cyanobacteria.

Table A8-1: (continued)

New Zealand guidelines for cyanobacteria in recreational fresh waters: Interim Guideline 2009 and 2018 Review

	Criteria	Y/N/NA	Response
	Evidence search		
	Are databases and other sources of evidence specified?	Y	Section 3 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)?	N	New literature was acquired through the personal knowledge of the research team and by searching Google Scholar
	Is it specified what date range the literature search covers? Is there a justification?	Y	2009-2017; justification not specified; New issues related to potentially toxic cyanobacteria have emerged that were not covered by the 2009 guidelines
	Are search terms and/or search strings specified?	Y	Section 3 Review
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?	Y	Section 3 Review
	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	Risk of bias not mentioned in Review or Guidelines
	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.		Unknown
	Does the organisation assess the overall certainty of the evidence and reach recommendations? If so, provide details.		Unknown

Table A8-1: (continued)

New Zealand guidelines for cyanobacteria in recreational fresh waters: Interim Guideline 2009 and 2018 Review

	Derivation of health-based guideline values		
	Is there justification for the choice of uncertainty and safety factors?		Appendix 2 Guidelines and Appendix 2 Review (microcystins)
	Are the parameter value assumptions documented and explained?		Appendix 2 Guidelines and Appendix 2 Review (microcystins)
	Are the mathematical workings/algorithms clearly documented and explained?		Appendix 2 Guidelines and Appendix 2 Review (microcystins)
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?		Appendix 2 Guidelines and Appendix 2 Review (microcystins)
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?		Appendix 2 Guidelines and Appendix 2 Review (microcystins)
	What processes are used when expert judgement is required and applied? Is the process documented and published?		Appendix 2 Guidelines and Appendix 2 Review (microcystins)
	Is dose response modelling (e.g. BMDL) routinely used?		Appendix 2 Guidelines and Appendix 2 Review (microcystins)
	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?		Appendix 2 Guidelines and Appendix 2 Review (microcystins)
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	N/A	Appendix 2 Guidelines and Appendix 2 Review (microcystins)

Table A8-1: (continued)

Guidelines for Canadian recreational water quality: Cyanobacteria and their toxins. Guideline technical document for public consultation ending November 2020.

	Criteria	Y/N/NA	Response
	Overall guidance/advice development process		
	Are the key stages of the organisation's advice development processes compatible with Australian processes?		NHMRC to review and complete
	Are the administrative processes documented and publicly available?		Unknown
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?	Y but not stated	Advisory committee details not provided. Conflict of interest not listed.
	Are funding sources declared?	Y	Health Canada
	Was there public consultation on this work? If so, provide details.	Y	Guideline technical document for public consultation ending Nov 2020.
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?	Y	The document was reviewed by external experts and subsequently revised. Peer review was not documented,
	Was the guidance/advice developed or updated recently? Provide details.		https://www.canada.ca/content/dam/hc-sc/documents/programs/consultation-cyanobacteria-toxins-recreational-water/consultation-cyanobacteria-toxins-recreational-water.pdf [Accessed February 2021]

Table A8-1: (continued)

Guidelines for Canadian recreational water quality: Cyanobacteria and their toxins. Guideline technical document for public consultation ending November 2020.

	Criteria	Y/N/NA	Response
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?		This guideline technical document evaluated the available information on cyanobacteria and their toxins with the intent of updating/recommending guideline value(s) for cyanobacteria toxins, total cyanobacteria cell counts, total cyanobacteria biovolume, and chlorophyll-a in recreational waters.
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?		Unknown
	Does the organisation use or undertake systematic literature review methods to identify and select data underpinning the advice? Are the methods used documented clearly?	NA	No details of literature review given.
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?		Unknown
	Are inclusion/exclusion criteria used to select or exclude certain studies from the review? If so, is justification provided?	NA	No details of literature review given.
	Does the organisation use or adopt review findings or risk assessments from other organisations? What process was used to critically assess these external findings?		Table 2 and Section 7 pp 24-30 Rationale
	Can grey literature such as government reports and policy documents be included?	NA	No details of literature review given.
	Is there documentation and justification on the selection of a toxicological endpoint for use as point of departure for health-based guideline derivation?		Section 7 pp 24-30 Rationale

Table A8-1: (continued)

Guidelines for Canadian recreational water quality: Cyanobacteria and their toxins. Guideline technical document for public consultation ending November 2020.

	Criteria	Y/N/NA	Response
	Evidence search		
	Are databases and other sources of evidence specified?	NA	No details of literature review given.
	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	No details of literature review given.
	Is it specified what date range the literature search covers? Is there a justification?	NA	No details of literature review given.
	Are search terms and/or search strings specified?	NA	No details of literature review given.
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?	NA	No details of literature review given.
	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 details about risk of bias given.
	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.		Approach taken for recreational waters refers to that outlined in Health Canada (2017). Guidelines for Canadian drinking water quality - cyanobacterial toxins. Prepared by the Federal-Provincial-Territorial Committee on Drinking Water of the Federal-Provincial-Territorial Committee on Health and the Environment, Ottawa, ON.
	Does the organisation assess the overall certainty of the evidence and reach recommendations? If so, provide details.		Unknown.

Table A8-1: (continued)

Guidelines for Canadian recreational water quality: Cyanobacteria and their toxins. Guideline technical document for public consultation ending November 2020.

	Criteria	Y/N/NA	Response
	Derivation of health-based guideline values		
	Is there justification for the choice of uncertainty and safety factors?		Section 7 pp 24-30 Rationale
	Are the parameter value assumptions documented and explained?		Section 7 pp 24-30 Rationale
	Are the mathematical workings/algorithms clearly documented and explained?		Section 7 pp 24-30 Rationale
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?		Section 7 pp 24-30 Rationale
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?		Section 7 pp 24-30 Rationale
	What processes are used when expert judgement is required and applied? Is the process documented and published?		Section 7 pp 24-30 Rationale
	Is dose response modelling (e.g. BMDL) routinely used?		Section 7 pp 24-30 Rationale
	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?		Section 7 pp 24-30 Rationale
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	N/A	Section 7 pp 24-30 Rationale

Table A8-1: (continued)

U.S. EPA (2019). Recommended human health recreational ambient water quality criteria or swimming advisories for microcystins and cylindrospermopsin.

