

US EPA ARCHIVE DOCUMENT

EPA's Drinking Water Health Advisories and Recreational Criteria for Cyanotoxins



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Presentation Overview

- Describe public health guidelines in place
- Discuss the toxicity assessment done for the three cyanotoxins listed in CCL
- Discuss the development of the Health Advisories
- Discuss current efforts to develop Ambient Water Quality Criteria for Recreational Exposures

Disclaimer

- The views expressed in this presentation are those of the author and do not necessarily represent the views or policies of the U.S. Environmental Protection Agency.

Why cyanobacterial HABs are important?

- The prevalence of HABs in freshwater is increasingly reported in the U.S. and worldwide
- Algal blooms can cause:
 - Hypoxia, leading to fish kills
 - Taste and odor problems in treated drinking water
 - Toxins at levels that may be of concern for human health
- HABs may contribute to economic losses to the fishing and recreation industries and increase costs for managing and treating potable water supplies
- Presence in finished drinking water
 - 2014: > 1 $\mu\text{g/L}$ total microcystins detected in finished water in a drinking water system on western Lake Erie
 - City of Toledo, OH (population ~500,000) issued a “do not drink” advisory.



Guidelines and Regulations for Drinking Water

- No federal regulations for cyanobacteria or cyanotoxins in drinking water in the U.S.
- Safe Drinking Water Act Requirements (SDWA Section 1412(b)(1))
 - [Contaminant Candidate List](#)
 - List of unregulated contaminants that are known or anticipated to occur in public water systems and may require a drinking water regulation.
 - EPA publishes the list every five years.
 - Cyanobacteria and their toxins included in CCL (CCL 1 , 2, 3 and draft 4)
 - [Unregulated Contaminant Monitoring Rule \(UCMR\)](#)
 - Collect data from selected public water systems.
 - EPA included 10 cyanotoxins in UCMR 4 for monitoring from 2018-2021.
 - [Regulatory Determination \(RD\)](#)
 - Determine whether or not to regulate; EPA publishes determinations every on a five year cycle.
 - RD 1, 2 and 3 – No Regulatory Decision - not sufficient information

Drinking Water Guidelines for Cyanotoxins

Authority/Country/State	Microcystins	CYL	Anatoxin-a	Saxitoxin
World Health Organization (WHO), 2003	1 µg/L MC-LR	-	-	-
Health Canada, 2002	1.5 µg/L MCs (proposed)	-	-	-
Brazil, 2005	1 µg/L MC-LR	15 µg/L	-	3 µg/L
Australia, 2009	1.3 µg/L MC-LR TE	1 µg/L	3 µg/L	3 µg/L
Singapore, Poland, Norway, China, Netherlands, Korea, Japan, Italy, France, Germany, Finland, Czech Republic	1 µg/L MC-LR	-	-	-
Ohio, 2015	0.3 µg/L bottle-fed infants and pre- school age children 1.6 µg/L school- age children and adults	0.7 µg/L bottle-fed infants and pre- school age children 3 µg/L school-age children and adults	20 µg/L	0.2 µg/L
Oregon	0.3 µg/L age 5 and younger 1.6 µg/L age 6 and older	0.7 µg/L age 5 and younger 3 µg/L age 6 and older	0.7 µg/L age 5 and younger 3 µg/L age 6 and older	0.3 µg/L age 5 and younger 1.6 µg/L age 6 and older
Minnesota	0.1 µg/L MC-LR	-	-	-

Cyanotoxins Toxicity Assessment

- Microcystins
- Cylindrospermopsin
- Anatoxin-a



Health Effects Assessment: Microcystins

- Most studied and widespread cyanobacterial toxin (microcystin-LR).
- More than 100 congeners exist.
- The toxicological database is almost exclusively limited to data on the -LR congener.

Noncancer Effects

- Human data suggest that the liver is the target organ of toxicity
- Studies in laboratory animals have demonstrated toxicity in the liver, kidney, and testes
 - Acute and short term studies, and sub-chronic studies
 - Liver, kidney, reproductive, and developmental effects
 - Chronic studies
 - Limited and have not reported significant effects

Cancer Effects

- Human epidemiological studies have reported an association between consumption of drinking water with cyanobacteria and microcystins and liver or colon cancer in certain areas of China.
- No chronic cancer bioassays designed to evaluate dose-response for the tumorigenicity of microcystins following lifetime exposures are available.
- Applying the EPA 2005 Guidelines for Carcinogen Risk Assessment, there is *inadequate information to assess the carcinogenic potential* of microcystins.

