Oregon Harmful Algae Bloom Surveillance (HABS) Program

Public Health Advisory Guidelines
Harmful Algae Blooms in Freshwater Bodies

Oregon Health Authority

Public Health Division
Office of Environmental Public Health
Research & Education Section

Public Health Advisory Guidelines for Harmful Algae Blooms in Freshwater Bodies

Oregon Health Authority Public Health Division
Office of Environmental Public Health

Table of Contents

Introduction

Cyanobacteria, also known as blue-green algae, are commonly found in many freshwater environments around the world. Some cyanobacteria species are referred to as toxigenic because they have the potential to produce toxins that can harm people, pets and wildlife.

Many Oregon water bodies are monitored for cyanobacterial harmful blooms (CyanoHABs). Historically the decision-making process for issuing and lifting health advisories varied according to the managing jurisdiction of a specific water body. In 2009 the Oregon Health Authority Public Health Division (OPHD) assumed responsibility for the decision-making process and for issuing and lifting public health advisories when cyanoHABs are detected.

The OPHD is working to gain a better understanding about the occurrence of cyanoHABs in Oregon and their impact on human health. Funding is through a five-year federal grant from the U.S. Centers for Disease Control and Prevention (CDC).

OPHD program objectives:

- Track freshwater and marine cyanoHABs with data provided by partner agencies
- Track cases of human and animal illnesses related to cyanoHABs
- Enter environmental and health data for OPHD tracking
- Build the capacity of our partners to monitor water bodies in a scientifically sound manner with the goal of protecting public health
- Provide technical assistance to partner agencies to assess health risks associated with algal toxins
- Educate and inform the public regarding health risks due to cyanoHABs
- Analyze data to identify areas vulnerable to cyanoHABs to prioritize prevention efforts

Purpose of this Document

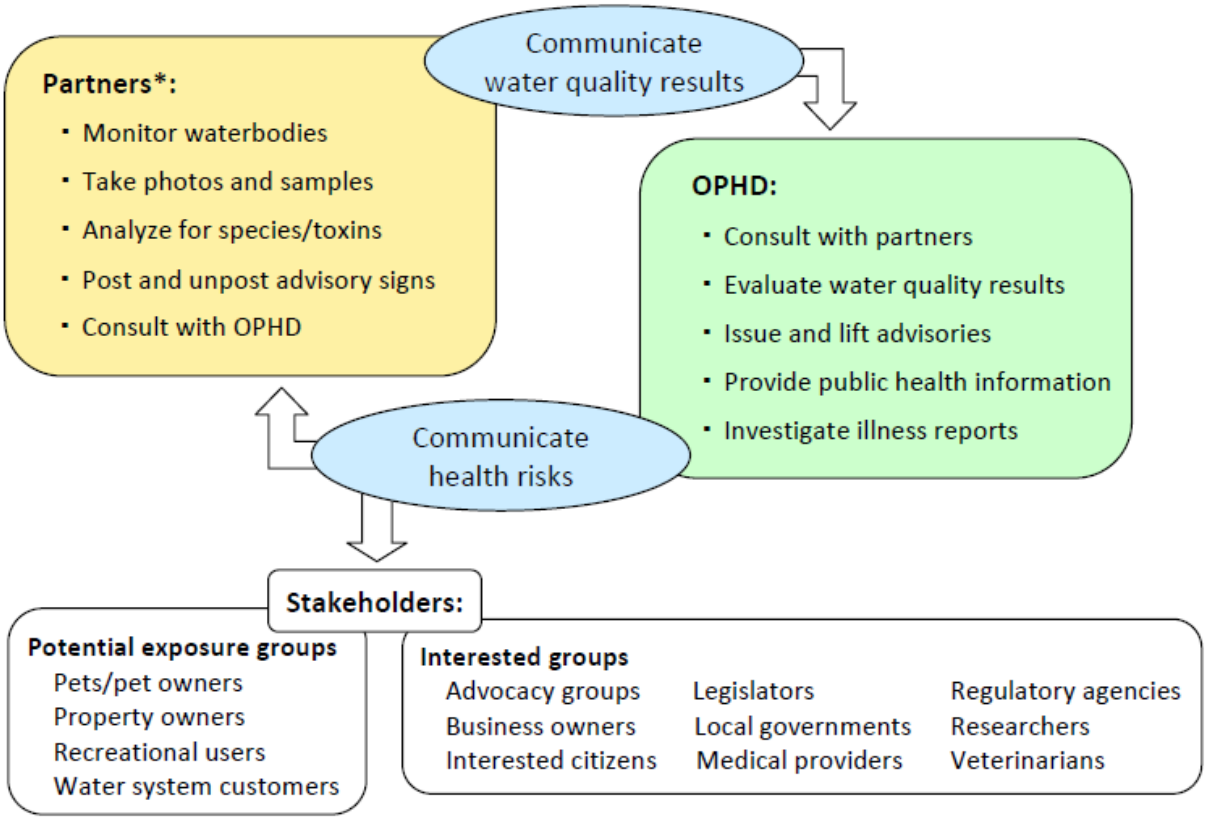
The purpose of this document is to explain the OPHD guidelines for issuing and lifting public health advisories that inform the public of potential health risks from exposure to toxic cyanobacteria in Oregon fresh water bodies.

The advisory process is based on a coordinated effort to monitor and detect cyanoHABs in Oregon's recreational fresh waters and the communication system to notify the public. OPHD authority for public health and safety fall under Title 36, Oregon Revised Statute (ORS), Chapter 431.035 to 431.530.

CyanoHAB Coordination Process

There are specific actions involved in monitoring and responding to cyanoHABs, which require mutual coordination and communication among the OPHD, its partners and stakeholders to complete the process. Figure 1 depicts the flow of activities among all entities involved in cyanoHAB incidents.

Figure 1. Activities involved in monitoring and responding to cyanoHABs



*Oregon Department of Environmental Quality, U.S. Forest Service, U.S. Army Corps of Engineers and other waterbody managers.

The main roles of the OPHD are to issue and lift health advisories based on water quality data provided by partners and to provide risk communication assistance.

Partners in this effort include the Oregon Department of Environmental Quality, U.S. Forest Service, U.S. Army Corps of Engineers and other waterbody managers.

For the purposes of the OPHD public health advisory process, stakeholders are classified in two sub-groups:

- **Potential exposure groups** have a greater opportunity for illness from cyanoHABs through recreational activities. Exposure can occur through ingestion, inhalation or skin contact with contaminated fresh water. More information regarding potential routes of exposure for recreational activities is provided in Appendix C.
- **Interested groups** have varying levels of need, involvement or interest in program operations or policies; are affected by the program; or are intended users of program outcomes/findings.

