Oregon Cyanobacteria Harmful Algae Bloom Surveillance (CHABS) Program

ADVISORY GUIDELINES
Cyanobacteria Blooms in Recreational Waters

Oregon Health Authority

Public Health Division
Center for Health Protection
Environmental Public Health Section

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Advisory Guidelines
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Introduction

Cyanobacteria, also known as blue-green algae, are commonly found in many fresh and saltwater 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.

Some Oregon water bodies are monitored for cyanobacteria harmful algae blooms (CyanoHABs). The number of waterbodies monitored is affected by available local, state, and federal resources and the costs associated with sampling and analysis. 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 (OHA) assumed responsibility for the decision-making process and for issuing and lifting public health advisories when CyanoHABs are detected.

The OHA is working to gain a better understanding about the occurrence of CyanoHABs in Oregon and their impact on human health. Funding for Oregon's Harmful Algae Bloom Surveillance program was through a five-year federal grant from the U.S. Centers for Disease Control and Prevention (CDC). That grant ceased in September of 2013. Currently program staff implement the highest priority activities such as the issuing and lifting of advisories with no dedicated funding.

OHA program objectives:

- Provide a single, statewide point of contact to all agencies and groups performing sampling and analysis
- Track freshwater CyanoHABs with data provided by partner agencies
- Track cases of human and animal illnesses related to CyanoHABs
- Enter environmental and health data for OHA tracking
- Build 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 cyanotoxins
- Educate and inform the public regarding health risks due to CyanoHABs

Background

The recreational use public health advisory guidelines in this document were developed and are modified based on the most current national data and references, and on monitoring data received from our waterbody partners and stakeholders.

These guidelines are used to educate the public and our partners about how and when OHA issues and lifts recreational use public health advisories. Public health advisories help to inform the public of the health risks associated with exposure to potentially toxic cyanobacteria in Oregon's recreational fresh waters.

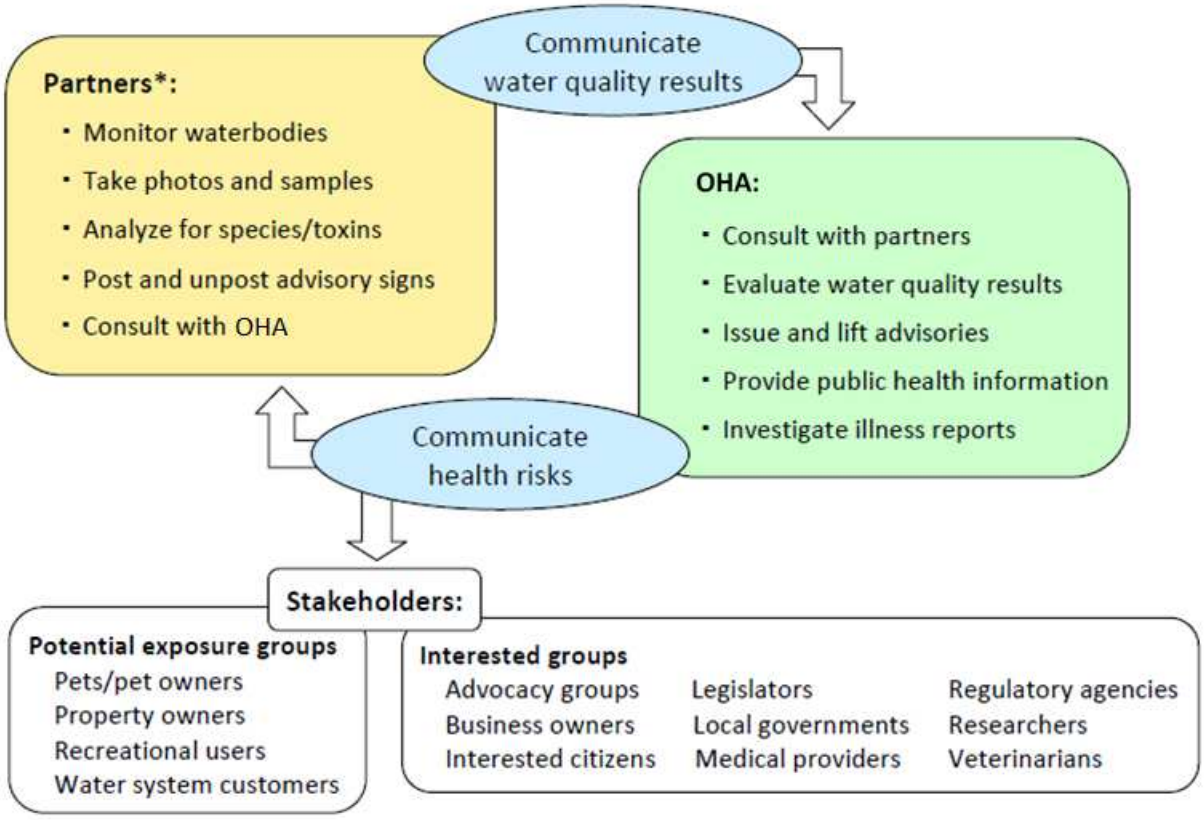
OHA authority for public health and safety fall under Title 36, Oregon Revised Statute (ORS), Chapter 431.035 to 431.530.