	Criteria	Y/N/NA	Response
	Overall guidance/advice development process		
	Are the key stages of the organisation's advice development processes compatible with Australian processes?		NHMRC to review and complete
	Are the administrative processes documented and publicly available?		Unknown.
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?		U.S. EPA staff. No conflicts of interest listed.
	Are funding sources declared?		US Government
	Was there public consultation on this work? If so, provide details.		No information given about public consultation.
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?		This document has undergone an EPA intra-agency peer-review process.
	Was the guidance/advice developed or updated recently? Provide details.		https://www.epa.gov/sites/production/files/2019-05/documents/hh-rec-criteria-habs-document-2019.pdf [Accessed February 2021]

Table A8-1: (continued)

U.S. EPA (2019). Recommended human health recreational ambient water quality criteria or swimming advisories for microcystins and cylindrospermopsin.

	Criteria	Y/N/NA	Response
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?	Y	The EPA is publishing these recommended values under CWA 304(a) for states to consider as the basis for swimming advisories for notification purposes in recreational waters to protect the public. The EPA envisions that if states decide to use the values as swimming advisory values they might do so in a manner similar to their current recreational water advisory programs. Alternatively, states may consider using these same values when adopting new or revised water quality standards (WQS).
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?	Y	See Table C-1
	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	U.S. EPA (2015a; 2015b)
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?	Y	U.S. EPA (2015a; 2015b)
	Are inclusion/exclusion criteria used to select or exclude certain studies from the review? If so, is justification provided?	Y	U.S. EPA (2015a; 2015b)
	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	U.S. EPA (2015a; 2015b)
	Can grey literature such as government reports and policy documents be included?	Y	U.S. EPA (2015a; 2015b)
	Is there documentation and justification on the selection of a toxicological endpoint for use as point of departure for health-based guideline derivation?	Y	U.S. EPA (2015a; 2015b)

Table A8-1: (continued)

U.S. EPA (2019). Recommended human health recreational ambient water quality criteria or swimming advisories for microcystins and cylindrospermopsin.

	Criteria	Y/N/NA	Response
	Evidence search		
	Are databases and other sources of evidence specified?	Y	For the Health Effects Support Documents (HESDs), the EPA conducted a comprehensive literature search from January 2013 to May 2014 using Toxicology Literature Online (TOXLINE), PubMed, and Google Scholar.
	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	Toxicology Literature Online (TOXLINE), PubMed, Google Scholar, Web of Science
	Is it specified what date range the literature search covers? Is there a justification?	Y	January 2013 to May 2014 and Sept 2015
	Are search terms and/or search strings specified?	Y	See Appendix C
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?	Y	English only
	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?	Y	No details given about risk of bias assessment.
	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	Section D.1.3 pp. D-3 to D-10.
	Does the organisation assess the overall certainty of the evidence and reach recommendations? If so, provide details.	Y	Section D.1.3 pp. D-3 to D-10.

Table A8-1: (continued)

U.S. EPA (2019). Recommended human health recreational ambient water quality criteria or swimming advisories for microcystins and cylindrospermopsin.

	Criteria	Y/N/NA	Response
	Derivation of health-based guideline values		
	Is there justification for the choice of uncertainty and safety factors?	Y	Section 6 and U.S. EPA (2015a; 2015b)
	Are the parameter value assumptions documented and explained?	Y	Section 6 and U.S. EPA (2015a; 2015b)
	Are the mathematical workings/algorithms clearly documented and explained?	Y	Section 6 and U.S. EPA (2015a; 2015b)
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?	Y	Section 6 and U.S. EPA (2015a; 2015b)
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?	Y	Section 6 and U.S. EPA (2015a; 2015b)
	What processes are used when expert judgement is required and applied? Is the process documented and published?	Y	Section 6 and U.S. EPA (2015a; 2015b)
	Is dose response modelling (e.g. BMDL) routinely used?	Y	Section 6 and U.S. EPA (2015a; 2015b)
	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	Section 6 and U.S. EPA (2015a; 2015b)
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	N/A	Section 6 and U.S. EPA (2015a; 2015b)

U.S. EPA (2015a). Health effects support document for the cyanobacterial toxin cylindrospermopsin. EPA/820/R-15/103. [online] Available at: https://www.epa.gov/sites/production/files/2017-06/documents/cylindrospermopsin-supportreport-2015.pdf. [Accessed February 2021]
U.S. EPA (2015b). Health Effects Support Document for the Cyanobacterial Toxin Microcystins. EPA/820/R-15/102. [online] Available at: https://www.epa.gov/sites/production/files/2017-06/documents/microcystins-support-report-2015.pdf. [Accessed February 2021]

Table A8-1: (continued)

World Health Organization (WHO) (2020). Cyanobacterial toxins: microcystins/saxitoxins/anatoxin-a/cylindrospermopsins. Background document for development of WHO Guidelines for drinking water quality and guidelines for safe recreational water environments.

	Criteria	Y/N/NA	Response
	Overall guidance/advice development process		
	Are the key stages of the organisation's advice development processes compatible with Australian processes?		NHMRC to review and complete
	Are the administrative processes documented and publicly available?		Unknown
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?	Y	Conflict of interest not declared
	Are funding sources declared?		Not specifically stated but assumed to be WHO
	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	The draft health criteria document was submitted to a number of scientific institutions and selected experts for peer review. Comments were carefully considered and addressed, as appropriate, taking into consideration the processes outlined in the Handbook for Guideline Development.
	Was the guidance/advice developed or updated recently? Provide details.		Microcystins (all accessed February 2021) https://apps.who.int/iris/bitstream/handle/10665/338066/WHO-HEP-ECH-WSH-2020.6-eng.pdf?sequence=1&isAllowed=y saxitoxins https://apps.who.int/iris/bitstream/handle/10665/338069/WHO-HEP-ECH-WSH-2020.8-eng.pdf?sequence=1&isAllowed=y anatoxin-a and analogues https://apps.who.int/iris/bitstream/handle/10665/338060/WHO-HEP-ECH-WSH-2020.1-eng.pdf?sequence=1&isAllowed=y cylindrospermopsins https://apps.who.int/iris/bitstream/handle/10665/338063/WHO-HEP-ECH-WSH-2020.4-eng.pdf?sequence=1&isAllowed=y

Table A8-1: (continued)

World Health Organization (WHO) (2020). Cyanobacterial toxins: microcystins/saxitoxins/anatoxin-a/cylindrospermopsins. Background document for development of WHO Guidelines for drinking water quality and guidelines for safe recreational water environments.