Table 1 outlines the roles and responsibilities for monitoring and responding to a cyanoHAB.

Table 1 - Roles and Responsibilities for Monitoring and Responding to a CyanoHAB

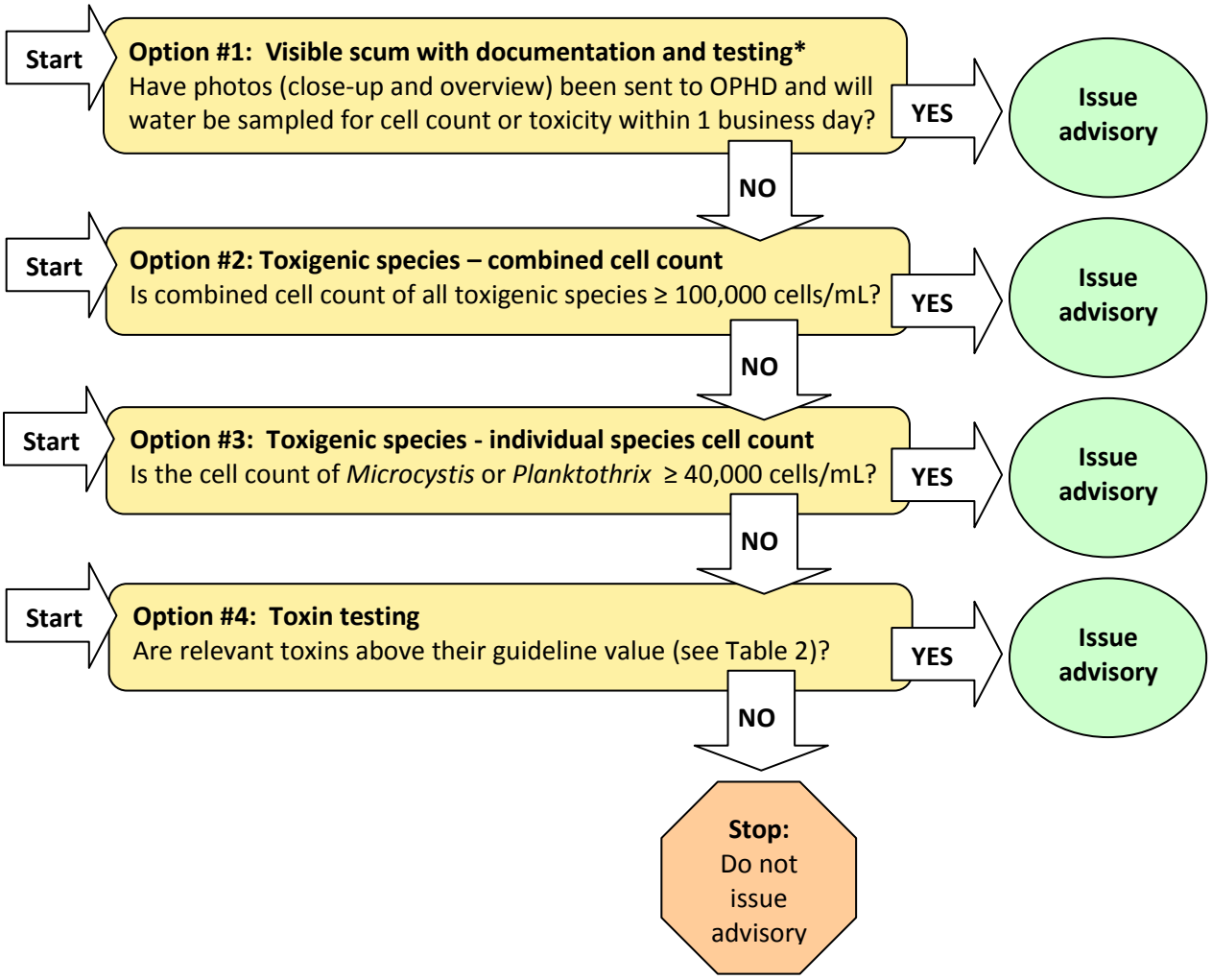
Activity	Lead role	Assist
Monitor	Partners monitor water bodies through on-site observations for evidence of cyanoHABs	OPHD provides guidance for establishing a monitoring program
Collect water samples	Partners use scientifically acceptable methods to obtain water samples	OPHD provides guidance in sampling techniques
Analyze samples	Partners contract with laboratories that are qualified to perform the required analyses	OPHD provides a list of laboratories with appropriate analytic capabilities
Issue or lift advisories	OPHD evaluates data quality and compares test results to established criteria and determines if an advisory should be issued or lifted	OPHD consults with local health departments before issuing or lifting advisories
Communicate Advisory Information	OPHD informs the general public through advisories issued to the media, via its website, an automated electronic list-serv and a toll-free hotline	Partners and local health departments inform their constituents of the health advisory status
Ongoing communication between the OPHD and partners occurs throughout the bloom season regarding advisory decisions, bloom reformation, water quality data transmissions and illness reports.		

Criteria for Issuing a Public Health Advisory

OPHD is responsible for the decision-making and communication process of issuing and lifting public health advisories. While waiting for the OPHD advisory process, local management may post educational signs as a precautionary measure to alert the public of the potential health risks associated with using the water during a cyanoHAB.

OPHD criteria for issuing a public health advisory depend on the method selected. Options include: visible scum (with supporting photographs and water analysis), cell counts or toxicity levels or a combination of two or more options.

Figure 2. OPHD process for issuing public health advisories for a cyanoHAB



*Note: If an advisory was issued based on Option 1 and initial sample results come back below guideline values after an advisory has already been issued (based on visual assessment), no additional sampling is required to lift the advisory. It will be lifted as soon as OPHD receives the initial laboratory results showing cell count or toxin concentrations are below guideline values.

Scum is defined as a visible mass of algae or cyanobacteria in stagnant or slow moving water. Scum accumulations of the greatest concern are those occurring at or near recreational access points.

OPHD guideline values for cyanobacterial cell counts and toxins are based on the World Health Organization risk categories and research in the field. More information regarding the rationale used to help determine when advisories should be posted is provided in Appendix A.

Toxin Based Monitoring Program: Option 4

Toxin testing provides the most accurate information in terms of protecting public health. Toxin testing also results in health advisory decisions that are based on actual human health risk rather than potential health risk.

Because cyanobacteria, even when present in concentrations above OPHD's threshold values, often do not produce toxins, it is anticipated that Option 4 will result in fewer and shorter duration public health advisories for a given water body. However, laboratory costs when using Option 4 are higher than those for Options 1 through 3. OPHD's cyanotoxin guideline values, listed in Table 2, are the basis for determining whether an advisory will be issued under Option 4. The OPHD Sampling Guidelines document contains detailed information on how to conduct a toxin-based monitoring program.