CyanoHAB Coordination Process

Specific actions are involved in monitoring, responding to and communicating information about CyanoHAB blooms.

Coordination among the OHA and its partners and stakeholders is paramount to complete the advisory process from identification, sampling and analysis of a bloom to notifying the public of a recreational use public health advisory. 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 role of the OHA is to issue and lift health advisories based on water quality data provided by partners and to provide risk communication.

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.

Stakeholders in the process are classified in two sub-groups:

- Exposure: Those with a greater risk of illness from cyanotoxins through recreational activities. The main routes of exposure are through ingestion and inhalation of affected water. Although cyanotoxins are not absorbed through the skin, people with sensitivities can develop a rash when coming into contact with a

CyanoHAB. More information regarding potential routes of exposure is provided in Appendix C.

- Interest: Those with varying levels of need, involvement or interest in program operations or policies, those affected by the program, or are intended users of program outcomes and findings.

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	OHA provides guidance on how to monitor for public health purposes and in identifying cyanobacteria
Collect water samples	Partners use scientifically acceptable methods to obtain water samples	OHA provides guidance on sampling techniques
Analyze samples	Partners contract with laboratories that are qualified to perform the required analyses	OHA provides a list of laboratories with appropriate analytic capabilities
Issue or lift advisories	OHA evaluates data and compares test results to established criteria to determine if an advisory should be issued or lifted	Partners respond to questions about waterbody status
Communicate advisory information	OHA informs the public through advisory news releases, GovDelivery messages, broadcast and print media, a toll-free hotline, the HABs website and educational materials	Partners and local health departments inform constituents of health advisory status through news releases and signage
Ongoing communication between the OHA and partners occurs throughout the bloom season regarding advisory decisions, bloom information, water quality data and illness reports.		

Protocol for Issuing a Recreational Use Public Health Advisory

OHA is responsible for the decision-making and communication process of issuing and lifting recreational use public health advisories.

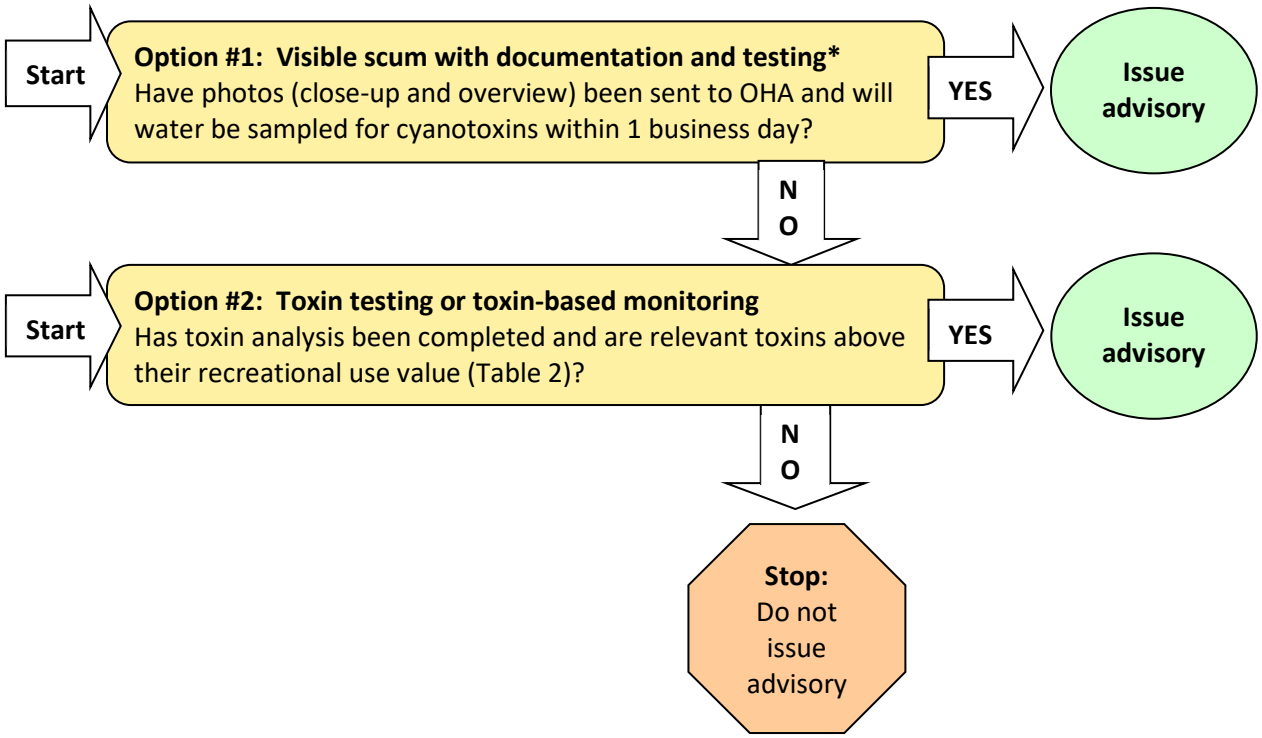
OHA criteria for issuing a public health advisory depend on the method selected by the water body manager. Options are:

- Visible scum with supporting photographs and toxin analysis within 1 business day
- Analysis showing cyanotoxin levels above OHA recreational use values (RUVs)

Scum is defined as a visible mass of cyanobacteria identified in the water body. Accumulations of greatest concern are those occurring at or near recreational access points.

