Public Health Advisory Guidance for Toxigenic Cyanobacteria in Recreational Waters

Currently, several water bodies in Oregon are monitored for toxigenic cyanobacteria. In past years, the decision-making process for issuing and lifting advisories varied with the managing jurisdiction of that water body. The intent of this document is to provide statewide public health guidelines for issuing and lifting advisories in recreational waters when toxigenic cyanobacteria are detected. While it is hoped these recommendations are applied consistently across Oregon, site-specific issues and flexibility in the decision-making process is emphasized. These guidelines are intended for recreational exposures only and not for water bodies that serve as drinking water sources. In addition, these guidelines are recommendations based on the best available information and subject to change if needed or as more information becomes available.

Toxigenic Cyanobacteria

Cyanobacteria, also known as blue-green algae, are commonly found in many freshwater systems across the world. The species of concern for these guidelines are referred to as toxigenic species, since they have the potential to produce toxins. The primary target organs for cyanotoxins are the liver and nervous system, although other health effects are possible.

Currently, at least 46 species of cyanobacteria have been shown to be toxic to vertebrates (Chorus & Bartrum, 1999). Some of the more common toxigenic genera include include *Microcystis*, *Anabaena*, *Aphanizomenon*, *Lyngbya*, *Nodularia, Planktothrix*, *Nostoc* and *Cylindrospermopsis.* The cyanotoxins that have been detected in non-marine waters of Oregon include microcystin, anatoxin-a and cylindrospermopsin. While cyanobacteria can produce other toxins, the focus of this section will be on microcystin and anatoxin-a, the most commonly detected cyanotoxins in Oregon lakes. It should be noted that cyanobacteria likely produce toxins that have not been characterized. A recent example is the discovery of a neurotoxic amino acid that can be produced by the majority of cyanobacteria (Cox et al., 2005).

Microcystin

Microcystins are the most commonly detected cyanotoxin across the globe (Chorus and Bartrum, 1999). 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 use a carrier similar to the bile acid carrier of 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).

A Tolerable Daily Intake (TDI) was calculated for microcystin-LR, since this variant has sufficient information to derive a guideline value and is thought to be one of the most toxic variants. A TDI is a level of exposure below which it is thought that no adverse health effects will occur. It is important to note that simply exceeding a TDI does not imply that a health effect is likely. Rather, the duration of exposure and concentration of toxin will be major determinants of toxicity. The basis for the TDI was a 13-week mouse study with observed liver changes (Fawell et al., 1994). The no observed adverse effect level (NOAEL), which was the basis for determining a guidance value, was 40µg microcystin per kg body weight per day. To calculate a TDI, the NOAEL was divided by a series of uncertainty factors to include potential for intraspecies variation (factor of 10), interspecies variation (factor of 10) and for a less-than-lifetime study (factor of 10). The equation is:

$$\text{TDI} = \frac{40\ \mu g/kg \bullet day^{-1}}{1000} = 0.04\ \mu g \text{ microcystin-LR per kg body weight per day}$$

The TDI is instrumental in determining guidance for taxa that are known to produce microcystins at high intracellular concentrations, such as *Microcystis* or *Planktothrix.* This process is described in Appendix A.

Anatoxin-a

Anatoxin-a is an alkaloid neurotoxin that is produced by some strains of *Anabaena*, *Aphanizomenon* and *Oscillatoria* (Chorus & Bartrum 1999). Anatoxin-a mimics the neurotransmitter acetylcholine, binds to nicotinic acetylcholine receptors and cannot be

degraded by the enzyme acetylcholinesterase. The molecular activity of anatoxin-a leads to over stimulation of muscle cells and possibly paralysis followed by asphyxiation (Carmichael 1997). In addition to anatoxin-a, anatoxin-a(s) and homoanatoxin have been identified from cyanobacteria and vary in their toxicity and mode of action.

The acute toxic properties of anatoxin-a are obvious, since it affects the nervous system. Available data indicate that it is unlikely to cause chronic toxicity from limited exposure (Fawell & James 1994). At this time, the database is insufficient for a derivation of a TDI as human exposure information and suitable animal tests are lacking.

Exposures 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 1).

Table 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 the 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.

At this time, there is insufficient information to determine the risk of consuming fish caught in waters with toxigenic cyanobacteria. 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 Magalhães et al., 2001). 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). It is recommended that people call the Department of Human Services for more information on fish consumption while advisories are in effect.

Issuing Advisories

In 2004 and previous years, lakes were posted when toxigenic cell densities exceeded 15,000 cells/mL (corresponding to an Alert Level III using World Health Organization recommendations). The guidance below recommends that agencies not use 15,000 cells/mL as an absolute criterion for posting advisories at recreational access points. The risk to recreational users at this cell density is considered low and includes symptoms such as skin irritation and gastrointestinal disorders, which are though to be related to lipopolysaccharide endotoxins found on cell walls. In a recent study, 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 (Pilotto, 2004). 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 systemic effects.