Table 2. Health advisory guideline values for cyanotoxins in Oregon's recreational waters

	Anatoxin-A (µg/L)	Cylindrospermopsin (µg/L)	Saxitoxin (µg/L)	Microcystin (µg/L)
Guideline Value	20	6	100	10

Note: OPHD has also developed dog-specific guideline values. They are for informational purposes only and are not to be used as a basis for issuing public health advisories. These guideline values can be found in Appendix C.

Special note: *Aphanizomenon flos-aquae* exemption from cyanotoxin-producing genus list

Aphanizomenon flos-aque (AFA) is a species of cyanobacteria commonly found in Oregon's fresh waters. Although some studies have shown this species to produce toxins in other parts of the world, subsequent evaluations of that work show that the species either was or likely was misidentified. **For the purpose of issuing public health advisories, AFA is excluded from calculation of combined cell counts of toxigenic species.** Other species of the genus *Aphanizomenon*, such as *A. gracile*, have been demonstrated to produce cyanotoxins. In recognition of this exemption the toxigenic genus list presented in Appendix B, Table B-1 describes *Aphanizomenon (Except A. flos-aquae)*.

Criteria for Lifting a Public Health Advisory

OPHD will lift advisories when tests show that cell counts and toxin concentrations are below the guideline values listed in Figure 2 (cell counts) and Table 2 (toxins).

Cell count is required in addition to toxin testing to ensure there is minimal potential for further toxin release. The accepted method for determining cell counts is Standard Methods Section 10200E and F (also called "SM10200"). The cost for species identification and cell counts is approximately $150.

Toxin analyses are required to lift public health advisories for cyanoHABs. **Be sure to analyze for cyanotoxins produced by the cyanobacteria present (see Appendix B, Table B-1)**. All cyanobacteria produce lipopolysaccharides that can cause skin irritation, but OPHD will not require testing for these toxins.

Cyanotoxin analyses currently available through commercial laboratories use a variety of comparable methods. These analyses may be quite costly, ranging from $150 to $350 depending

on the method and equipment used. For microcystin, saxitoxin, and cylindrospermopsin determination, the ELISA method is least expensive. ELISA methods are not currently available for anatoxin-a. When testing for toxins, ensure the lab uses a method detection level less than the guideline values in Table 2.

Note: OPHD will not accept field-ready test kits for microcystin as a basis for lifting an advisory. However, the kits may be useful for monitoring the progress of a bloom throughout the season.

Public Notification Methods

Several notification methods are used by the OPHD, concurrently, in the issuing and lifting of public health advisories. The specific methods used are as follows:

Phone Alerts: Phone calls are immediately made to the highest priority contacts to ensure that advisory information reaches the local area first. These contacts include:

- County health department staff
- Partner agency communications staff that have jurisdiction over the affected lake/reservoir.

Email: An email is sent to a large list of stakeholders including interested citizens, resort owners, advocacy groups, public officials and others. Access to this list is open to all interested Oregonians.

News Releases: OPHD issues statewide news releases which may be picked up and reported by broadcast and print media outlets across Oregon. These releases contain information about the nature and location of the advisory, possible health effects, recommended protective actions and where people can obtain more information. Statewide news releases are also issued when advisories are lifted.

Program Web page: The program maintains a website that provides real-time access to advisory information, resources for water samplers and prevention tips. Advisory information (both issuing and lifting) is immediately posted to the program website. The website is available at ***www.healthoregon.org/hab***.

Hotline: A statewide toll-free telephone service (877-290-6767) provides updated advisory information to the public, which is particularly helpful for those individuals without Internet access.

Program Contact Information

Email: habhealth@state.or.us
Phone: (971) 673-0440 Toll Free: (877) 290-6767 and press 0
Website: ***www.healthoregon.org/hab***

Appendix A: Rationale for and history of standards to issue and lift recreational public health advisories for cyanoHABs

In 2004 and previous years, lakes were posted when harmful algae cell densities exceeded 15,000 cells/mL. In 2005, a decision was made to no longer use 15,000 cells/mL threshold as an absolute criterion for posting advisories at recreational access points.

The risk to recreational users at a cell density of 15,000 cells/mL is considered low and includes minor health symptoms such as skin irritation, which are though to be related to lipopolysaccharide endotoxins found on cell walls. In a study by Pilotto et. al, (Pilotto et al., 2004) acute skin irritant effects were tested over a range of cell densities (< 5000 cells/mL to > 200,000 cells/mL) after application of cyanobacterial extracts. Genera tested included *Anabaena*, *Microcystis*, *Cylindrospermopsis* and *Nodularia*. Approximately 15% of the people reacted to the extracts with mild, self-limiting reactions. Furthermore, no dose-response relationship was established. The absence of a dose-response relationship, and therefore a threshold, makes it difficult to recommend quantitative guidance. Consequently, the focus of advisory postings is on the risk posed by cyanotoxins and the potential for more serious health effects such as nervous system or gastrointestinal disorders.

Advisory guidelines for algae blooms dominated by *Microcystis* or *Planktothrix*:

A focused risk assessment was conducted to characterize the risk associated with swimming in waters that are dominated by *Microcystis* or *Planktothrix* cyanobacteria. The equation and parameters are described below:

$$\text{Concentration of toxin } (\mu g/L) = \frac{\text{TDI} \times \text{BW}}{\text{IR}}$$

where:

TDI (tolerable daily intake) = 0.05 µg/kg/day
BW (body weight) = 20 kg
IR (ingestion rate) = 0.1 L

The TDI was developed by the Oregon Public Health Division (OPHD) based on oral administration of microcystin-LR via drinking water in rats and effects on the liver (Heinze, 1999). A body weight (BW) of 20 kg was used to represent a child. An ingestion rate (IR) was based on EPA guidance for incidental ingestion of surface waters, in which 0.05 L is accidentally ingested per one-hour event (Dang, 1996). For this guidance, it was assumed that a child would swim for up to two hours in a single day.

By use of the parameters described above, the equation results in 10 µg/L of microcystin toxin.

According to World Health Organization guidance, 10 µg/L would correspond to approximately 40,000 cells/mL if *Microcystis* were the dominant species (Chorus and Bartram, 1999). *Planktothrix* was included in the additional guidance, since it has the potential to contain higher endocellular microcystin compared with *Microcystis* (Codd et al., 2005).

Advisory guidelines for algae blooms not dominated by *Microcystis* or *Planktothrix*:
At 100,000 cells/mL, the World Health Organization lists a moderate probability of adverse health effects, based in part on the ability of cyanotoxins to reach levels of concern. As the cell density increases, the potential for frequently occurring cyanobacteria to form scum may increase toxin production by 1000x in a few hours (Chorus and Bartram, 1999).