The difference between Options 1 and 2 is the time between when the CyanoHAB is identified and when an advisory is issued. If Option 1 is used an advisory is issued as soon as visible scum is identified. If toxin analysis determines levels below OHA's RUVs, the advisory is lifted immediately. If levels are above, the advisory stays in place until additional toxin analysis shows levels below the RUVs. If Option 2 is used, an advisory would only be issued if cyanotoxin levels are above OHA's RUVs once data is submitted. Option 1 is used when waterbody managers are interested in a more health protective approach.

Figure 2. OHA process for issuing public health advisories for a CyanoHAB



OHA RUVs for cyanotoxins are based on information from the Environmental Protection Agency (EPA) and toxicological review of peer-reviewed scientific literature. More information about how OHA derived RUVs is provided in Appendix C. More information regarding the rationale used to help determine when advisories should be issued or lifted is provided in Appendix A.

Additional Guidance on the Toxin Based Monitoring Program: Option 2

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

Because cyanobacteria do not always produce toxins, even when blooms are large, it is anticipated that Option 2 will result in fewer and potentially more targeted public health advisories for a given water body.

OHA's cyanotoxin RUVs listed in Table 2, are the basis for determining whether an advisory is issued. The OHA Sampling Guidelines document contains detailed information on how to conduct a toxin-based monitoring program.

Table 2. Health advisory RUVs for cyanotoxins in Oregon recreational waters (µg/L)

*RUVs**	*Microcystin*	*Anatoxin-a*	*Saxitoxin*	*Cylindrospermopsin*
	8	15	8	15

*See Appendix B for the detailed rationale behind these RUVs.

OHA has also developed dog-specific RUVs. They are for informational purposes only to educate pet owners about the susceptibility of dogs to cyanotoxins and are not used as a basis for issuing public health advisories. These RUVs can be found in Appendix C.

Note: While waiting for laboratory analysis to determine if a recreational use public health advisory should be issued, local water body management may post educational and/or caution signs as a precautionary measure, to alert the public of potential health risks associated with recreating in a water body during a CyanoHAB.

OHA has educational posters on the HAB webpage to use all year round, especially on waterbodies where blooms have been identified in the past. You can find an informational poster about blooms in Oregon here:
https://www.oregon.gov/oha/PH/HEALTHYENVIRONMENTS/RECREATION/HARMFULALGAEBLOOMS/Documents/HABSinOregon_FINAL_Web.pdf
There is also a poster created specifically for dogs in English:
https://www.oregon.gov/oha/PH/HEALTHYENVIRONMENTS/RECREATION/HARMFULALGAEBLOOMS/Documents/HAB-dog-safety.pdf
and in Spanish:
https://www.oregon.gov/oha/PH/HEALTHYENVIRONMENTS/RECREATION/HARMFULALGAEBLOOMS/Documents/HAB-dog-safety-sp.pdf

Aphanizomenon flos-aquae

Aphanizomenon flos-aquae (AFA) is a species of cyanobacteria commonly found in Oregon's fresh waters. Since 2012, studies have shown that AFA can produce cyanotoxins in other parts of the world, and current toxin testing of AFA here in Oregon has determined that toxins can be produced in Oregon waters where AFA is present. Given the uncertainty relative to the amount of toxin produced by AFA, OHA no longer supports the exclusion of AFA from the list of potentially toxigenic species used to determine which toxin tests to conduct. As before, other species of the genus *Aphanizomenon*, such as *A. gracile* have been demonstrated to produce cyanotoxins. Table B-1 in appendix B has a list of cyanobacteria found in Oregon and the toxins OHA recommends be analyzed for.

Advisory protocol for very large, geographically unique waterbodies

For these waterbodies OHA will, to the extent possible based on available data, tailor recreational advisories geographically on very large and unique lakes (e.g., Lake Billy Chinook, Upper Klamath Lake, Detroit Lake, Tenmile Lake, etc.) that lend themselves to partial vs. whole lake advisories. These tailored advisories can simultaneously provide protection of public health where risk is high, while allowing recreational activities to continue in unaffected areas where exposure is low. Tailored advisories will be evaluated by OHA on a case-by-case basis working with waterbody managers and using satellite imagery tools to inform the advisories issued.

Protocol for Lifting a Public Health Advisory

Table 3 summarizes the lifting criteria for advisories issued based on the type of monitoring that led to the advisory.

