

Appendix to the CCHAB Proposed Changes to the Statewide Voluntary Guidance on CyanoHABs in Recreational Waters, January 2016.

Appendix A. Description of cyanotoxin triggers in recreational waters.

This appendix describes the basis for the concentration levels selected to trigger the actions in the decision tree. The voluntary guidance relies on the science presented in OEHHA's risk assessment for microcystin, anatoxin-a and cylindrospermopsin (OEHHA 2012). Risk management decisions were used to integrate and expand the OEHHA action levels into a tiered response framework. Under this framework, increasing concentrations of cyanotoxins in recreational waters will prompt increasing public health warnings to users of the waterbody. Some of the triggers are not based on OEHHA's risk assessment but consider other important information such as animal poisoning reports and successful approaches used in other areas.

Development of this framework was a collaborative effort within CCHAB. Risk management decisions involve balancing the risk of low-level toxin exposures with the risks of closing waterbodies to the public, including economic, social and health impacts. Policy issues are also considered in risk management. The approach described here is designed to be feasible, useful and protective of public health.

Table A.1. CyanoHAB Triggers for Recreational Water.

| | Toxin (µg/L) | | |
|---------------------------|-----------------------|----------------|----------------|
| | Caution Trigger Level | Warning Tier I | Danger Tier II |
| Microcystins ¹ | 0.8 | 6 | 20 |
| Anatoxin-a | Detect ² | 20 | 90 |
| Cylindrospermopsin | 1 | 4 | 17 |

¹Microcystins refers to the sum of all measured microcystin variants.

²Must use an analytical method that detects <1 µg/L anatoxin-a.

Microcystin

The trigger level of 0.8 µg/L microcystin prompts increased monitoring and the placement of a caution sign stating that people should stay away from scum and pets and livestock should be kept away from the water and scum. The trigger level is based on the Office of Environmental Health Hazard Assessment's (OEHHA) action level of 0.8 µg/L (OEHHA 2012). The action level represents a concentration in recreational water that is not expected to lead to adverse health effects. This is based on the best available science and very health-protective assumptions. OEHHA's action level is based on the short-term Heinze 1999 study in rats, which reported a Lowest Observable

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Adverse Effect Level (LOAEL) of 50 µg/kg-d. The endpoint was moderate liver pathology. The next highest dose (150 µg/kg-d) showed moderate to severe liver pathology. OEHHA calculated a 95% lower confidence limit of the Benchmark Dose (BMDL) of 6.4 µg/kg-d to represent the dose of microcystin that serves as the point of departure to estimate a safe dose for humans. An Uncertainty Factor (UF) of 1000 was applied to the BMDL, resulting in a Reference Dose (RfD) of 6×10^{-3} µg/kg-d, which estimates the dose of microcystin that is not expected to produce any adverse liver effects in humans. The UF of 1000 is the product of the following individual uncertainty factors: 10 for extrapolating from rat to human (assumes that humans could be 10 times more sensitive to microcystin than rats), 10 for the different sensitivities in humans (assumes the most sensitive person could be 10 times more susceptible to microcystin than the average person) and 10 for an incomplete toxicological database. The exposure scenario is a child swimming in recreational waters for 5 hours per day (30.25 kg child ingesting 0.05 L water per hour, or 0.25 L per day). OEHHA's risk assessment reflects a conservative, health-based approach and is described in detail in OEHHA (2012).

Managers should be aware of the risk to dogs and livestock when the microcystin trigger level is exceeded. Animals have been poisoned by microcystin at recreational waters in California. Exposure in dogs and livestock is unpredictable because they may consume scum at the shoreline and drying algal mats that wash up on shore. They are also exposed by cleaning cyanotoxin-containing material from their coats after being in the water. These materials may have much higher concentrations of microcystin compared to water levels. Dogs and livestock should be kept out of the water and away from the shoreline when the microcystin trigger level is exceeded.

The Tier I level of 6 µg/L microcystin in recreational waters would prompt the placement of a warning sign stating that swimming is not recommended and that pets and livestock should be kept away from the water. The Tier I level is based on OEHHA's calculated BMDL from the Heinze (1999) study (6.4 µg/kg-d; OEHHA 2012), a UF of 300 and a lower exposure rate. The cumulative UF of 300 includes the following factors: 10 for extrapolating from rodent data to humans, 10 for the differing sensitivities within the human population and 3 for an incomplete toxicological database. Using a UF of 3 for an incomplete toxicological database is a common approach in human health risk assessment and is often used by OEHHA (OEHHA 2008). Applying the cumulative UF of 300 to the BMDL of 6.4 µg/kg-d results in an RfD of 2×10^{-2} µg/kg-d. The exposure scenario is a child swimming in recreational waters for 2 hours per day (30.25 kg child ingesting 0.05 L water per hour, or 0.1 L per day). The Tier I level represents a health-based and conservative approach.