	Criteria	Y/N/NA	Response
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?	Y	
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?	Y	
	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	
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?		Unknown
	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?	N	
	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	

Table A8-1: (continued)

World Health Organization (WHO) (2020). Cyanobacterial toxins: microcystins/saxitoxins/anatoxin-a/cylindrospermopsins. Background document for development of WHO Guidelines for drinking water quality and guidelines for safe recreational water environments.

	Criteria	Y/N/NA	Response
	Evidence search		
	Are databases and other sources of evidence specified?	N/A	Not literature 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)?	N/A	
	Is it specified what date range the literature search covers? Is there a justification?	N/A	
	Are search terms and/or search strings specified?	N/A	
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?	N/A	
	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	
	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	
	Does the organisation assess the overall certainty of the evidence and reach recommendations? If so, provide details.	Y	

Table A8-1: (continued)

World Health Organization (WHO) (2020). Cyanobacterial toxins: microcystins/saxitoxins/anatoxin-a/cylindrospermopsins. Background document for development of WHO Guidelines for drinking water quality and guidelines for safe recreational water environments.

	Criteria	Y/N/NA	Response
	Derivation of health-based guideline values		
	Is there justification for the choice of uncertainty and safety factors?	Y	Details in Background Documents
	Are the parameter value assumptions documented and explained?	Y	
	Are the mathematical workings/algorithms clearly documented and explained?	Y	
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?	Y	Discussion about methodologies and detection limits.
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?		Unknown
	What processes are used when expert judgement is required and applied? Is the process documented and published?		Unknown
	Is dose response modelling (e.g. BMDL) routinely used?		Unknown
	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?		Unknown
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	N/A	

Table A8-1: (continued)

California Government (2019). California voluntary guidance for response to HABs in recreational inland waters.

	Criteria	Y/N/NA	Response
	Overall guidance/advice development process		
	Are the key stages of the organisation's advice development processes compatible with Australian processes?		NHMRC to review and complete
	Are the administrative processes documented and publicly available?		Unknown
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?		Document prepared by Blue Green Algae Work Group of the State Water Resources Control Board (SWRCB), the California Department of Public Health (CDPH), and Office of Environmental Health and Hazard Assessment (OEHHA). No details about conflict of interest
	Are funding sources declared?		Californian Government… but not specifically declared in the document
	Was there public consultation on this work? If so, provide details.		Acknowledgement of participation of the stakeholders in the State-wide Blue-Green Algae Workgroup implies public consultation,
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?		Unknown
	Was the guidance/advice developed or updated recently? Provide details.		https://mywaterquality.ca.gov/monitoring_council/meetings/2016feb/cchab_appendixa.pdf [Accessed February 2021]

Table A8-1: (continued)

California Government (2019). California voluntary guidance for response to HABs in recreational inland waters.

	Criteria	Y/N/NA	Response
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?		See Appendix A at URL provided above
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?		Reference to WHO (1999) values for warning levels
	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	No
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?		Unknown
	Are inclusion/exclusion criteria used to select or exclude certain studies from the review? If so, is justification provided?	N/A	
	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	For anatoxin-a they refer to Oregon Health Authority; for Tier II microcystin they refer to WHO.
	Can grey literature such as government reports and policy documents be included?	Y	Utilise documents from Office of Environmental Health and Hazard Assessment, Californian EPA
	Is there documentation and justification on the selection of a toxicological endpoint for use as point of departure for health-based guideline derivation?		See Appendix A at URL provided above
	Evidence search		
	Are databases and other sources of evidence specified?	N/A	
	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)?	N/A	No literature search is presented.
	Is it specified what date range the literature search covers? Is there a justification?	N/A	
	Are search terms and/or search strings specified?	N/A	
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?	N/A	

Table A8-1: (continued) California Government (2019). California voluntary guidance for response to HABs in recreational inland waters.

	Criteria	Y/N/NA	Response
	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/A	
	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/A	
	Does the organisation assess the overall certainty of the evidence and reach recommendations? If so, provide details.	N/A	
	Derivation of health-based guideline values		
	Is there justification for the choice of uncertainty and safety factors?	Y	Appendix A URL provided; A higher cumulative UF (600) was used for cylindrospermopsin compared to that for microcystin (UF=300) because more data is available for microcystin compared with cylindrospermopsin.
	Are the parameter value assumptions documented and explained?		Appendix A URL provided; Microcystin, anatoxin-a and cylindrospermopsin: water ingestion rate 0.25L/d (Alert) and 0.1 L/d (Action Tier 1); Anatoxin-a weigh to child in derivation 20 kg (Action Tier 1) and 30.25 kg (Action Tier 2); For microcystin and cylindrospermopsin 30.35 kg child used in derivations.
	Are the mathematical workings/algorithms clearly documented and explained?		Appendix A URL provided
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?		Appendix A URL provided; specify analytical method chosen must detect < 1µg/L anatoxin-a
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?	Y	Discuss heightened risk to animals and livestock due to consumption of scum and mats containing concentrated toxins.
	What processes are used when expert judgement is required and applied? Is the process documented and published?		Appendix A URL provided
	Is dose response modelling (e.g. BMDL) routinely used?		Unknown
	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?		Unknown
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	N/A	Unknown

Table A8-1: (continued) Commonwealth of Massachusetts (2021). Guidelines for cyanobacteria in freshwater recreational water bodies.

	Criteria	Y/N/NA	Response
	Overall guidance/advice development process		
	Are the key stages of the organisation's advice development processes compatible with Australian processes?		NHMRC to review and complete
	Are the administrative processes documented and publicly available?		Unknown
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?		Unknown
	Are funding sources declared?		Government of Massachusetts
	Was there public consultation on this work? If so, provide details.		Unknown
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?	N	
	Was the guidance/advice developed or updated recently? Provide details.		URL provided at end of table.
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?	N	Limited background introduction
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?	Y	WHO (2003)
	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	
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?	N	
	Are inclusion/exclusion criteria used to select or exclude certain studies from the review? If so, is justification provided?	N/A	Not systematic literature review
	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	California, Vermont, WHO, Australia
	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	WHO TDI used

Table A8-1: (continued)

Commonwealth of Massachusetts (2021). Guidelines for cyanobacteria in freshwater recreational water bodies.

	Criteria	Y/N/NA	Response
	Evidence search		
	Are databases and other sources of evidence specified?	N	
	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)?	N	
	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?	N	
	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	
	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	
	Does the organisation assess the overall certainty of the evidence and reach recommendations? If so, provide details.	N	

Table A8-1: (continued)

Commonwealth of Massachusetts (2021). Guidelines for cyanobacteria in freshwater recreational water bodies.