Table 3. Criteria for lifting advisories

Monitoring option used to generate advisory	*Lifting criteria*
Option 1: Visible Scum	Cyanotoxin results from initial sample below RUVs
Option 2: Toxin based monitoring	Cyanotoxin results below RUVs AND either there is a commitment to continue bi-weekly sampling until bloom gone OR bloom is visibly gone
Toxin Based monitoring on waterbodies used for drinking water (and other scenarios where sampling is more frequent than bi-weekly)	When lab analysis from a second sample shows cyanotoxin results below RUVs. *Certain instances may require OHA to determine the number of consecutive samples necessary to lift (done on a case-by-case basis)*

Cyanobacteria can release their toxins during bloom formation and as the bloom is declining. Cyanotoxins, like microcystin and cylindrospermopsin can take some time to degrade even after a bloom has dispersed. It is possible therefore, for visual observations to indicate that a bloom has disappeared and still have toxins present. To reduce the risk of exposure to the public from lingering toxins, in all cases, toxin analysis must be completed to lift an advisory.

If an advisory is issued based on Option 1 (visible scum) and initial sample results verify that toxins are below RUVs, OHA will immediately lift the advisory. In this case OHA advises continued visual assessment of the bloom and resampling if a change in bloom condition or size is observed.

If an advisory is issued based on Option 2 (toxin results above RUVs) and testing is bi-weekly or less frequent, OHA will lift the advisory as soon as regular toxin testing indicates that total (intracellular and extracellular) toxin levels are below RUVs as long as there is a commitment to continue bi-weekly monitoring. In this case, even though the advisory has been lifted, OHA advises continued toxin-based monitoring every other week until the bloom is gone to ensure toxin levels remain below RUVs. If continued sampling shows an increase in toxins above RUVs, a second advisory would be issued. If sampling shows toxin levels are below RUVs and the bloom has visually dispersed, OHA will lift the advisory immediately.

We recommend contacting your lab for the most current cost of analyses and for preservation and shipping instructions for your sample. Be sure to choose a laboratory that can analyze for cyanotoxins produced by the cyanobacteria present (see Appendix B, Table B-1).

Lifting Protocol for Frequently Sampled Waterbodies

Permanent drinking water rules for cyanotoxin sampling and analysis will provide OHA with raw water analyses on a biweekly or more frequent basis throughout the season for susceptible water bodies used as drinking water sources. Concurrently, data from other waterbodies such as Upper Klamath Lake are submitted on a more frequent than normal basis as part of a monitoring partnership among tribes and local, state, and federal agencies.

Frequent sampling and analysis have confirmed the high variability of toxin levels during the life of a bloom. This variability can lead to the increased issuing and lifting of recreational advisories we call bouncing advisories. Bouncing advisories are resource intensive and can cause advisory fatigue. For these reasons, OHA has changed the recreational use advisory protocol for lifting advisories on frequently sampled waterbodies which will reduce the recurrence of advisories throughout the season.

When frequent sampling and analysis occur, OHA will determine on a case-by-case basis the number of consecutive samples necessary to lift a recreational use advisory. In most cases, an advisory will be lifted when lab analysis from a second sample shows that the cyanotoxins present continue to be below OHA RUVs.

Laboratories

Commercial laboratories use a variety of comparable methods currently available to analyze for cyanotoxins. When requesting toxin testing, ensure the lab uses a method detection level less than the RUVs in Table 2. Note: OHA will not accept field-ready test kits (dipsticks, etc.) for cyanotoxins as a basis for lifting an advisory. However, these kits may be useful for monitoring the progress of a bloom throughout the season.

Analysis can be costly depending on the method and equipment used. Lab staff can provide you with the most current cost of toxin analyses prior to submitting a sample. In general, the ELISA method is least expensive for determining levels of cyanotoxin in the bloom. ELISA methods are not currently available for anatoxin-a. However, Abraxis has introduced a micro-titer plate format (96T) receptor-binding assay (RBA) kit for anatoxin-a. The kit provides two protocols. The EZ protocol requires no sample preparation and has a range of 5 - 500 ppb. If a lower limit of detection is required, the enhanced sensitivity (ES) SPE sample concentration may be performed. This kit provides a real-time, economical, accurate and sensitive alternative for research and monitoring programs.

Note: All cyanobacteria produce lipopolysaccharides that can cause skin irritation, so there is no need to test for them.

Public Notification Methods

OHA uses several concurrent notification methods in the issuing and lifting of public health advisories. The specific methods are as follows:

Email: An email alert is sent to the following:

- Health department administrators and officials
- Tribal leaders and tribal health directors

News Releases: OHA 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.

GovDelivery listserv messages: A GovDelivery message is sent to notify members about a health advisory issue or lift immediately after the advisory news release is issued. List serv recipients can also choose to receive a text message as part of this notification process. Currently this listserv has nearly 6,000 members. OHA recommends subscribing to GovDelivery to receive real-time information about HAB advisories issued and lifted across the state. Subscribe to email alerts.