Criteria for lifting public health advisories
Both cell counts and toxin concentrations will need to be laboratory-confirmed as being below threshold values in order to lift a public health advisory. The presence of toxin is what causes illness, while the presence of toxigenic cyanobacteria represents the potential for toxin release. Because cyanobacteria can release their toxins as the bloom is declining and toxins can take some time to degrade once released, it is possible to have cell counts that are below advisory threshold and yet still have toxins present, and therefore risk to the public's health.

Several northern California studies conducted between 2005 and 2009 have demonstrated that microcystin concentrations greater than the 10 µg/L advisory threshold can be present in rivers and reservoirs where cell counts are below advisory threshold values (Kann and Corum, 2009). Other research (Manganelli et al., 2010) also suggests that cell count alone is not a good predictor of human health risk. In fact, the State of Washington's Department of Ecology uses only toxin testing data as a basis for public health advisories. The requirement of toxin and cell counts before lifting an advisory is consistent with the OPHD goal of public health protection.

Between August 21 and August 30, 2009, four dogs died of acute anatoxin poisoning shortly after drinking water from Elk Creek and the Umpqua River, near the confluence of these two streams at Elkton, Oregon. Water samples collected from the area on September 1, 2009 had no detectable toxigenic cyanobacteria. However, other samples collected from the same areas on the same day revealed detectable levels of anatoxin-A (0.5 µg/L). Microcystin was measured at an average concentration of 15 µg/L (1.5 times above the advisory threshold of 10 µg/L). There was no visible bloom or scum reported in that area of the creek when these fatalities occurred.

This case study demonstrates that lethal concentrations of cyanobacterial toxin can be present in the absence of detectable toxigenic cyanobacterial cells. This case study and other research (Kann and Corum, 2009; Manganelli et al., 2010) demonstrate the importance of measuring both toxin and cells before an advisory is lifted.

Appendix B: Toxigenic cyanobacteria and related toxin information

A variety of species of cyanobacteria are capable of producing toxins that are harmful to people, pets and wildlife (Chorus and Bartram, 1999). The most common toxigenic genera observed during cyanoHABs in Oregon are *Microcystis* and *Anabaena. Microcystis* is capable of producing microcystin (a liver toxin) and anatoxin (a nervous system toxicant). Anabaena, in addition to those produced by microcystis can also produce cylindrospermopsin (a liver toxin) and saxitoxin (a nervous system toxin). A complete listing of toxigenic cyanobacteria that are considered when issuing health advisories in Oregon is presented in Table B-1.

Note: Table B-1 is at the genus level, not the species level. Not all species of a given genus produce all of the toxins listed for that genus. Once the species involved in a specific bloom have been identified, OPHD recommends that water body mangers contact OPHD to determine exactly which toxins could be involved.

Table B-1. Toxigenic cyanobacteria (data are derived from evidence of toxin production presented in (Chorus and Bartram, 1999; Carey et al., 2007; Funari and Testai, 2008; Voloshko et al., 2008)).

	Hepatotoxins			Neurotoxins	
	Microcystin	Nodularin	Cylindro-spermopsin	Anatoxin-a	Saxitoxin
Anabaena	+		+	+	+
Anabaenopsis	+				
Aphanizomenon (Except A. flos-aquae)			+	+	+
Arthrospira	+				
Cyanobium	+				
Cylindrospermopsis			+		+
Gloeotrichia	+				
Hapalosiphon	+				
Limnothrix	+				
Lyngba					+
Microcystis	+			+	
Nodularia		+			
Nostoc	+				
Oscillatoria	+			+	
Phormidium	+			+	
Planktothrix	+			+	+
Raphidiopsis			+	+	
Schizothrix					
Synechocystis	+				
Umezakia			+		

The primary cyanotoxins of concern in Oregon are microcystin and anatoxin because they have been the toxins most frequently tested and detected. However, OPHD will also require testing for other cyanotoxins listed in Table B-1 to lift an advisory when genera reported to produce those toxins are present. Health advisories are not issued solely for algal production of

lipopolysaccharides (LPS) as these compounds are produced by most algal species and exposure to LPS compounds typically produce mild, self-limiting rashes in people.

Microcystin

Microcystins are the most commonly detected cyanotoxin across the globe. Cyanobacteria that are known to produce microcystins include *Microcystis, Planktothrix, Oscillatoria, Nostoc, Anabaena, Anabaenopsis* and *Hapalosiphon*. Microcystins are cyclic heptapeptides with about 60 known structural variants (Rinehart et al., 1994). These structural variations have significant influence on the toxicity and physio-chemical properties of the toxin. The most studied variant is microcystin-LR.

The mechanism of toxicity of microcystins is the inhibition of protein phosphatases which can cause internal hemorrhaging of the liver. While the inhibition of protein phosphatases may be generally cytotoxic, the microcystins primarily target liver cells since they enter cells through a bile acid carrier most abundant on liver cells. Exposure to microcystin has the potential to cause acute and chronic injury, depending on the dose and duration of duration of exposure. Sub-acute damage to the liver is likely to go unnoticed up to levels that are near severe acute damage (Chorus et al., 2000). Two aspects of chronic damage include progressive injury to the liver and tumor-promoting capacity. Microcystins alone have not been classified as carcinogenic. However, microcystins are considered to be tumor promoters based on studies in mice that were initiated with a known carcinogen (Falconer and Buckley, 1989).

Most of the mammalian poisonings from the ingestion of microcystin have involved livestock. Symptoms reported from cattle that were exposed to *Microcystis aeruginosa* include generalized weakness, hyperthermia, anorexia, diarrhea, pale mucous membranes, mental derangement, muscle tremors, coma and death within a few days (Short and Edwards, 1990). Symptoms reported from British military recruits exposed to a bloom of *M. aeruginosa* during an exercise in a reservoir included abdominal pain, vomiting, diarrhea, sore throat, blistering of the mouth and pneumonia (Turner et al., 1990).

OPHD used a 28-day rat study (Heinze, 1999) as the critical study for determination of a tolerable daily intake (TDI). In this study, researchers treated rats with purified microcystin LR in drinking water for 28 days and then measured several endpoints. The Heinze study identified a lowest observable adverse effect level (LOAEL) of **50 µg/kg-day**.

Provisional Acute Tolerable Daily Intake

HABS used the LOAEL identified in the Heinze study (Heinze, 1999) described above (50 µg/kg-day) to derive a provisional acute TDI of **0.05 µg/kg-day** as follows:

$$\text{ATDI} = \frac{\text{LOAEL}}{\text{UF}}$$

Where:
ATDI = Acute Tolerable Daily Intake (0.05 µg/kg-day)
LOAEL = Lowest Observable Adverse Effect Level (50 µg/kg-day)
UF = Uncertainty Factors (1,000 Total = 10 for LOAEL to NOAEL adjustment, 10 for interspecies variability * 10 for intraspecies variability).