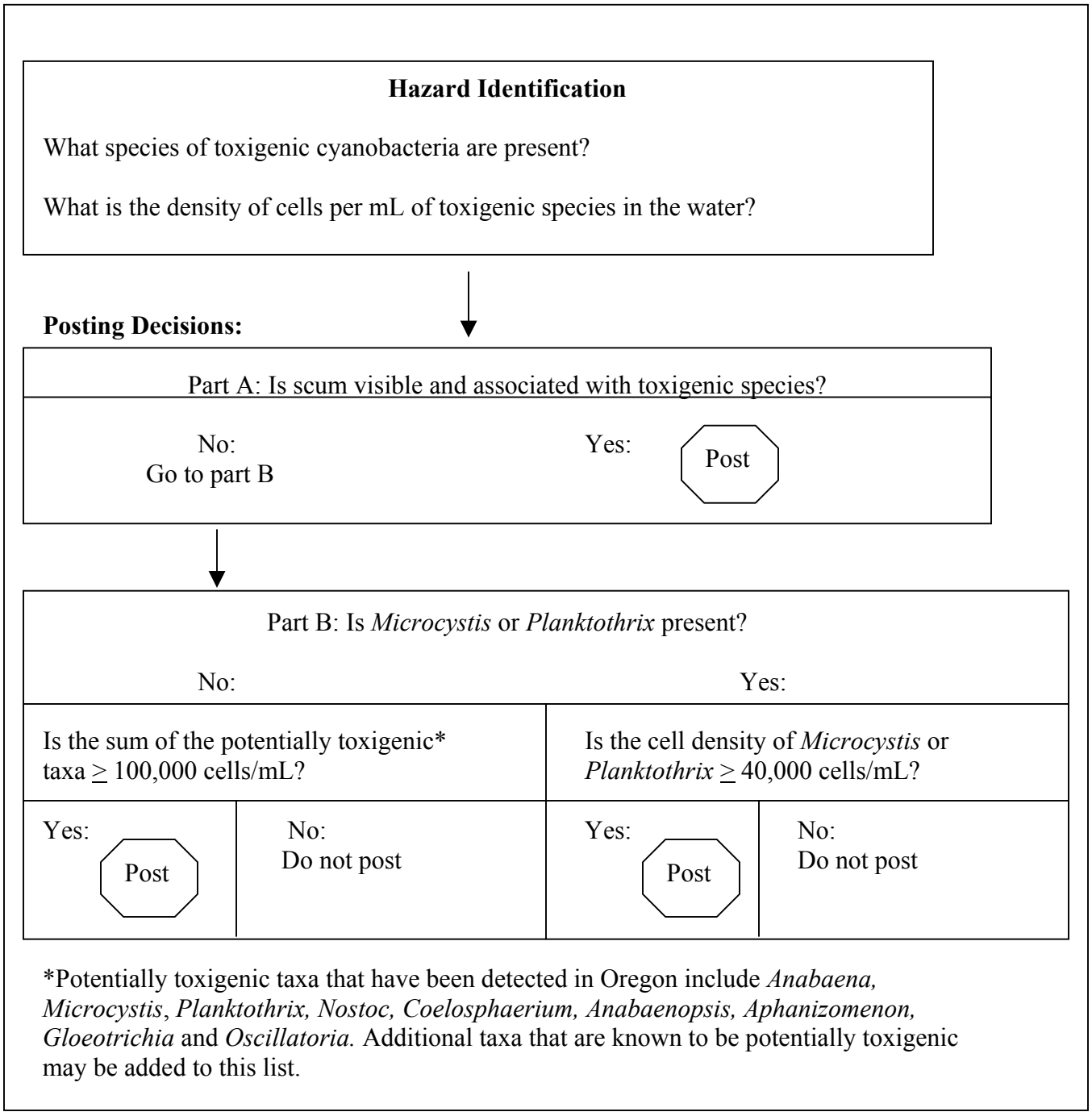
Despite the lack of quantitative guidance to address the potential for mild reactions to cyanobacteria, such as skin irritation, DHS recommends that posters and pamphlets be available to advise the public about these possibilities. Information should be posted and visible at kiosks, bulletin boards and other suitable locations that describe these effects and symptoms. Additional suggested information for these postings or pamphlets include:

- advice that if symptoms persist or become more severe over time, to contact their medical provider
- notice that not all waters can be monitored all the time and scummy, turbid or discolored waters should be avoided
- notice that algae cells trapped beneath clothing may be more likely to cause skin reactions and washing with clean water is recommended
- warning that people with nasal-bronchial allergies may be more susceptible to skin irritation from cyanobacteria
- warning that children, immunocompromised individuals and the elderly are more susceptible to gastrointestinal disturbances

Figure 1 depicts a flowchart of guidelines to assist in deciding whether to post or not post a waterbody. The issuance of advisories is based solely on cell density determinations and not dependent upon the analysis of toxins. However, the analysis of toxin data is recommended to better understand the systems being monitored, the potential health implications and to document historical trends for future advisories.