Program Website: The program maintains a website where advisory information is immediately posted, providing access to up-to-date information on the issuing and lifting of HAB advisories in Oregon. The public and others can also access resources for water samplers, prevention tips, frequently asked questions, and general information about CyanoHABs. 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 individuals who are traveling, or those without Internet access.

Program Contact Information

Email: habhealth@state.or.us
Phone: (971) 673-0440, Toll Free: (877) 290-6767 and press 4
Website: ***www.healthoregon.org/hab***

Appendix A: Rationale used to determine when advisories should be issued and lifted for CyanoHABs

The use of cell count data to issue and lift recreational advisories has been a concern for many. Specifically, there is no standard method for performing cell counts that provides assurance that cells are counted consistently across laboratories. Current research with concurrence from the Environmental Protection Agency (EPA) points out that there is uncertainty about the relationship between cell counts and the level of toxins produced. Other research (Manganelli et al., 2010) 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 cyanotoxin testing data as a basis for public health advisories.

Between August 21 and August 30, 2009, four dogs died of acute anatoxin-a 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 at the time of 10 μg/L). There was no visible bloom or scum reported in that area of the creek when these fatalities occurred. This case demonstrates that lethal concentrations of cyanotoxins can be present in the absence of detectable toxigenic cyanobacterial cells. Due to the uncertainty associated with cell densities, level of toxin production and exposure to people and pets, OHA has removed cell count data from the advisory issuing and lifting protocol.

Appendix B: Toxigenic cyanobacteria and related cyanotoxin information

A variety of genera 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 *Dolichospermum.*

Microcystis can produce microcystin (liver toxin) and anatoxin-a (neurotoxin). *Dolichospermum*, in addition to producing microcystin and anatoxin-a, can also produce cylindrospermopsin (liver toxin) and saxitoxin (neurotoxin). A complete listing of toxigenic cyanobacteria considered when issuing health advisories in Oregon is presented in Table B-1 on page 9.

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

	Hepatotoxin (liver toxins)			*Neurotoxins*	
	Microcystin	Nodularin	Cylindro-spermopsin	Anatoxin-a	Saxitoxin
Anabaenopsis	+				
Aphanizomenon	+		+	+	+
Arthrospira	+				
Cyanobium	+				
Cylindrospermopsis			+		+
Dolichospermum	+		+	+	+
Gloeotrichia	+				
Hapalosiphon	+				
Limnothrix	+				
Lyngba					+
Microcystis	+			+	
Nodularia		+			
Nostoc	+				
Oscillatoria	+			+	
Phormidium	+			+	
Planktothrix	+			+	+
Raphidiopsis			+	+	
Schizothrix					
Synechocystis	+				
Umezakia			+		
Woronichinia	+			+	

Note: Table B-1 is at the genus level. Not all species of a given genus produce all the toxins listed for that genus. Once the species involved in a specific bloom have been identified, OHA recommends that water body mangers contact OHA to determine exactly which toxins could be involved. Taxonomy for many types of cyanobacteria is currently being revised. This guidance reflects taxonomy as of 1/2017.

The primary cyanotoxins of concern in Oregon are microcystin, anatoxin and cylindrospermopsin because they have been the toxins most frequently tested and detected. However, small amounts

of saxitoxin have also been detected in Oregon. OHA recommends testing for the cyanotoxins listed in Table B-1 to issue and lift advisories when genera that 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 sensitive people.

Microcystin

Background

Microcystins are the most commonly detected cyanotoxin in the world. Cyanobacteria known to produce Microcystins include *Microcystis, Planktothrix, Oscillatoria, Nostoc, Dolichospermum, Anabaenopsis* and *Hapalosiphon*. Microcystins are cyclic heptapeptides with about 60 known structural variants (Rinehart et al., 1994). These 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 dose and 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 (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 included abdominal pain, vomiting, diarrhea, sore throat, blistering of the mouth and pneumonia (Turner et al., 1990).

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

Provisional Tolerable Daily Intake

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

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

Where:

TDI = 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 individual variability)

This TDI is intended for use with acute or short-term exposure scenarios and may not be protective for chronic or long-term exposures. This recommended TDI should be considered provisional and will be updated to conform to federal guidelines or standards when they are issued, or whenever additional toxicological information becomes available.

Additional support for this TDI: The EPA has used this same TDI as their reference dose (RfD) for microcystins based on currently available research.

Provisional Recreational Use Value

OHA used the TDI of 0.05 µg/kg-day to derive a provisional **recreational use value of 8 µg/L for microcystin**:

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

Where:

TDI = Tolerable Daily Intake (0.05 µg/kg-day)
BW = Mean body weight of children 6 to < 11 years (31.8 kg) (U.S. EPA 2011)
IR = Recreational water incidental ingestion rate for children (0.21 L/d) at approximately the 90th percentile (U.S. EPA 2011; U.S. EPA 1997)

The TDI was developed by OHA based on oral administration of microcystin-LR via drinking water in rats and effects on the liver (Heinze, 1999).