	Criteria	Y/N/NA	Response
	Derivation of health-based guideline values		
	Is there justification for the choice of uncertainty and safety factors?	Y	Based on WHO 2003
	Are the parameter value assumptions documented and explained?	Y	
	Are the mathematical workings/algorithms clearly documented and explained?	Y	limited
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?	N	
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?	N	
	What processes are used when expert judgement is required and applied? Is the process documented and published?		
	Is dose response modelling (e.g. BMDL) routinely used?	N	
	What is the organisation’s policy for dealing with substances for which a non-threshold mode of action may be applicable in humans? Has the policy been articulated and recorded?		
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	N/A	

Commonwealth of Massachusetts (2021). Guidelines for cyanobacteria in freshwater recreational water bodies. [online] Available at: https://www.mass.gov/info-details/guidelines-for-cyanobacteria-in-freshwater-recreational-water-bodies [Accessed February 2021]

Table A8-1: (continued)

Oregon Health Authority (2019). Oregon harmful algae bloom surveillance (HABS) program. Recreational use public health advisory guidelines. Cyanobacterial blooms in freshwater bodies. May 2019.

	Criteria	Y/N/NA	Response
	Overall guidance/advice development process		
	Are the key stages of the organisation's advice development processes compatible with Australian processes?		NHMRC to review and complete
	Are the administrative processes documented and publicly available?		Unknown
	Was the work overseen by an expert advisory committee? Are potential conflicts of interest of committee members declared, managed and/or reported?		Unclear, document prepared by Oregon Health Authority.
	Are funding sources declared?		Unclear but most likely Oregon Government
	Was there public consultation on this work? If so, provide details.		Unknown
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?	N	
	Was the guidance/advice developed or updated recently? Provide details.		https://www.oregon.gov/oha/PH/HEALTHYENVIRONMENTS/RECREATION/HARMFULALGAEBLOOMS/Documents/2019%20Advisory%20Guidelines%20for%20Harmful%20Cyanobacterial%20Blooms%20in%20Recreational%20Waters.pdf [Accessed February 2021]

Table A8-1: (continued)

Oregon Health Authority (2019). Oregon harmful algae bloom surveillance (HABS) program. Recreational use public health advisory guidelines. Cyanobacterial blooms in freshwater bodies. May 2019.

	Criteria	Y/N/NA	Response
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?	Y	
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?	Y	U.S. EPA (2006); Washington Department of Health (2008); NZ Ministry of Health (2002)
	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	
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?	N	
	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	U.S. EPA (2006); Washington Department of Health (2008); NZ Ministry of Health (2002); details of critical assessment not given
	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/A	
	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)?	N/A	
	Is it specified what date range the literature search covers? Is there a justification?	N/A	
	Are search terms and/or search strings specified?	N/A	
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?	N/A	

Table A8-1: (continued)

Oregon Health Authority (2019). Oregon harmful algae bloom surveillance (HABS) program. Recreational use public health advisory guidelines. Cyanobacterial blooms in freshwater bodies. May 2019.

	Criteria	Y/N/NA	Response
	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	
	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	
	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	Appendix B pp 13-20 URL given above
	Are the parameter value assumptions documented and explained?	Y	Appendix B pp 13-20 URL given above
	Are the mathematical workings/algorithms clearly documented and explained?	Y	Appendix B pp 13-20 URL given above
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?	N	Appendix B pp 13-20 URL given above
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?	N	Appendix B pp 13-20 URL given above
	What processes are used when expert judgement is required and applied? Is the process documented and published?		Appendix B pp 13-20 URL given above
	Is dose response modelling (e.g. BMDL) routinely used?	N	Appendix B pp 13-20 URL given above
	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?		Unknown; Appendix B pp 13-20 URL given above
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	N/A	

Table A8-1: (continued)

Washington State Department of Health (2008). Washington State provisional recreational guidance for microcystins (Provisional) and anatoxin-a (Interim/Provisional). Final Report.; Washington State Department of Health (2011). Washington State provisional recreational guidance for cylindrospermopsin and saxitoxin. Final Report.

	Criteria	Y/N/NA	Response
	Overall guidance/advice development process		
	Are the key stages of the organisation's advice development processes compatible with Australian processes?		NHMRC to review and complete
	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	Conflicts of interest no listed
	Are funding sources declared?	Y	Washington Department of Ecology
	Was there public consultation on this work? If so, provide details.		No details of public consultation
	Is the advice peer reviewed? If so, is the peer review outcome documented and/or published?		No details of peer review
	Was the guidance/advice developed or updated recently? Provide details.		Microcystins and anatoxin-a (2008) https://www.doh.wa.gov/Portals/1/Documents/4400/334-177-recguide.pdf [Accessed February 2021] cylindrospermopsin and saxitoxin (2011) https://www.doh.wa.gov/portals/1/documents/4400/332-118-cylindrosax%20report.pdf [Accessed February 2021]

Table A8-1: (continued)

Washington State Department of Health (2008). Washington State provisional recreational guidance for microcystins (Provisional) and anatoxin-a (Interim/Provisional). Final Report.; Washington State Department of Health (2011). Washington State provisional recreational guidance for cylindrospermopsin and saxitoxin. Final Report.

	Criteria	Y/N/NA	Response
	Evidence review parameters		
	Are decisions about scope, definitions and evidence review parameters documented and publicly available?	Y	
	Is there a preference for data from studies that follow agreed international protocols or meet appropriate industry standards?	Y	U.S. EPA (2006); refer to guidelines from other countries
	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	
	If proprietary/confidential studies or data are considered by the agency, are these appropriately described/recorded?		Unknown
	Are inclusion/exclusion criteria used to select or exclude certain studies from the review? If so, is justification provided?		Not detailed
	Does the organisation use or adopt review findings or risk assessments from other organisations? What process was used to critically assess these external findings?		U.S. EPA (2006); details of critical assessment not given
	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	
	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)?	N/A	Not a literature search
	Is it specified what date range the literature search covers? Is there a justification?	N/A	
	Are search terms and/or search strings specified?	N/A	
	Are there any other exclusion criteria for literature (e.g. publication language, publication dates)? If so, what are they and are they appropriate?	N/A	

Table A8-1: (continued)

Washington State Department of Health (2008). Washington State provisional recreational guidance for microcystins (Provisional) and anatoxin-a (Interim/Provisional). Final Report.; Washington State Department of Health (2011). Washington State provisional recreational guidance for cylindrospermopsin and saxitoxin. Final Report.