This recommended ATDI should be considered provisional and will be updated either to conform to federal standards or when additional toxicological information becomes available.

Additional Support for this ATDI

The TDI developed by WHO (0.04 µg/kg-day) based on the Fawell, et al. study (Fawell et al., 1999a) is very similar to the provisional acute value (0.05 µg/kg-day) proposed here. OEHHA's selection (CalEPA, 2012) of the Heinze study (Heinze, 1999) also supports OPHD's decision to use the same study. A chronic (18 month) mouse toxicity study of microcystin LR in drinking water identified a NOAEL of 3 µg/kg-day (Ueno et al., 1999), very similar to the estimated 5 µg/kg-day NOAEL based on the Heinze study OPHD used to develop this provisional ATDI.

Summary

Based on the ATDI calculated above, the guideline value for microcystin in recreational water bodies is **10 µg/L**.

Anatoxin-a

Background

OPHD reviewed available literature on the toxicology of anatoxin-a (Astrachan et al., 1980; Astrachan and Archer, 1981; Fawell and James, 1994; Chorus and Bartram, 1999; Fawell et al., 1999b; Duy et al., 2000; Rogers et al., 2005; Codd et al., 2005; Falconer and Humpage, 2005; van Apeldoorn et al., 2007; Burch, 2008; Pegram et al., 2008) as well as accepted and proposed threshold values used in other governmental jurisdictions (New Zealand Ministry of Health, 2002; USEPA, 2006; Washington Department of Health, 2008). OPHD selected a study conducted by Fawell et al. (Fawell and James, 1994; Fawell et al., 1999b) as the critical study for derivation of a TDI. In this study, groups of 10 male and 10 female mice were orally treated with anatoxin-a every day for 28 days at 4 doses (0, 100, 500, and 2,500 µg/kg-day). The mice were then observed for health effects over the course of the experiment and many health-related endpoints and physiological parameters were measured (Fawell and James, 1994; Fawell et al., 1999b). Three animals died over the course of the study. One of the deaths was not related to treatment but rather resulted from animals fighting in their cages. Two of the deaths, one at 500 µg/kg-day and one at 2,500 µg/kg-day, could have been related to treatment. None of the surviving animals had any observable adverse health effects. Therefore, OPHD selected **100 µg/kg-day** as the no observable adverse effect level (NOAEL).

Provisional Tolerable Daily Intake

OPHD used the NOAEL identified in the Fawell et.al. study (Fawell and James, 1994; Fawell et al., 1999b) described above (100 µg/kg-day) to derive a provisional TDI of **0.1 µg/kg-day** as follows:

$$\mathrm{TDI} = \frac{\mathrm{NOAEL}}{\mathrm{UF}}$$

Where:

TDI = Tolerable Daily Intake (0.1 µg/kg-day)

NOAEL = No Observable Adverse Effect Level (100 µg/kg-day)

UF = Uncertainty Factors (1,000 Total = 10 for interspecies variability * 10 for intraspecies variability * 10 for limitations in the database).

OPHD applied a total uncertainty factor of 1,000. This uncertainty is a composite of 3 types of uncertainty around this TDI. First, the critical study was conducted in mice, which may have physiological differences in the way they absorb, distribute, metabolize and excrete anatoxin-a relative to humans. Mice may also be more or less sensitive to anatoxin-a toxicity than humans. Therefore, an uncertainty factor of 10 was applied to account for these potential interspecies differences in sensitivity to anatoxin-a. Second, humans could have considerable inter-individual variability in their sensitivity to anatoxin-a. For example, a child may be more sensitive than an adult or people with unidentified genetic traits may be more sensitive than the general population. Therefore, another uncertainty factor of 10 was applied to account for this intraspecies variability. Finally, OPHD applied an additional uncertainty factor of 10 due to limitations in the database. Very few applicable studies have been conducted with the intent to identify dose-response relationships to anatoxin-a administered orally. Therefore, this uncertainty factor accounts for the possibility that additional studies in the future may reveal that anatoxin-a is more toxic than has been suggested in the currently available literature.

This recommended TDI should be considered provisional because of the paucity of toxicity data. OHA will update this TDI when more toxicity information becomes available.

Additional Studies Supporting this TDI

OPHD only identified two primary studies that employed oral administration of anatoxin-a: the Fawell, et.al. study selected as the critical study (Fawell and James, 1994; Fawell et al., 1999b), and an older study conducted by Astrachan, et al. (Astrachan et al., 1980; Astrachan and Archer, 1981). Independent reviews (Duy et al., 2000; Codd et al., 2005) of this Astrachan, et al. study have derived a TDI of 0.51 µg/kg-day, a value similar within a factor of 5 to the TDI selected (0.1 µg/kg-day). California's Environmental Protection Agency (CalEPA) has proposed an oral reference dose of 0.5 µg/kg-day (CalEPA, 2012), a value similar within a factor of 5 to the TDI selected here. Other toxicity studies (Rogers et al., 2005) have been conducted using non-oral (mainly intraperitoneal injection) routes of exposure. Because human exposures to anatoxin-a in Oregon is expected to be primarily through ingestion, either in drinking water or accidental ingestion of surface water while recreating, OPHD only considered studies using the oral route of exposure.

Provisional Recreational Water Guideline Value

OPHD used the TDI of 0.1 µg/kg-day to derive a provisional recreational water guideline value of **20 µg/L**:

$$\text{Guideline Value} = \frac{\text{TDI} \times \text{BW}}{\text{IR}}$$

Where:
Guideline Value = 20 µg/L
TDI = Tolerable Daily Intake (0.1 µg/kg-day)
BW = Body weight (20 kg)
IR = Ingestion rate (0.1 L/day)

OPHD used a body weight of 20 kg to represent a child. An ingestion rate (IR) was based on guidance from the Agency for Toxic Substances and Disease Registry (ATSDR) for incidental ingestion of surface waters, in which 0.05 L is accidentally ingested per one-hour event (ATSDR,

2005). For this guidance, it was assumed that a child would swim for up to two hours in a single day.

This proposed recreational water guideline value is based on a provisional TDI. Therefore, this recreational water guideline value should also be considered provisional and subject to change should the provisional TDI be updated to accommodate new scientific information.

Additional Studies Supporting a Recreational Water Guideline Value

CalEPA has also proposed a recreational water guideline value for swimmers. This value was derived using a higher TDI (0.5 µg/kg-day), however the result (50 µg/L) (CalEPA, 2012) is similar within a factor of 2.5 to the recreational water guideline value proposed for Oregon (20 µg/L).