If *Microcystis* or *Planktothrix* is not the dominant species in a sample, DHS recommends advisories be posted if cell densities of total toxigenic cyanobacteria equal or exceed 100,000 cells/mL, or if scums containing toxigenic cyanobacteria are observed. At 100,000 cells/mL, the World Health Organization lists a moderate probability of adverse

Figure 1. Proposed Guidance for Recreational Contact with Cyanobacteria



*Potentially toxigenic taxa that have been detected in Oregon include *Anabaena, Microcystis*, *Planktothrix, Nostoc, Coelosphaerium, Anabaenopsis, Aphanizomenon, Gloeotrichia* and *Oscillatoria.* Additional taxa that are known to be potentially toxigenic may be added to this list.

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 scums may increase toxin production by 1000x in a few hours (Chorus and Bartrum,

1999). Toxigenic genera that are common scum producers include *Microcystis, Anabaena, Anabaenopsis, Planktothrix and Aphanizomenon* (Codd et al., 2005).

A lower guideline of 40,000 cells/mL was recommended for issuing advisories based on cell densities that are dominated by *Microcystis* and *Planktothrix*. This lower guideline is based on the premise that these two genera are more likely to produce microcystin toxin compared to other genera, such as *Anabaena* (Codd et al., 2005; Chorus and Bartrum, 1999) and the observation that almost all *Microcystis* strains are toxic (Carmichael, 1995). To derive the guideline of 40,000 cells/ml, a risk assessment approach was employed based on recreational exposure to microcystin toxin to a child (Appendix A).

Currently, no TDI or reference dose has been established for anatoxin-a, prohibiting the quantitative approach that was used for microcystin. Detection of anatoxin-a or any other cyanotoxin in recreational waters should be handled on a case-by-case basis, involving expert consultation for public health and lake access decisions.

Lifting advisories

Cyanotoxins, if produced, are found within the cell during most of a bloom event. However, toxin may be released into the water when the cells die and lyse. The released toxin will dilute and eventually degrade over time. However, the risk of exposure to dissolved toxin immediately following the peak of a bloom must be addressed since cyanotoxins have been detected in the water phase as a result of extracellular release, even though the producer cells (i.e. cell density) are absent or found in low numbers (Lawton, 1994). An additional risk factor is that the water will appear more suitable for recreational activities as clarity increases, thus elevating the potential for exposure during this period.

It is recommended that an advisory be lifted after a waiting period of **two** weeks once the cell density of potentially toxigenic blue-green algae falls below the thresholds established in Part B of the Guidelines (Figure 1) and with sufficient evidence that the bloom is continuing to decline. Evidence of a declining bloom can include decreasing cell density of potentially toxigenic cyanobacteria and increasing lake clarity.

An advisory may be lifted **one** week after the cell density of potentially toxigenic blue-green algae falls below the thresholds established in Part B of the Guidelines (Figure 1) if toxin analysis indicates that microcystin is below 8 ug/L for species capable of producing microcystin and anatoxin-a is below 3 ug/L detected for species capable of producing anatoxin-a. It is recommended that if the dominant species of an advisory is known in the scientific literature to produce anatoxin-a and microcystin, that both toxins be tested prior to lifting an advisory before the two-week waiting period.

The advisory should remain in place until a final quantitative sample confirms the decreasing trend of potentially toxigenic blue-green algae and restrictions should remain in place whenever scums are visible. In some situations, there may be reason to prolong the advisory beyond the recommended waiting period. This may result from reported

illnesses associated with recreational contact, the persistence of toxin, historic concerns at a particular water body (such as the Diamond Lake 2001 event), or other factors. Furthermore, it is likely that certain water bodies will have site-specific issues that require consultation among stakeholders to determine suitable actions to address an advisory.

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Appendix A. Risk Assessment for deriving quantitative guidance for 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:

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

where,

TDI (tolerable daily intake) = 0.04 µg/kg/day
BW (body weight) = 20 kg
IR (ingestion rate) = 0.1 L

The TDI was developed by the World Health Organization based on repeated oral administration of microcystin-LR in mice and effects on the liver (Fawell and James, 1994). 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.

Using the parameters described above, the equation results in 8 µg/L of microcystin toxin. According to World Health Organization guidance, 8 µg/L would correspond to approximately 40,000 cells/mL if *Microcystis* were the dominant species (Chorus & Bartrum, 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).