The mean body weight (BW) of 31.8 kg was used to represent a child between the age of 6 and 11 years. An incidental ingestion rate (IR) was based on EPA guidance for incidental ingestion of recreational water for children at the 90th percentile.

The RUV for microcystin was the result of new research on exposure factors provided by the Environmental Protection Agency (EPA), specifically affecting body weight and ingestion rate factors.

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

Summary

OHA adopted a health-based RUV for microcystin:

- Tolerable Daily Intake: 0.05 µg/kg-day
- **Recreational Use Value: 8 µg/L**

The primary limitation in the database relates to chronic toxicity. Because OHA only intends to apply these RUVs in acute or short-term exposure scenarios, there is no extrapolation from acute

to chronic toxicity. Therefore, OHA considered the uncertainty factor for database limitations to be unnecessary.

Anatoxin-a

Background

OHA 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).

OHA 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 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 during 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, OHA selected 100 µg/kg-day as the no observable adverse effect level (NOAEL).

Provisional Tolerable Daily Intake

OHA 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 Individual variability * 10 for limitations in the database)

This TDI is intended only for use in acute or short-term exposure scenarios because the toxicity study upon which this TDI is based was short-term. Because most exposures in Oregon are acute or short-term, an acute or short-term TDI is the most useful.

OHA applied a total uncertainty factor of 1,000. This number is a composite of 3 types of uncertainty about 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 individual variability in their sensitivity to anatoxin-a. For example, a child may be more sensitive than an adult or people with certain genetic traits may be more sensitive than the general population. Therefore, another uncertainty factor of 10 was applied to account for this individual variability. Finally, OHA applied an additional uncertainty factor of 10 due to limitations in the database. Very few applicable studies have been conducted 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: OHA 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, OHA only considered studies using the oral route of exposure.

Provisional Recreational Use Value

OHA used the TDI of 0.1 µg/kg-day to derive a provisional **recreational use value of 15 µg/L for anatoxin-a:**

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

Where:

TDI = Tolerable Daily Intake (0.1 µg/kg-day)
BW = Mean body weight of children 6 to < 11 years (31.8 kg) (U.S. EPA 2011)
IR = Recreational water incidental ingestion rate for children (0.21 L/d) at approximately the 90th percentile (U.S. EPA 2011; U.S. EPA 1997)

The RUV for anatoxin-a was the result of new research on exposure factors provided by the Environmental Protection Agency (EPA) for microcystin and cylindrospermopsin, specifically affecting body weight and ingestion rate factors. These same factors were used to calculate the RUV for anatoxin-a.

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

Summary

OHA adopted health-based RUVs for anatoxin-a:

- Tolerable Daily Intake: 0.1 µg/kg-day
- **Recreational Use Value: 15 µg/L**

As noted above, very few studies have been done to quantify the oral dose-response to anatoxin-a. Therefore, these RUVs 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 associated with paralytic shellfish poisoning (PSP). This family 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) developed toxic equivalency factors (TEFs), based on toxicity in mice, so 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).

OHA adopted 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. Previously few waterbody managers tested for this cyanotoxin because it was considered an insignificant threat in the Northwest. 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 was important to determine whether this cyanotoxin was also present in Oregon. Since development of RUVs for saxitoxins in recreational waters by OHA, this toxin has been detected in Oregon waters. OHA asks water body managers to provide saxitoxin data when a waterbody contains taxa of cyanobacteria associated with this toxin.

EFSA established an acute RfD for STX-eq of 0.5 µg STX-eq/kg-day (EFSA, 2009). This acute RfD is based on available intoxication reports in humans across the European population. This acute RfD represents an estimated NOAEL.

Provisional Tolerable Daily Intake

OHA used the RfD/NOAEL described above (0.5 µg/kg-day) to derive a provisional TDI of 0.05 µg/kg-day as follows:

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

Where:

TDI = Tolerable Daily Intake (0.05 µg/kg-day)
NOAEL = No Observable Adverse Effect Level (0.5 µg/kg-day)

UF = Uncertainty Factors (10 for limitations in the database).

This TDI is based on an acute toxicity study, so it is only applicable to acute or short-term exposure scenarios. OHA applied a total uncertainty factor of 10 for database limitations[1]. This is the only study of its kind for saxitoxin and additional studies may find a lower RfD.

For humans, no uncertainty factor for interspecies variability was needed since the data were from human illnesses. OHA also did not apply an uncertainty factor for individual variability since the EFSA study covered the general population which included sensitive individuals.

Provisional Recreational Use Value

OHA used the TDI of 0.05 µg/kg-day to derive a provisional **recreational use value of 8 µg/L for SXT-eq:**

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

Where:

TDI= Acute oral reference dose (0.05 µg STX-eq/kg-day)
BW = Mean body weight of children 6 to < 11 years (31.8 kg) (U.S. EPA 2011)
IR = Recreational water incidental ingestion rate for children (0.21 L/d) at approximately the 90th percentile (U.S. EPA 2011; U.S. EPA 1997)

The RUV for saxitoxin was the result of new research on exposure factors provided by the Environmental Protection Agency (EPA) for microcystin and cylindrospermopsin, specifically affecting body weight and ingestion rate factors. These same factors were used to calculate the RUV for saxitoxin.