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The OEHHA action level is conservative and its use as a posting trigger could lead to constant public warnings on waterbodies, which could obscure the need for caution when toxin concentrations increase. Policy and economic issues are also considered in risk management. Local authorities must weigh very low risks of toxic exposures with the high risks of closing waterbodies to the public, including economic, social and health impacts. The approach described here provides a highly useful tiered response to public health protection from microcystin exposure in recreational waters. The Tier I trigger is in the general range of OEHHA’s microcystin subchronic action levels for water intake by dogs and livestock (OEHHA 2012). However, because these animals often consume scum and mats containing concentrated toxins, the action trigger level should be used for the protection of dogs and livestock from microcystin poisoning.

The Tier II level of 20 µg/L microcystin would prompt the placement of a sign stating that there is a present danger and that people, pets and livestock should stay out of the water and away from water spray. This level is based on risk management objectives rather than a purely health-based conservative approach. California water bodies support some of the highest microcystin levels in the world, with microcystins measured in the tens of thousands µg/L during bloom seasons in some areas. This guidance provides the Tier II “danger” level to convey the higher risk of critical liver impacts associated with higher microcystin levels in California waters. The concentration of 20 µg/L microcystin has been suggested as a warning level by the World Health Organization (WHO; WHO 1999). WHO’s warning level is based on an earlier subchronic mouse study by Fawell et al. (1994; 1999a). Although OEHHA (2012) and USEPA (2015) found the later study by Heinze (1999; described above) to be a stronger study for the basis of health advisories, the Fawell study was acknowledged as a good study by both agencies. The WHO’s warning level of 20 µg/L has been employed internationally for over a decade. There have been limited reports of human illness associated with recreational exposure to cyanobacterial bloom waters. Most of the reported human cases have involved rashes and gastrointestinal symptoms (Backer et al., 2015). The California Tier II level of 20 µg/L is intended as a severe warning level and is prompted by the historical, intermittent occurrences of very high microcystin levels in California waters.

Table A.2. Basis of suggested triggers for microcystin in Table A.1.

| Basis of Trigger | Trigger (µg/L) | POD (µg/kg-d) | Total UF | RfD (µg/kg-d) | IR (L/d) | BW (kg) | Study |
|--|-----------------------|----------------------|------------------|----------------------|-----------------|----------------|--------------|
| OEHHA's Action Level | 0.8 | 6.4 ^b | 1000 | 6 x 10 ⁻³ | 0.25 | 30.25 | Heinze 1999 |
| Modified OEHHA Action Level ^a | 6 | 6.4 ^b | 300 ^c | 2 x 10 ⁻² | 0.1 | 30.25 | Heinze 1999 |

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| | | | | | | | |
|--|----|----|----|----|----|----|----|
| Risk Management: <i>WHO Warning Level</i> | 20 | -- | -- | -- | -- | -- | -- |
|--|----|----|----|----|----|----|----|

^a OEHHA's BMDL with UF = 300 and lower exposure.

^b Calculated BMDL from Heinze (1999) data.

^c The UF is lower because a factor of 3 was used to account for limited database.

POD = Point of Departure, the study dose representing the lower end of the observed range of adverse effects.

IR = Ingestion Rate, how much water is assumed to be ingested by members of the target population

BW = Body Weight, average for the target population being considered

Anatoxin-a

The trigger level for anatoxin-a is identified as any detection of the toxin in recreational waters. The chemical analysis must be able to detect anatoxin-a at levels below 1 µg/L in order for the trigger level to be useful. Concentrations above the trigger level will prompt increased monitoring and the placement of a caution sign stating that people should stay away from scum and pets and livestock should be kept away from the water and scum. The guidance for the trigger level is based on the precautionary approach in risk management. With this approach, known vulnerabilities may be addressed despite the absence of sufficient scientific evidence of risk. Anatoxin-a is a potent and very fast-acting neurotoxin. The toxin is responsible for numerous domestic animal and wildlife deaths. The trigger level is a precautionary measure, intended to prompt local managers to continue monitoring anatoxin-a concentrations to detect any increase. The anatoxin-a trigger level is also intended to protect dogs and livestock from acute poisoning as described below.

There is a heightened danger to dogs and livestock whenever anatoxin-a is present in a waterbody. Dogs and livestock may be particularly susceptible to acute lethality from anatoxin-a. Animal poisonings have been observed when anatoxin-a was present at low levels in California waterbodies. Animals can be exposed to high anatoxin-a concentrations by consuming scum at the shoreline and drying algal mats that wash up on shore. They are also exposed by cleaning cyanotoxin-containing material from their coats after being in the water. These materials may have high anatoxin-a concentrations even though the toxin levels are low in the water. Dogs and livestock should be kept out of the water and away from the shoreline when anatoxin-a is present.