Summary

OPHD adopted health-based guideline values for anatoxin-A:

- Tolerable Daily Intake: 0.1 µg/kg-day
- Recreational Water Advisory Guideline Value: **20 µg/L**

As noted above, very few studies have been done to quantify the oral dose-response to anatoxin-a. Therefore, these guideline values should be viewed as provisional and subject to revisions pending further research relevant to anatoxin-a toxicity.

Saxitoxins

Background

Saxitoxins (STXs) are a family of biological toxins that are associated with paralytic shellfish poisoning (PSP). This family of toxins includes saxitoxin (STX), neosaxitoxin (neoSTX), gonyautoxins, (GTX), C-toxins (C), 11-hydroxy-STX and decarbamoylsaxitoxins (dcSTXs)(van Apeldoorn et al., 2007). Because individual STXs vary in their toxicity, the European Food Safety Authority (EFSA) has developed toxic equivalency factors (TEFs), based on toxicity in mice, so that individual toxin concentrations can be considered relative to the toxicity of STX (EFSA, 2009). The proposed TEFs are: STX = 1, NeoSTX = 1, GTX1 = 1, GTX2 = 0.4, GTX3 = 0.6, GTX4 = 0.7, GTX5 = 0.1, GTX6 = 0.1, C2 = 0.1, C4 = 0.1, dc-STX = 1, dc-NeoSTX = 0.4, dc-GTX2 = 0.2, GTX3 = 0.4, and 11-hydroxy-STX = 0.3 (EFSA, 2009). OPHD recommends adoption of these TEFs as the method for reporting STX-equivalents (STX-eq) results for public health analysis in Oregon. Most labs report total saxitoxins, which is also acceptable.

OPHD has not previously developed a health-based threshold value for STXs in Oregon's waters. Few water body managers have tested for this cyanotoxin because it has been considered an insignificant threat in Oregon. However from 2009 to 2011, 4 of 30 Washington State lakes sampled tested positive for saxitoxin (Hardy and Farrer, 2011). Given the documented presence of saxitoxin in Washington, it is important to determine whether this cyanotoxin is also present in Oregon. To this end, HABS will be asking water body managers to provide saxitoxin data when their water body contains taxa of cyanobacteria associated with saxitoxin. In anticipation of these data, HABS developed human health-based guidance values for recreational water.

Provisional Recreational Water Guideline Value

People recreating in surface water will most likely come into intense contact with STXs for a few hours or less. This type of exposure is best characterized as "acute." The EFSA has established an acute RfD for STX-eq of 0.5 µg STX-eq/kg-day (EFSA, 2009). OPHD used this acute RfD to calculate a provisional recreational water guideline value of **100 µg STX-eq/L**:

$$\text{Guideline Value} = \frac{\text{ARfD} \times \text{BW}}{\text{IR}}$$

Where:
Guideline Value = 100 µg STX-eq/L
ARfD = Acute oral reference dose (0.5 µg STX-eq/kg-day)
BW = Body weight (20 kg)
IR = Ingestion rate (0.1 L/day)

OPHD used a body weight of 20 kg to represent a child. An ingestion rate (IR) was based on guidance from the Agency for Toxic Substances and Disease Registry (ATSDR) for incidental ingestion of surface waters, in which 0.05 L is accidentally ingested per one-hour event (ATSDR, 2005). For this guidance, it was assumed that a child would swim for up to two hours in a single day.

This provisional recreational water guideline value is based on EFSA's acute RfD. This provisional value is subject to change should additional toxicological information become available in the future.

Additional Studies Supporting Recreational Water Guideline Value

The approach described here is mirrored by the Department of Health for the State of Washington, which also used EFSA's acute RfD as the basis for their recreational water guidance value of 75 µg STX-eq/L (Washington Department of Health, 2011). The difference in final values is that Oregon used 20 kg as the assumed body weight of a child while Washington used 15 kg. To be consistent with recreational values for other toxins, Oregon chose to stay with 20 kg for the likely body weight of a child who is old enough to be swimming for two hours per day.

Summary

OPHD adopted a recreational water advisory guideline value of **100 µg STX-eq/L** for saxitoxins.

As noted above, this guideline value should be viewed as provisional and subject to revisions pending further research relevant to STX toxicity.

Cylindrospermopsin

Background

OPHD has not previously developed a health-based threshold value for cylindrospermopsin in Oregon's waters. Few water body managers have tested for this cyanotoxin because it has been considered an insignificant threat in Oregon. However in 2011, a water body in Washington tested positive for cylindrospermopsin (Hardy and Farrer, 2011). Given the documented presence of cylindrospermopsin in Washington, it is important to determine whether this cyanotoxin is also present in Oregon. To this end, HABS will be asking water body managers to provide cylindrospermopsin data when their water body contains taxa of cyanobacteria

associated with cylindrospermopsin. In anticipation of these data, HABS developed human health-based guidance values for recreational water.

Provisional Recreational Water Guideline Value

To derive a recreational water guideline value OPHD applied the U.S. Environmental Protection Agency's (EPA's) proposed subchronic oral reference dose (RfD) of 0.03 micrograms cylindrospermopsin per kilogram body weight per day (µg/kg-day) (USEPA, 2006) as follows**:**

$$\text{Guideline Value} = \frac{\text{RfD} \times \text{BW}}{\text{IR}}$$

Where:
Guideline Value = 6 µg/L
RfD = Oral reference dose (0.03 µg/kg-day)
BW = Body weight (20 kg)
IR = Ingestion rate (0.1 L/day)

OPHD used a body weight of 20 kg to represent a child. An ingestion rate (IR) was based on guidance from the Agency for Toxic Substances and Disease Registry (ATSDR) for incidental ingestion of surface waters, in which 0.05 L is accidentally ingested per one-hour event (ATSDR, 2005). For this guidance, it was assumed that a child would swim for up to two hours in a single day.

This provisional recreational water guideline value is based on a proposed subchronic RfD. There is very little information in the toxicological literature about chronic or acute exposures and resultant health outcomes. Therefore, this recreational water guideline value should be considered provisional and subject to change should the EPA or other federal agency update this RfD or develop additional RfDs for acute or chronic exposure.

Additional Studies Supporting Recreational Water Guideline Value

This provisional recreational water guideline value is similar to those proposed by other governmental bodies. CalEPA proposed a recreational water guideline value of 4 µg/L (CalEPA, 2012). The Department of Health for the State of Washington has proposed a recreational water guideline value of 4.5 µg/L (Washington Department of Health, 2011). Brazil has a recreational guidance value of 15 µg/L (Burch, 2008). These values are similar to the provisional recreational water guideline value proposed for Oregon (6 µg/L).