	Criteria	Y/N/NA	Response
	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	
	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	
	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	
	Are the parameter value assumptions documented and explained?	Y	
	Are the mathematical workings/algorithms clearly documented and explained?	Y	
	Does the organisation take into consideration non-health related matters to account for feasibility of implementing the guideline values (e.g. measurement attainability)?	N	
	Is there documentation directing use of mechanistic, mode of action, or key events in adverse outcome pathways in deriving health-based guideline values?		Unknown
	What processes are used when expert judgement is required and applied? Is the process documented and published?		Unknown
	Is dose response modelling (e.g. BMDL) routinely used?	N	
	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?		Unknown
	If applicable: For carcinogens, what is the level of cancer risk used by the organisation to set the health-based guideline value?	N/A	

6.9 Appendix 9: Suggested Resources for Guideline Implementation

While not identified as part of this project it was recognised, during the search for guidelines developed by multiple jurisdictions, that a collation of resource material developed by other agencies may provide additional material that would be useful for agencies or organisations required to implement the guidelines. The suggestions in Table A9-1 are not exhaustive but were considered good representative examples of the resources developed elsewhere that may be utilised by councils or water authorities to implement the guidelines.

Table A9-1: Suggested resources for authorities (e.g. councils, government) to implement guidelines for cyanobacteria in recreational freshwater with examples from the grey literature.

	Some selected (not exhaustive) examples from existing literature	**Comments**
PRE-PLANNING		
Local action plan	The Scottish Government (2012).	
OBSERVATION		
Cyanobacteria field identification	Kannan, M.S. and Lenca, N. (2013). *Field guide to algae and other "scums" in ponds, lakes, streams and rivers.* Wisconsin Department of Health Services (2019). *Harmful algal blooms toolkit.*	Excellent guide to algae, floating macroscopic plants
ACTION and ADVICE		
Fact sheet	Minnesota Department of Health (2019). *Harmful algal blooms (HABs).* SEQ Water (2016). *Blue-green algae recreation management procedure summary.*	Lots of examples from US States
Sampling advice	The Scottish Government (2012). California State Water Resources Control Board, Department of Public Health, and Office of Environmental Health and Hazard Assessment (2008). Arkansas Energy and Environment (2019). *Harmful algal bloom management plan.* Water NSW (2021b). *Water NSW Guidelines to management response to freshwater, marine and estuarine harmful algal blooms, Procedures for monitoring, application of alert levels and communication.* New Zealand Ministry for the Environment (2009). *New Zealand guidelines for cyanobacteria in recreational fresh waters: Interim Guideline 2009.*	NZ have good information and photos of benthic cyanobacteria

Table A9-1: (continued)

Monitoring advice	California State Water Resources Control Board, Department of Public Health, and Office of Environmental Health and Hazard Assessment (2008). Colorado Lake and Reservoir Management Association (2015) *Guidance document for harmful algal blooms in Colorado.* Water NSW (2021b). *Water NSW Guidelines to management response to freshwater, marine and estuarine harmful algal blooms, Procedures for monitoring, application of alert levels and communication.* New Zealand Ministry for the Environment (2009). *New Zealand guidelines for cyanobacteria in recreational fresh waters: Interim Guideline 2009.*	
Veterinarian advice	California Office of Health Hazard Assessment (OEHHA) (2017). *Blue-green algae: A veterinarian reference.* Michigan Department of Agriculture and Rural Development (2021a). *Factsheet Harmful algal blooms: Veterinarians.* Minnesota Department of Health (2019). *Harmful algal blooms (HABs).* Vermont Department of Health (2015). *Cyanobacteria (blue-green algae) guidance for Vermont communities.* Wisconsin Department of Health Services (2019). *Harmful algal blooms toolkit.*	Veterinarian fact sheet Veterinarian fact sheet
Dog owner advice	Environment Canterbury Regional Council (2021) *Keeping dogs safe from toxic algae.* Centers for Disease Control and Prevention (2021). *Animal safety alert poster.* Michigan Department of Agriculture and Rural Development (2021b). *Factsheet Harmful algal blooms: Pets and livestock.* Wisconsin Department of Health Services (2019). *Harmful algal blooms toolkit.*	Poster for dog owners Dog owner fact sheet

Table A9-1: (continued)

Physician advice	Oregon Health Authority (2021). *Cyanotoxin resources for drinking water.* California Water Quality Monitoring Council (2021). *Human health and HABs.*	Fact sheets for health care providers, health facilities, vulnerable people, general population
	California Department of Public Health (2020). *Harmful algal blooms (HABs): Information for physicians.* Centres for Disease Control (2021). *Physician reference for cyanobacterial blooms.*	Physician's guide
General homeowner advice	Oregon Health Authority (2021). *Cyanotoxin resources for drinking water.* California Government/U.S. EPA (2021). *Look out for harmful algal blooms poster.*	Publicity poster
Livestock advice	New South Wales Department of Primary Industries (2021). *Blue-green algae.* Agriculture Victoria (2021). *Blue-green algae and irrigation water.*	
Irrigation advice	New South Wales Department of Primary Industries (2021). *Blue-green algae.* Agriculture Victoria (2021). *Blue-green algae and irrigation water.* National Collaborating Centre for Environmental Health (2017). *Irrigating food crops with water containing cyanobacteria blooms.*	
Signage examples	Colorado Lake and Reservoir Management Association (2015) *Guidance document for harmful algal blooms in Colorado.* Arkansas Energy and Environment (2019). *Harmful algal bloom management plan.* New Zealand Ministry for the Environment (2009). *New Zealand guidelines for cyanobacteria in recreational fresh waters: Interim Guideline 2009.*	

Table A9-1: (continued)