The Tier I level of 20 µg/L anatoxin-a in recreational waters would prompt the placement of a warning sign stating that swimming is not recommended and that pets and livestock should be kept away from the water. The Tier I level is based on Oregon's recreational guideline for anatoxin-a, which incorporates a conservative approach (Farrer et al.,

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2015). The Oregon Health Authority (OHA) based their guideline on the short-term oral study in mice by Fawell et al., (1999b). The mice were examined for a wide range of toxicological endpoints both during and at the end of the study. There was no statistically significant difference between the control group and any of the dosed groups for any of these endpoints. However there were two unexplained deaths in the study -- one each in the mid- and high-dose groups. Anatoxin-a was not suspected in these deaths but it was not possible to rule it out. Therefore OHA set the lowest dose, 100 µg/kg-d, as the No-Observed Adverse Effect level (NOAEL; Farrer et al., 2015). A UF of 1000 was applied to the NOAEL, resulting in an RfD of 0.1 µg/kg-d. The UF of 1000 is the product of the following individual uncertainty factors: 10 for extrapolating from rodent to human, 10 for the differing sensitivities within the human population and 10 for an incomplete toxicological database. The exposure scenario was a child swimming in recreational waters for 2 hours per day (20 kg child ingesting 0.05 L water per hour, or 0.1 L per day). OHA's risk assessment reflects a conservative, health-based approach using the best available science.

The OHA guideline was chosen as the Tier I trigger as a precautionary approach in the risk management of anatoxin-a. This concentration level is considered precautionary because it is more restrictive than the health-based OEHHA Action Level of 90 µg/L, described below. The Tier I level may be updated as more information becomes available. **As noted above, dogs and livestock are susceptible to acute anatoxin-a poisoning at water concentrations that are below the Tier I level due to high exposures in animals.** The action trigger level should be used for the protection of dogs and livestock from anatoxin-a poisoning.

The Tier II level of 90 µg/L anatoxin-a would prompt the placement of a sign stating that there is a present danger and that people, pets and livestock should stay out of the water and away from water spray. The Tier II level is based on OEHHA's action level for human exposure to anatoxin-a in recreational waters (OEHHA 2012). OEHHA's action level was also based on the short-term oral study in mice by Fawell et al., (1999b). As described above, there was no statistically significant difference between the control group and any of the dosed groups for a wide array of endpoints. OEHHA did not consider the two unexplained mortalities described above to be treatment related. The mice in this study were exposed daily through oral gavage, which is a somewhat stressful technique that can lead to unintended mortalities. OEHHA identified the highest dose, 2,500 µg/kg-d, as the NOAEL (OEHHA 2012). A UF of 1000 was applied to the NOAEL, resulting in an RfD of 2.5 µg/kg-d. The UF of 1000 is the product of the following individual uncertainty factors: 10 for extrapolating from rodent to human, 10 for the differing sensitivities within the human population and 10 for an incomplete toxicological database. The exposure scenario included a child swimming in recreational waters for 5 hours per day (30.25 kg child ingesting 0.05 L water per hour,

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or 0.25 L per day). OEHHA also considered exposures through inhalation and skin contact (OEHHA 2012). OEHHA's risk assessment reflects a conservative, health-based approach using the best available science.

Table A.3. Basis of suggested triggers for anatoxin-a in Table A.1.

| Basis of Trigger | Trigger (µg/L) | POD (µg/kg-d) | Total UF | RfD (µg/kg-d) | IR (L/d) | BW (kg) | Study |
|--|----------------|---------------|----------|---------------|----------|---------|----------------------|
| Risk Management: <i>Precautionary Approach</i> | Detect | -- | -- | -- | -- | -- | -- |
| Risk Management: <i>OHA's Guideline</i> | 20 | 100 | 1000 | 0.1 | 0.1 | 20 | Fawell et al., 1999b |
| OEHHA's Action Level ^a | 90 | 2,500 | 1000 | 2.5 | 0.25 | 30.25 | Fawell et al., 1999b |

^a OEHHA's action level for anatoxin-a is not solely based on oral exposure (i.e., ingestion rate; IR). The action level also includes dermal and inhalation exposures. See OEHHA 2012 for details on the incorporation of dermal and inhalation exposures into the 90 µg/L action level.

POD = Point of Departure, the study dose representing the lower end of the observed range of adverse effects.