Summary

OPHD adopted **6 µg/L** as a health-based guideline values for cylindrospermopsin in recreational water. As noted above, these guideline values should be viewed as provisional and subject to revisions pending further research relevant to cylindrospermopsin toxicity.

Acknowledgements

These threshold values and this document have been reviewed by the OPHD's cyanoHABs Science Advisory Committee. This is a volunteer committee with experts in the fields of toxicology, limnology and phycology. Members of the committee are listed here:

David Stone, Ph.D. – Oregon State University
Wayne Carmichael, Ph.D. – Professor Emeritus, Wright State University
Al Johnson, Limnologist - U.S. Forest Service
Jacob Kann, Ph.D. – Aquatic Ecosystem Sciences, LLC
Theo Dreher, Ph.D. – Oregon State University
Kurt Carpenter, Hydrologist - U.S. Geological Survey

Appendix C: Exposure pathways

The primary exposure pathway of concern for exposure to cyanotoxins is through ingestion of water. Dermal effects are possible from the lipopolysaccharides found on cell surfaces, however the cyanotoxins are not likely to cross the skin barrier and enter the bloodstream. Inhalation and aspiration of toxin is possible, especially through activities where the toxin is aerosolized, such as water skiing or splashing.

Ingestion of water can occur through both incidental and intentional ingestion pathways. Incidental ingestion is more likely in recreational waters, especially in turbid or discolored lakes. The risk of incidental ingestion is particularly high for children playing in near-shore areas where scums tend to accumulate. Exposure levels can be broadly defined as high, moderate and low based on recreational activity (Table C-1).

Table C-1. Level of recreational activity (modified from(Queensland Health, 2001))

Level of Exposure	*Recreational Activity*
High	Swimming, diving, water skiing
Moderate	Canoeing, sailing, rowing
Low to none	Fishing, pleasure cruising, picnicking, hiking

A possible scenario for human intentional ingestion of recreational water that should be considered is the use of lake water for drinking or cooking purposes by campers and hikers. It is possible that some campers or hikers have the mistaken belief that boiling, filtering or treating contaminated water with camping equipment will make it potable. This scenario should be addressed in informational and advisory signs.

Risk for exposure to cyanobacterial toxins may also occur when people draw in-home water directly from a lake or reservoir. Private treatment systems are not proven effective in removing algae toxins.

Public Drinking Water Systems

Drinking water could be another important exposure pathway for cyanotoxins. Occasionally, cyanoHABs occur in waters that serve as drinking water sources. OPHD has developed provisional acute toxicity values for cyanotoxins in drinking water (Table C-2). Drinking water containing toxins above the acute values in Table 1 could cause immediate harm to public health. Although these are not enforceable Maximum Contaminant Levels (MCLs), OPHD recommends that public water systems use them as “Do Not Drink” thresholds. For microcystin, the World Health Organization has also developed a chronic toxicity value of 1 µg/L. For more guidance specific to drinking water system operators, see http://public.health.oregon.gov/HealthyEnvironments/DrinkingWater/Operations/Treatment/Pages/algae.aspx. For more information about the derivation of these guideline values, please contact OPHD at 971-673-0400 or HAB.health@state.or.us.

Table C-2. Provisional acute drinking water toxicity values

Cyanotoxin	Anatoxin-a	Cylindrospermopsin	Microcystin	Saxitoxin
Drinking Water Guidance Value (µg/L)	3	1	1	3

Fish Consumption

At this time, there is insufficient information to determine the risk of consuming fish caught in waters with a cyanoHAB. Studies have shown that toxins mainly accumulate in the liver and viscera of fish, although microcystin has been detected in the fillet (Vasconcelos, 1999; de Magalhaes et al., 2001; Kann, 2008; Washington Department of Ecology, 2010; Kann et al., 2011). At a minimum, the organs and skin should be removed and discarded prior to cooking fillets. In addition, shellfish have been shown to accumulate cyanotoxins in edible tissue (Vasconcelos, 1999).

Risk to Animals

Animals are also sensitive to cyanotoxins. The main route of exposure occurs through ingestion when pets and wildlife drink water from a harmful algae-filled lake or pond and by licking their fur after swimming. If toxins are being produced at the time animals drink the water, the animals can become very ill and even die.

Because dogs are a sensitive companion animal and there have been confirmed dog deaths due to cyanoHABs, OPHD has developed dog-specific guideline values for cyanotoxins in recreational water (Table C-3).

Table C-3. Dog-specific guideline values for cyanotoxins in recreational waters

Cyanotoxin	Anatoxin-a	Cylindrospermopsin	Microcystin	Saxitoxin
Dog Guidance Value (µg/L)	0.6	0.2	0.2	3

OPHD does not intend to use these dog-specific guideline as the basis for public health advisories. Rather, they are offered as a resource to veterinarians and veterinary associations to use as they deem appropriate. OPHD may use these values to aid discussions with individual veterinarians or pet owners. Contact OPHD for details about the derivation of these dog-specific values.

Appendix D: References

van Apeldoorn, M.E., van Egmond, H.P., Speijers, G.J.A., and Bakker, G.J.I. (2007). Toxins of cyanobacteria. Molecular Nutrition & Food Research *51*, 7–60.

Astrachan, N.B., and Archer, B.G. (1981). Simplified monitoring of anatoxin-a by reverse-phase high performance liquid chromatography and the sub-acute effects of anatoxin-a in rats. In The Water Environment: Algal Toxins and Health, W.W. Carmichael, ed. (New York, NY: Plenum Press), pp. 437–446.

Astrachan, N.B., Archer, B.G., and Hilbelink, D.R. (1980). Evaluation of the subacute toxicity and teratogenicity of anatoxin-a. Toxicon : Official Journal of the International Society on Toxinology *18*, 684–688.

ATSDR (2005). Public Health Assessment Guidance Manual (Atlanta, GA: US Department of Health and Human Services).

Burch, M.D. (2008). Effective doses, guidelines & regulations. Advances in Experimental Medicine and Biology *619*, 831–853.

CalEPA (2012). Toxicological Summary and Suggested Action Levels to Reduce Potential Adverse Health Effects of Six Cyanotoxins (Sacramento, CA: California Environmental Protection Agency).

Carey, C.C., Haney, J.F., and Cottingham, K.L. (2007). First report of microcystin-LR in the cyanobacterium Gloeotrichia echinulata. Environmental Toxicology *22*, 337–339.

Chorus, I., and Bartram, J. (1999). Toxic cyanobacteria in water: a guide to their public health consequences, monitoring and management. WHO.

Chorus, I., Falconer, I.R., Salas, H.J., and Bartram, J. (2000). HEALTH RISKS CAUSED BY FRESHWATER CYANOBACTERIA IN RECREATIONAL WATERS. Journal of Toxicology and Environmental Health, Part B *3*, 323–347.