General public advice **Including media**	California State Water Resources Control Board, Department of Public Health, and Office of Environmental Health and Hazard Assessment (2008). The Scottish Government (2012). Colorado Lake and Reservoir Management Association (2015) *Guidance document for harmful algal blooms in Colorado.* Water NSW (2021b). *Water NSW Guidelines to management response to freshwater, marine and estuarine harmful algal blooms, Procedures for monitoring, application of alert levels and communication.* New Zealand Ministry for the Environment (2009). *New Zealand guidelines for cyanobacteria in recreational fresh waters: Interim Guideline 2009.*	
Sources of specialist advice for each state	New Zealand Ministry for the Environment (2009). *New Zealand guidelines for cyanobacteria in recreational fresh waters: Interim Guideline 2009.*	
List of analytical laboratories and capability	Arkansas Energy and Environment (2019). *Harmful algal bloom management plan.* New Zealand Ministry for the Environment (2009). *New Zealand guidelines for cyanobacteria in recreational fresh waters: Interim Guideline 2009.*	
Alert de-escalation	Water NSW (2021b). *Water NSW Guidelines to management response to freshwater, marine and estuarine harmful algal blooms, Procedures for monitoring, application of alert levels and communication.*	

References for Table A9-1:

Agriculture Victoria (2021). Blue-green algae and irrigation water. [online] Available at: https://agriculture.vic.gov.au/farm-management/water/blue-green-algae-in-water/bluegreen-algae-and-irrigation-water [Accessed February 2021]

Arkansas Energy and Environment (2019). Harmful algal bloom management plan. [online] Available at: https://www.adeq.state.ar.us/water/pdfs/HAB-ResponsePlan-Manual-bookmarks-2019-12-12-Final.pdf [Accessed February 2021]

California Department of Public Health (2020). Harmful algal blooms (HABs): Information for physicians. [online] Available at: https://mywaterquality.ca.gov/habs/resources/docs/humanhealth/hab_physician_guide_may2020.pdf [Accessed February 2021]

California Government/U.S. EPA (2021). Look out for harmful algal blooms poster. [online] Available at: https://mywaterquality.ca.gov/habs/resources/docs/habs-infographic-detailed-2019_CA%20version.pdf [Accessed February 2021]

California Office of Health Hazard Assessment (OEHHA) (2017). Blue-green algae: A veterinarian reference. [online] Available at: https://oehha.ca.gov/risk-assessment/fact-sheet/blue-green-algae-veterinarian-reference [Accessed February 2021]

California State Water Resources Control Board, Department of Public Health, and Office of Environmental Health and Hazard Assessment (2008). Blue green algae work group. Cyanobacteria in California recreational water bodies. Providing voluntary guidance about harmful algal blooms, their monitoring, and public notification. DRAFT. [online] Available at: https://www.waterboards.ca.gov/water_issues/programs/bluegreen_algae/docs/bga_volguidance.pdf [Accessed February 2021]

California Water Quality Monitoring Council (2021). Human health and HABs. [online] Available at: https://mywaterquality.ca.gov/habs/resources/human_health.html [Accessed February 2021]

Centers for Disease Control and Prevention (2021). Animal safety alert poster. [online] Available at: https://www.cdc.gov/habs/pdf/algal_bloom_poster.pdf [Accessed February 2021]

Centres for Disease Control (2021). Physician reference for cyanobacterial blooms. [online] Available at: https://www.cdc.gov/habs/pdf/habsphysician_card.pdf [Accessed February 2021]

Colorado Lake and Reservoir Management Association (2015) Guidance document for harmful algal blooms in Colorado. Prepared by the 2015 Board of Directors, Colorado Lake & Reservoir Management Association. [online] Available at: http://www.clrma.org/files/springconference/CLRMA%20Luncheon.2015.HAB%20Guidance%20Document.pdf [Accessed February 2021]

Environment Canterbury Regional Council (2021) Keeping dogs safe from toxic algae. [online] Available at: https://ecan.govt.nz/your-region/your-environment/water/health-warnings/keeping-dogs-safe-from-toxic-algae/ [Accessed February 2021]

Kannan, M.S. and Lenca, N. (2013). Field guide to algae and other "scums" in ponds, lakes, streams and rivers. 2nd edition. Northern Kentucky University. [online] Available at: https://www.townofchapelhill.org/home/showdocument?id=28866 [Accessed February 2021]

Michigan Department of Agriculture and Rural Development (2021a). Factsheet Harmful algal blooms: Veterinarians. [online] Available at: https://www.michigan.gov/documents/egle/egle-wrd-swas-habs-vethandout_663644_7.pdf [Accessed February 2021]

Michigan Department of Agriculture and Rural Development (2021b). Factsheet Harmful algal blooms: Pets and livestock. [online] Available at: https://www.michigan.gov/documents/egle/egle-wrd-swas-habs-ownerhandout_663645_7.pdf [Accessed February 2021]

Minnesota Department of Health (2019). Harmful algal blooms (HABs). [online] Available at: https://www.health.state.mn.us/diseases/hab/index.html [Accessed February 2021]

National Collaborating Centre for Environmental Health (2017). Irrigating food crops with water containing cyanobacteria blooms. [online] Available at: https://ncceh.ca/sites/default/files/Irrigating_Food_Crops_Water_Containing_Cyanobacteria-Oct_2017.pdf [Accessed February 2021]

New South Wales Department of Primary Industries (2021). Blue-green algae. [online] Available at: https://www.dpi.nsw.gov.au/agriculture/water/quality/pubs-and-info/blue-green-algae [Accessed February 2021]

New Zealand Ministry for the Environment (2009). New Zealand guidelines for cyanobacteria in recreational fresh waters: Interim Guideline 2009 Appendix 2. [online] Available at: https://www.mfe.govt.nz/publications/fresh-water-environmental-reporting/guidelines-cyanobacteria [Accessed February 2021]

Oregon Health Authority (2021). Cyanotoxin resources for drinking water. [online] Available at: https://www.oregon.gov/oha/PH/HealthyEnvironments/DrinkingWater/Operations/Treatment/Pages/algae.aspx [Accessed February 2021]

SEQ Water (2016). Blue-green algae recreation management procedure summary. [online] Available at: https://www.seqwater.com.au/sites/default/files/2019-09/Seqwater%20Blue%20Green%20Algae%20Recreation%20management%20procedure%20-%20summary.pdf [Accessed February 2021]

The Scottish Government (2012). Cyanobacteria (blue-green algae) in inland and inshore waters: assessment and minimisation of risks to public health. Revised guidance 2012. [online] Available at: https://www.gov.scot/binaries/content/documents/govscot/publications/advice-and-guidance/2012/04/cyanobacteria-blue-green-algae-inland-inshore-waters-assessment-minimisation-risks-public-health/documents/cyanobacteria-blue-green-algae-inland-inshore-waters-assessment-minimisation-risks-public-health-revised-guidance-2012/cyanobacteria-blue-green-algae-inland-inshore-waters-assessment-minimisation-risks-public-health-revised-guidance-2012/govscot%3Adocument/00391470.pdf [Accessed February 2021]