IR = Ingestion Rate, how much water is assumed to be ingested by members of the target population

BW = Body Weight, average for the target population being considered

Cylindrospermopsin

The trigger level of 1 µg/L cylindrospermopsin prompts increased monitoring and the placement of a caution sign stating that people should stay away from scum, and pets and livestock should be kept away from the water and scum. The trigger level is based on a precautionary approach to the risk management of cylindrospermopsin. This toxin has been linked to a widespread outbreak of critical illness in humans following oral exposure (Byth 1980; Griffiths and Saker 2003). The details of the exposure concentrations are unknown but the outbreak supports the use of caution in managing risk associated with cylindrospermopsin. Additionally, less toxicological information is available for this cyanotoxin compared to microcystin. The trigger level concentration (1 µg/L) is intended to alert water managers to the possibility of toxic bloom formation.

Managers should be aware of the risk to dogs and livestock when the cylindrospermopsin trigger level is exceeded. Exposure in animals is unpredictable because they often consume material that can be very high in cylindrospermopsin (scums, mats, cyanobacteria stuck on their coats). We are not aware of any animal poisonings associated with exposure to cylindrospermopsin in California recreational waters. However, as a precaution, dogs and livestock should be kept out of the water and away from the shoreline when the cylindrospermopsin trigger level is exceeded.

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The Tier I level of 4 µg/L cylindrospermopsin in recreational waters would prompt the placement of a warning sign stating that swimming is not recommended and that pets and livestock should be kept away from the water. The Tier I level is based on OEHHA's action level for human exposure to cylindrospermopsin in recreational waters (OEHHA 2012). OEHHA's action level is based on the subchronic study in mice by Humpage and Falconer (2003). OEHHA calculated a BMDL of 33 µg/kg-d. The endpoint was increased kidney weight, indicating mild impaired kidney function. A UF of 1000 was applied to the BMDL, resulting in an RfD of 3.3×10^{-2} µg/kg-d. The UF of 1000 is the product of the following individual uncertainty factors: 10 for extrapolating from rat to human, 10 for the differing sensitivities within the human population and 10 for an incomplete toxicological database. The exposure scenario is a child swimming in recreational waters for 5 hours per day (30.25 kg child ingesting 0.05 L water per hour, or 0.25 L per day). OEHHA's risk assessment reflects a conservative, health-based approach. The Tier I level is below OEHHA's cylindrospermopsin subchronic action levels for water intake by dogs and livestock. However, because these animals often consume scum and mats containing concentrated toxins, the action trigger level should be used for the protection of dogs and livestock from cylindrospermopsin poisoning.

The Tier II level of 17 µg/L cylindrospermopsin would prompt the placement of a sign stating that there is a present danger and that people, pets and livestock should stay out of the water and away from water spray. The Tier II level is based on OEHHA's BMDL from the Humpage and Falconer (2003) study described above. However, a lower UF for limited toxicological database is used (6) than was used in the OEHHA action level (10). The cumulative UF of 600 was applied to the BMDL (33 µg/kg-d; Humpage and Falconer 2003), resulting in an RfD of 5.5×10^{-2} µg/kg-d. The UF of 600 is the product of the following individual uncertainty factors: 10 for extrapolating from rodent data to humans, 10 for the differing sensitivities within the human population and 6 for an incomplete toxicological database. The exposure scenario is a child swimming in recreational waters for 2 hours per day (30.25 kg child ingesting 0.05 L water per hour, or 0.1 L per day). The Tier II level is health-based and conservative.

Note that a higher cumulative UF (600) was used to modify the OEHHA action level for cylindrospermopsin compared to that used to modify the OEHHA action level for microcystin (UF=300). This is because more data is available for microcystin compared to cylindrospermopsin. The UF specific to a limited database was 6 for the modified cylindrospermopsin level and 3 for the modified microcystin level.

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Table A.4. Basis of suggested triggers for cylindrospermopsin in Table A.1.

| Basis of Trigger | Trigger (µg/L) | POD (µg/kg-d) | Total UF | RfD (µg/kg-d) | IR (L/d) | BW (kg) | Study |
|--|----------------|---------------|------------------|---------------|----------|---------|-----------------------------|
| Risk Management: <i>Precautionary Approach</i> | 1 | -- | -- | -- | -- | -- | -- |
| OEHHA's Action Level | 4 | 33 | 1000 | 3.3E-02 | 0.25 | 30.25 | Humpage and Falconer (2003) |
| Modified OEHHA Action Level ^a | 17 | 33 | 600 ^b | 5.5E-02 | 0.1 | 30.25 | Humpage and Falconer (2003) |

^a UF is lowered from 1000 to 600.

^b The UF is lower because a factor of 6 was used to account for limited database.

POD = Point of Departure, the study dose representing the lower end of the observed range of adverse effects.

IR = Ingestion Rate, how much water is assumed to be ingested by members of the target population

BW = Body Weight, average for the target population being considered

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