OHA applies this SXT-eq RUV to total saxitoxin results. This provisional RUV is based on EFSA's acute RfD. This value is subject to change should additional toxicological information become available in the future.

Summary

OHA adopted a RUV of 8 µg STX-eq/L for saxitoxins. As noted above, this value should be viewed as provisional and subject to revisions pending further research relevant to STX toxicity.

Cylindrospermopsin

Background

Previously, few waterbody managers tested for this cyanotoxin because it had been considered an insignificant threat in the Northwest. However, in 2011, a water body in Washington tested positive for cylindrospermopsin (Hardy and Farrer, 2011). Since 2011, cylindrospermopsin has

[1]OHA did not originally apply the uncertainty factor for database limitations to the TDI for saxitoxins. Application of this uncertainty factor dropped OHA's previous TDI and all RUVs based on that TDI (recreational water RUVs and drinking water GVs) by a factor of 10. OHA applied the database limitation uncertainty factor in this revision in keeping with the Ohio EPA, which first applied this uncertainty factor in 2014.

been detected in Oregon above the RUV established by OHA. Given the documented presence of cylindrospermopsin in Washington and Oregon, OHA asks waterbody managers to provide cylindrospermopsin data when a waterbody contains taxa of cyanobacteria associated with this toxin.

Tolerable Daily Intake

To develop a TDI for cylindrospermopsin, OHA used the same study by Humpage et. al., 2003 that the EPA selected as the critical study in development of their 10-day Health Advisory for cylindrospermopsin. This 11-week study used male Swiss albino mice in which groups of mice were dosed with 0, 30, 60, 120, or 240 µg/kg-day (10 mice per dose group) of purified cylindrospermopsin by daily gavage. Authors monitored food and water consumption and body weights throughout the study. At nine weeks, authors conducted clinical exams with a focus on physiological and behavioral signs of toxicity. Near the end of the study an extensive panel of parameters was measured in serum and urine along with hematological endpoints. No deaths were reported in the study. Upon necropsy, organs were weighed, and all tissues were examined histologically. The most sensitive endpoint observed was kidney weight, which increased in a dose-dependent manner starting at 60 µg/kg-day. The EPA selected 60 µg/kg-day from this study as the LOAEL and 30 µg/kg-day as the NOAEL [23].

Consistent with EPA's Health Advisory methodology, OHA applied a total uncertainty factor of 300 to the NOAEL of 30 µg/kg-day. The total UF of 300 was a composite of an UF of 10 for interspecies variability, 10 for individual variability, and 3[2] for database limitations. OHA used the NOAEL of 30 µg/kg-day to derive a provisional TDI of 0.1 µg/kg-day as follows:

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

Where:

TDI = Tolerable Daily Intake (0.1 µg/kg-day)
NOAEL = No Observable Adverse Effect Level (30 µg/kg-day)
UF = Uncertainty Factors (300).

The EPA has also adopted this same TDI as their reference dose (RfD) for Cylindrospermopsin.

Provisional Recreational Use Value

To derive a recreational use value, OHA applied exposure factors to the TDI derived above (0.1 µg/kg-day) as follows:

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

Where:

TDI = Oral reference dose (0.1 µg/kg-day)
BW = Mean body weight of children 6 to < 11 years (31.8 kg) (U.S. EPA 2011)

[2] The previous assessment of cylindrospermopsin included a database limitation factor of 10. An uncertainty factor of 3 was used in the current 10-day Health Advisory issued by the EPA's Office of Water on June 17, 2015. To be consistent with EPA guidance, OHA adopted this uncertainty factor which resulted in an increase in the TDI from the previous value by an approximate factor of 3.

IR = Recreational water incidental ingestion rate for children (0.21 L/d) at approximately the 90th percentile (U.S. EPA 2011; U.S. EPA 1997)

The mean body weight (BW) of 31.8 kg was used to represent a child between the age of 6 and 11 years. An incidental ingestion rate (IR) was based on EPA guidance for incidental ingestion of recreational water for children at the 90th percentile.

The RUV for cylindrospermopsin was the result of new research on exposure factors provided by the Environmental Protection Agency (EPA), specifically affecting body weight and ingestion rate factors.

Summary

OHA adopted a RUV of 15 µg/L for cylindrospermopsin based on EPA criteria. As noted above, this value should be viewed as provisional and subject to revisions pending further research relevant to cylindrospermopsin toxicity.

Appendix C: Exposure pathways

The primary pathway for exposure to cyanotoxins is ingestion of water. Dermal effects are possible from the lipopolysaccharides found on cell surfaces, however, 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. The risk of incidental ingestion is particularly high for children playing in near-shore areas where scum tends 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

Two possible scenarios for human intentional ingestion of recreational water should be considered. One is lake water used for drinking or cooking purposes by campers and hikers. Boiling, or use of camping style equipment for filtering or treating affected water will not make it potable, and in fact, can make the toxins more concentrated. The second risk for exposure occurs when people draw in-home water directly from a lake or river. Many private treatment systems have not been proven effective in removing cyanotoxins. This exposure information is addressed in all advisory news releases, educational materials and signs.