Vermont Department of Health (2015). Cyanobacteria (blue-green algae) guidance for Vermont communities. Appendix F: Cyanobacteria in Vermont: What Veterinarians Should Know pp. 31-32. [online] Available at: https://www.healthvermont.gov/sites/default/files/documents/2016/12/ENV_RW_CyanobacteriaVeterinarians.pdf [Accessed February 2021]

Water NSW (2021b). Guidelines to management response to freshwater, marine and estuarine harmful algal blooms, Procedures for monitoring, application of alert levels and communication. [online] Available at: https://ehq-production-australia.s3.ap-southeast-2.amazonaws.com/829009d10fe83566b2b840c8aa60a7c15c43009c/documents/attachments/000/103/326/original/Guidelines_to_management_response_to_freshwater__marine_and_estuarine_harmful_algal_blooms_-_WaterNSW_-_2018.pdf?X-Amz-Algorithm=AWS4-HMAC-SHA256&X-Amz-Credential=AKIAIBJCUKKD4ZO4WUUA%2F20210301%2Fap-southeast-2%2Fs3%2Faws4_request&X-Amz-Date=20210301T024232Z&X-Amz-Expires=300&X-Amz-SignedHeaders=host&X-Amz-

Signature=f78b34531601170a7b53319ab254db67eed25cc2aff26c9ec579f466c7c5a477 [Accessed February 2021]

Wisconsin Department of Health Services (2019). Harmful algal blooms toolkit. [online] Available at: https://www.dhs.wisconsin.gov/library/p-00853.htm [Accessed February 2021]

6.10 Appendix 10: Primary Studies with Evidence of Health Outcomes for Dogs following Exposure in Recreational Water

Table A10-1: Primary studies providing evidence of health outcomes for animals following exposure to freshwater cyanobacteria in recreational situations.

Authors	Type of study and purpose	Comments
Observational Studies		
Fastner *et al*., 2018	Report of 12 dogs presenting with acute neurotoxicosis after swimming in a German lake. Three dogs died and post-mortem assessments of two of the dogs found anatoxin-a and filaments identical to *Tychonema* sp. in the stomach contents. No other neurotoxic substances were found. At the lake where the dog intoxications occurred large areas of water moss (*Fontinalis antipyretica*) were found and *Tychonema* sp. was found in the moss.	The study found a strong positive association between the dog poisonings and the presence of neurotoxic anatoxin-a in the stomach of two poisoned dogs and also filaments of *Tychonema* sp. The time period between dog exposure and environmental sampling is not clear.
Gugger *et al*., 2005	Report of two dog deaths following drinking from a river in France. The stomach, intestine and liver were analysed for cyanobacterial toxins. Anatoxin-a was detected in the livers of the poisoned dogs and *Phormidium favosum* was identified in one of the dog's stomach contents. Sediments, stones and surfaces at the river where the dogs were drinking were covered by a thick biofilm containing several benthic species of filamentous, non-heterocystous cyanobacteria. Several cyanobacterial strains were isolated and *Phormidium favosum* was identified as the producer of anatoxin-a.	The study found a strong positive association between the dog poisonings and detection of neurotoxic Anatoxin-a in the livers of the poisoned dogs and the benthic *Phormidium favosum* was identified in one of the dog's stomach contents. Anatoxin-a was determined by two analytical methods to discriminate anatoxin-a in phenylalanine-containing matrices such as liver samples. There were several days between dog exposure and collection of environmental samples.
Lurling and Faassen, 2013	Report of death of three dogs after swimming in Lake Amstelmeer, the Netherlands, that was covered in a massive bloom of *Microcystis aeruginosa*. The water and scum samples from the lake and the vomit from one of the dogs contained *Microcystis* aggregates. Cyanobacterial samples and the vomit also contained microcystins but no nodularin.	The study found a positive association between the dog poisonings and the presence of microcystin toxins and *Microcystis* colony aggregates in the dogs' vomit. The toxins were also confirmed from the *Microcystis aeruginosa* bloom in the lake.
Manning *et al*., 2020	Report of mass dog deaths after swimming in a lake in Austin, Texas, USA. Mats of benthic cyanobacteria were clustered along the shoreline. *Geitlerinema*, *Limnothrix*, *Pseudanabaena* and *Phormidium* were isolated from benthic mats. Dihydroanatoxin-a detected in high concentrations in the mats but only trace levels were in the water column. No analysis of cyanobacteria or cyanobacterial toxins in the dogs.	The study found an association between mass dog poisonings and potential exposure to neurotoxic benthic cyanobacteria, without strong confirmation of individual exposure. There were two days between dog exposure and follow-up environmental sampling.

Table A10-1: (continued)

Authors	Type of study and purpose	Comments
Mez *et al*., 1997	The study provided detailed analysis of environmental samples from alpine lakes in Switzerland in an area where cattle deaths had been reported. *Oscillatoria limosa* and *Phormidium konstantinosium* were the dominant benthic cyanobacteria in dense mats on sediments and submerged rocks. A microcystin was identified in the mats and in the lake water. Samples from the mats were positive in a protein phosphatase inhibition assay, reacted with antibodies against microcystins in an ELISA assay and were hepatotoxic in a mouse bioassay. Environmental sampling had been done previously in 1995. Cattle deaths had occurred over several decades.	The study found a weak and inconclusive association between the cattle poisonings and exposure to toxic benthic cyanobacteria. Intoxication due to alpine plants was excluded and negative results were found from searches for bacterial and fungal pathogens as well as for xenobiotic hepato- and neurotoxins.
Puschner *et al*., 2008	Report of death of three dogs in two separate outbreaks (total of 6 dogs) following swimming in a river in California and a pond in Ontario. Water samples were collected at both sites. Water samples from both sites contained *Planktothrix* sp. Stomach contents from one affected dog from Ontario and all three from California contained anatoxin-a. The Ontario pond water and all Californian water samples contained anatoxin-a. The following were ruled out, by analysis of the dog stomach contents or livers, as potential neurotoxicants: zinc phosphide, strychnine, organophosphorus and carbamate insecticides. Also, the Ontario dog was tested negative for mycotoxins penitrem A and roquefortine.	The study found a strong positive association between the dog poisonings and the presence of neurotoxic anatoxin-a in the stomachs of 4 of the 6 poisoned dogs. Environmental samples were collected a few days after dog deaths reducing the reliability of exposure assessment.
Case Studies		
Faassen *et al*., 2012	Report of death of three dogs and two birds after swimming in Lake Ljmeer, Netherlands. At the time of exposure, the lake was infested with the benthic cyanobacteria, *Phormidium* spp. An investigation of one of the dogs indicated neurotoxicosis and its stomach contained *Phormidium* filaments. Anatoxin-a was detected in the *Phormidium* mat and in the dog's stomach contents. Traces of homoanatoxin-a were also detected in the algae. No cyanobacterial toxins were found in the birds' stomachs.	The study found a strong positive association between dog neurotoxic poisonings and exposure to anatoxin-a from benthic *Phormidium* sp. One limitation with the study was the delay of two weeks between the dog's exposure and the collection of collection of cyanobacterial material from the lake.
Hoff *et al*., 2007	One page report of the Ontario case detailed in Puschner (2008).	