Codd, G.A., Morrison, L.F., and Metcalf, J.S. (2005). Cyanobacterial toxins: risk management for health protection. Toxicol Appl Pharmacol *203*, 264–272.

Dang, W. (1996). The Swimmer Exposure Assessment Model (SWIMODEL) and its use in estimating risks of chemical use in swimming pools (US Environmental Protection Agency).

Duy, T.N., Lam, P.K., Shaw, G.R., and Connell, D.W. (2000). Toxicology and risk assessment of freshwater cyanobacterial (blue-green algal) toxins in water. Reviews of Environmental Contamination and Toxicology *163*, 113–185.

EFSA (2009). Scientific Opinion: Marine biotoxins in shellfish -- Saxitoxin group. The EFSA Journal *1019*, 1–76.

Falconer, I.R., and Buckley, T.H. (1989). Tumour promotion by Microcystis sp., a blue-green alga occurring in water supplies. Medical Journal of Australia *150*, 351–352.

Falconer, I.R., and Humpage, A.R. (2005). Health risk assessment of cyanobacterial (blue-green algal) toxins in drinking water. International Journal of Environmental Research and Public Health *2*, 43–50.

Fawell, J.F., and James, H.A. (1994). Toxins from blue-green algae: Toxicological assessment of anatoxin-a and a method for its determination in reservoir water.

Fawell, J.K., Mitchell, R.E., Everett, D.J., and Hill, R.E. (1999a). The Toxicity of Cyanobacterial Toxins in the Mouse: I Microcystin-LR. Hum Exp Toxicol *18*, 162–167.

Fawell, J.K., Mitchell, R.E., Hill, R.E., and Everett, D.J. (1999b). The toxicity of cyanobacterial toxins in the mouse: II anatoxin-a. Human & Experimental Toxicology *18*, 168–173.

Funari, E., and Testai, E. (2008). Human health risk assessment related to cyanotoxins exposure. Crit Rev Toxicol *38*, 97–125.

Hardy, J., and Farrer, D. (2011). Personal communication.

Heinze, R. (1999). Toxicity of the cyanobacterial toxin microcystin-LR to rats after 28 days intake with the drinking water. Environmental Toxicology *14*, 57–60.

Kann, J. (2008). Microcystin Bioaccumulation in Klamath River Fish and Freshwater Mussel Tissue: Preliminary 2007 Results (Ashland, OR: Aquatic Ecosystem Sciences, LLC.).

Kann, J., Bowater, L., Johnson, G., and Bowman, C. (2011). Preliminary 2010 Microcystin Bioaccumulation Results for Klamath River Salmonids (Updated 4-7-2011). (Ashland, OR: Aquatic Ecosystem Sciences, LLC. Karuk Tribe Department of Natural Resources).

Kann, J., and Corum, S. (2009). Toxigenic Microcystis aeruginosa bloom dynamics and cell density/chlorophyll a relationships with microcystin toxin in the Klamath River, 2005-2008 (Karuk Tribe Department of Natural Resources).

de Magalhaes, V.F., Soares, R.M., and Azevedo, S.M.F.O. (2001). Microcystin contamination in fish from the JacarepaguaÂ Lagoon (Rio de Janeiro, Brazil): ecological implication and human health risk. Toxicon *39*, 1077–1085.

Manganelli, M., Scardala, S., Stefanelli, M., Vichi, S., Mattei, D., Bogialli, S., Ceccarelli, P., Corradetti, E., Petrucci, I., Gemma, S., et al. (2010). Health risk evaluation associated to Planktothrix rubescens: An integrated approach to design tailored monitoring programs for human exposure to cyanotoxins. Water Research *44*, 1297–1306.

New Zealand Ministry of Health (2002). Cyanobacteria Data Sheet.

Pegram, R.A., Nichols, T., Etheridge, S., Humpage, A., LeBlanc, S., Love, A., Neilan, B., Pflugmacher, S., Runnegar, M., and Thacker, R. (2008). Cyanotoxins Workgroup report. Advances in Experimental Medicine and Biology *619*, 317–381.

Pilotto, L., Hobson, P., Burch, M.D., Ranmuthugala, G., Attewell, R., and Weightman, W. (2004). Acute skin irritant effects of cyanobacteria (blue-green algae) in healthy volunteers. Australian and New Zealand Journal of Public Health *28*, 220–224.

Queensland Health (2001). Cyanobacteria in Recreational and Drinking Waters. Environmental Health Assessment Guidelines (Envirnmental Health Unit).

Rinehart, K., Namikoshi, M., and Choi, B. (1994). Structure and biosynthesis of toxins from blue-green algae (cyanobacteria). Journal of Applied Phycology *6*, 159–176.

Rogers, E.H., Hunter, E.S., Moser, V.C., Phillips, P.M., Herkovits, J., MuÃ±oz, L., Hall, L.L., and Chernoff, N. (2005). Potential developmental toxicity of anatoxin-a, a cyanobacterial toxin. Journal of Applied Toxicology : JAT *25*, 527–534.

Short, S.B., and Edwards, W.C. (1990). Blue-green algae toxicoses in Oklahoma. Veterinary and Human Toxicology *32*, 558–560.

Turner, P.C., Gammie, A.J., Hollinrake, K., and Codd, G.A. (1990). Pneumonia associated with contact with cyanobacteria. BMJ *300*, 1440–1441.

Ueno, Y., Makita, Y., Nagata, S., Tsutsumi, T., Yoshida, F., Tamura, S.-I., Sekijima, M., Tashiro, F., Harada, T., and Yoshida, T. (1999). No chronic oral toxicity of a low dose of microcystin-LR, a cyanobacterial hepatotoxin, in female BALB/c mice. Environmental Toxicology *14*, 45–55.

USEPA (2006). Toxicological Reviews of Cyanobacterial Toxins: Anatoxin-a (External Review Draft) (US Environmental Protection Agency).

Vasconcelos, V.M. (1999). Cyanobacterial toxins in Portugal: effects on aquatic animals and risk for human health. Brazilian Journal of Medical and Biological Research *32*, 249–254.

Voloshko, L.N., Plyushch, A.V., and Titova, N.N. (2008). Toxins of Cyanobacteria (Cyanophyta). International Journal on Algae *10*, 14–33.

Washington Department of Ecology (2010). Blue-Green Algae Toxins in Washington Lakes: Screening Fish Tissues for Microcystins and Anatoxin-a (Ecology).

Washington Department of Health (2008). Washington State Recreational Guidance for Microcystins (Provisional) and Anatoxin-a (Interim/Provisional) (Olympia, WA: Washington Department of Health).

Washington Department of Health (2011). Washington State Recreational Guidance for Cylindrospermopsin (Provisional) and Saxitoxin (Provisional) (Health).