Note: There is currently one manufacturer of in-home filtering equipment that certifies the reduction or elimination of microcystin in affected water. More information about this filtration system can be found through NSF Contaminant Reduction Claims Guide.

Table C-2. Acute or short-term drinking water cyanotoxin toxicity values (µg/L)

Drinking Water Guidance Value:	*Microcystin*	*Cylindrospermopsin*	*Saxitoxin*	*Anatoxin-a*
Adults	1.6	3	1.6*	3
Ages 5 years and younger	0.3	0.7	0.3	0.7

http://www.nsf.org/consumer-resources/water-quality/water-filters-testing-treatment/contaminant-reduction-claims-guide.

Public Drinking Water Systems

Drinking water is another exposure pathway of concern for cyanotoxins. Occasionally, CyanoHABs occur in recreational waters used as drinking water sources. OHA's Drinking Water Program has adopted the acute toxicity values for cyanotoxins in drinking water established by the EPA (Table C-2). Drinking water containing cyanotoxins above the acute values in Table C-2 could cause immediate harm to public health. Although these are not enforceable Maximum Contaminant Levels (MCLs), OHA recommends that public water systems use them as "Do Not Drink" thresholds.

For information regarding these guideline values, contact OHA at 971-673-0440 or HAB.health@state .or.us. For more guidance specific to drinking water system operators, visit: http://public.health.oregon.gov/HealthyEnvironments/DrinkingWater/Operations/Treatment/Pages/algae.aspx.

Note: Rounding conventions are consistent with EPA's 10-day Health Advisories

*OHA's previous drinking water guidance value for saxitoxin was 3 µg/L and was based on guidance used in other countries and not a TDI. This new drinking water value is based on the TDI established in Appendix B.

Table C-3 lists the exposure factors used to calculate drinking water Guideline Values (GVs) using the TDIs established in Appendix B. The equation used to calculate drinking water GVs is identical to the equation used to calculate RUVs in Appendix B.

Table C-3. Exposure factors used to calculate drinking water GVs

Parameter	Adults	Children 5 and younger
Body Weight	80 kilograms	---
Intake Rate	2.5 liters	---
Body Weight-Normalized Intake Rate	---	0.15 liters/kilogram-body weight per day

Note: OHA adopted EPA's exposure factors used in their derivation of 10-day Health Advisories for microcystin and cylindrospermopsin and applied them to the TDIs OHA derived for anatoxin-a and saxitoxins as well. Although drinking water treatment facilities are only required to sample for

microcystin and cylindrospermopsin, the levels for saxitoxin and anatoxin-a can be used for informational purposes.

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, and small amounts of 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, organs and skin should be removed and discarded, and fillets rinsed with clean water prior to cooking or freezing fillets. Caution should be taken with shellfish as cyanotoxins have been shown to accumulate in edible tissue (Vasconcelos, 1999).

Risk to Animals

Animals are extremely sensitive to cyanotoxins when present and can become very ill or potentially die due to exposure at very low levels. The primary route of exposure to these toxins is through ingestion. Ingestion occurs when pets and wildlife drink water from a cyanobacteria-filled lake or pond, lick their fur after swimming, or eat dried cells that accumulate along the shoreline.

Because dogs are cyanotoxin sensitive animals and dog deaths have been confirmed due to CyanoHABs, OHA developed dog-specific RUVs for cyanotoxins in recreational water (Table C-4).

Table C-4. Dog-specific RUVs for cyanotoxins (µg/L)

Dog RUV:	*Anatoxin-a*	*Cylindrospermopsin*	*Microcystin*	*Saxitoxin*
	0.4	0.4	0.2	0.02

Note: All dog-specific RUVs have been changed in this revision because California EPA's estimate of the amount of water an exercising dog consumes per kilogram body weight was updated in 2012 (from 0.168 to 0.255 L/kg-day). Current dog-specific RUVs are now consistent with the California EPA update. The dog-specific value for saxitoxins was further modified by application of an uncertainty factor to the dog-specific TDI for interspecies differences in sensitivity between humans (the species in the critical study) and dogs.

OHA does not use these dog-specific RUVs as the basis for public health advisories. Rather, they are offered as a resource to veterinarians and veterinary associations to use as appropriate, when treating dogs believed to have been exposed to cyanotoxins. OHA will use these values and potential exposure scenarios in discussions with individual veterinarians or pet owners, to educate them on the vulnerability of pets to cyanotoxin exposure. Contact OHA for details about the origin of these dog-specific values.

Note: Pet owners should be aware that the RUVs for dogs is below the GVs for drinking water affected by cyanotoxins. Because of this, OHA recommends owners supply their pets with bottled water or water from alternative sources when a drinking water advisory is in place.

Appendix D: References

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