Table A10-1: (continued)

Authors	Type of study and purpose	Comments
Puschner *et al.*, 2010	Case report of a dog with acute onset of paraparesis after swimming in a pond and ingesting algae from a nearby bucket of water. The dog deteriorated and was euthanized. *Phormidium* spp. was identified in the algal material from the bucket and the dog's stomach contents. Gastric contents of the dog, bucket contents, pond water, bile and urine were positive for anatoxin-a.	The study found a strong positive association between dog neurotoxic poisoning and confirmed exposure via drinking water and stomach contents containing anatoxin-a and *Phormidium* spp.
Puschner *et al.*, 2017	Case report of dermatitis in a dog after exposure to a lake in California, USA. First report of skin-related reaction in an animal following recreational exposure to lakes with visible algal blooms. Basic dermatology assessment excluded parasitic, fungal and bacterial organisms. A range of cyanobacterial organisms were found in the lake water. Lake water was found to contain debromoaplysiatoxin and low concentrations of anatoxin-a. The skin irritation was completely resolved within a few weeks after the dog was prevented from access to the lake.	The study is novel in finding an association, but not strong, between dermatitis in a dog and potential immersion exposure to cyanobacteria in a lake with blooms.
Rankin *et al.*, 2013	Case report of dog being hospitalised two days after swimming through an algal scum in a lake. The dog was observed to drink the water and lick the water and algal scum from its coat. After 8 days the dog was discharged. Surface scum and dog faeces collected 8 days post-exposure contained 38, 627 ppb and 217 ppb microcystin-LA, respectively.	The study found an association of dog poisoning from potential exposure via ingestion of microcystin toxins from swimming in an algal scum. Exposure confirmed from dog faeces and presence in lake water.
Sebbag *et al.*, 2013	Case report of dog presenting one day after swimming in a lake with vomiting, inappetence, weakness and lethargy. The dog had ingested a large amount of water and was covered in green material. Blood results from the dog were consistent with acute hepatic failure. *Microcystis* spp. was identified in the water sample collected from the lake. This is the first report of a dog to survive treatment after exposure.	The study found an association of dog poisoning and exposure to potentially toxic *Microcystis*. There was identification of cyanobacterial organism and no quantification of cyanobacteria in lake water. No toxin analyses were performed on the water samples or dog vomit.
Simola *et al.*, 2012	Case report of dog death following exposure to sea water containing blue-green algae. Exact exposure route uncertain. The dog may have consumed algal scum or drunk contaminated water. Nodularin was detected in liver and kidney samples. No environmental samples were collected but *Nodularia spumigena* is the main toxin-producing species in the Baltic Sea area.	The study found an association of the dog poisoning from potential exposure via ingestion of nodularin toxins, detected in liver and kidney samples. No environmental samples were collected to confirm exposure to *Nodularia spumigena.*

Table A10-1: (continued)

Authors	Type of study and purpose	Comments
Trevino-Garrison *et al*., 2015	Collation of six dog poisoning cases in Kansas, USA, 2011. Only three cases undertook cyanobacterial identification – two cases identified *Microcystis* spp. on hair or in vomit.	The study found a weak association only of poisonings and exposure to cyanobacteria or cyanotoxins. No information was given about types of cyanobacteria or cyanotoxins in the environmental samples. No information is provided about cyanotoxin analyses in the affected dogs.
Van der Merwe *et al*., 2012	Case report of a dog presenting with vomiting and diarrhea one day after drinking from a lake. Dog deteriorated and was euthanized. Lake water and algal scum samples were dominated by *Microcystis aeruginosa*. Microcystin concentrations in the lake water were extremely high (up to 126,000 ng/mL). Microcystins also detected in vomit and liver.	The study found a positive association of dog poisoning from potential exposure via ingestion of microcystin toxins from a lake with *M. aeruginosa* scum. Environmental samples were collected as part of a weekly monitoring program. The two water samples analysed for total microcystins by ELISA were collected 4 and 12 days before the dog's exposure.
Wood *et al*., 2007	Report of death of 5 dogs after contact with river water. A post-mortem of one dog revealed large amounts of froth in the respiratory tract and algal material in the stomach. Filaments of *Phormidium* sp. were identified in the environmental samples and the dog's stomach. Anatoxin-a and homoanatoxin-a and the degradation products, dihydro-anatoxin-a and dihydro-homoanatoxin-a, were detected in the dog's stomach contents and the benthic cyanobacterial mats.	The study found a strong positive association between dog poisonings and confirmed exposure via contact with water and stomach contents containing anatoxins and benthic *Phormidium* sp. filaments. Environmental samples were collected within a few days of the dog deaths, so no immediate confirmation of environmental exposure.
Wood *et al*., 2010	Case report of one dog death after ingesting benthic algal mat material from a river. *Planktothrix* sp. was identified as the causative organism. Microcystins were identified in the mat material.	The study found a positive association of dog poisoning with exposure via ingestion of benthic *Planktothrix* sp. and microcystins in the mat material. No confirmation of toxins in the animal.
Wood *et al*., 2017	Case report of one dog death after contact with floating algal mats at a farm pond. Samples of the floating algal mat found the dominant cyanobacteria was *Phormidium autumnale.* Environmental samples (pond water and algal mat) contained moderate levels of anatoxin-a and high levels of dihydroanatoxin-a.	The study found a positive association of dog poisoning with exposure to benthic *Phormidium* mats containing anatoxin-a and dihydroanatoxin-a. Environmental samples were collected within a few days of the dog death so there was no immediate confirmation of environmental exposure.