Health Effects Assessment: Cylindrospermopsin

Noncancer Effects

- Human data on oral toxicity of cylindrospermopsin suggests liver and kidney as the target organs.
- Animal laboratory studies focused on hepatic and renal toxicity
 - Acute, short-term, and subchronic studies demonstrate the liver and kidney as target organs.
 - No chronic studies were identified.

Cancer

- Applying the 2005 EPA Guidelines for Carcinogen Risk Assessment, there is *inadequate information to assess the carcinogenic potential* of cylindrospermopsin.
 - No human or chronic cancer bioassays in laboratory animals are available

Health Effects Assessment: Anatoxin-a

Noncancer Effects

- Human data on oral toxicity suggests the nervous system as the target organ.
- Acute and short-term animal laboratory studies are limited.
- No chronic studies were identified.
- Not enough information on sensitive endpoints and associated dose-response relationships to develop an RfD.

Cancer

- There are no cancer, genotoxicity, acute or chronic exposure studies on anatoxin-a, thus there is inadequate information to assess carcinogenic potential.

EPA Drinking Water Health Advisories for Cyanotoxins

- Microcystins
- Cylindrospermopsin

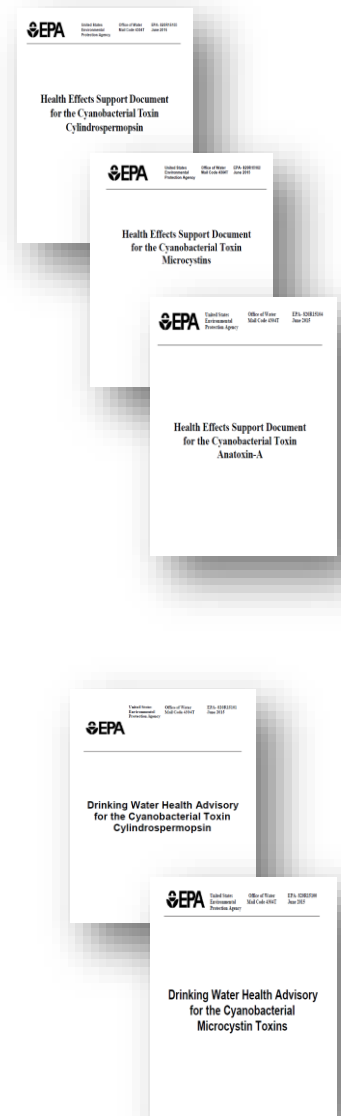


EPA Health Advisories

- Informal technical guidance, **non-regulatory** concentrations estimated for specific exposure durations:
 - Short term exposures: one-day and ten-day (children)
 - One-day HA assumes a single acute exposure; derived from a study of less than 7 days' duration
 - Ten-day HA assumes a limited period of one to two weeks exposure; derived from a study of less than 30-days duration.
 - Estimates of DWI/BW ratio for birth to < 12 months of age using 90th percentile values in Table 3-19 in the 2011 U.S.EPA Exposure Factors Handbook.
 - Chronic Exposures: lifetime (for adults)
 - Derived from a chronic study of 2 years duration, but subchronic studies may be used by adjusting the uncertainty factor employed in the calculation.
 - Updated BW represents the mean weight for adults ages 21 and older. EPA updated the default DWI to 2.5 L/d, rounded from 2.546 L/d, based on values in Table 3-33 in the EPA's Exposure Factors Handbook .
 - Carcinogenic
- Inference:
 - Concentration in drinking water that is not expected to cause any adverse non carcinogenic effects for a specific exposure period.

Cyanotoxins Health Advisories Development

- 2012 – Joint effort with Health Canada
- 2013 - Literature Review and Health Effects Support Documents (HESD) for microcystin, cylindrospermopsin and anatoxin-a development
 - Comprehensive review of the health effects information.
 - Provides the health effects basis for the development of HAs.
- 2014 -2015 External Peer Reviews HESDs for Anatoxin-a, Cylindrospermopsin and Microcystins
 - Peer reviewers affirmed there is inadequate information to develop an HA for anatoxin-a
 - Peer reviewers confirmed there is adequate information to develop HAs for microcystins and cylindrospermopsin
- 2015 –Development of HA for Microcystins and Cylindrospermopsin
- June 17th, 2015 – HAs Published



EPA Drinking Water HAs for Microcystins

- Stressor: microcystin-LR, considered a surrogate for all microcystins
 - Data are most complete
 - LR is the same or more toxic than other congeners, based on available data
- Key Study Selected: Heinze, 1999; 28 day drinking water study in rats
- Exposure pathway: oral ingestion of drinking water
- Most sensitive endpoint: liver toxicity
 - Increase in liver weight and in liver enzymes
- POD: 50 µg/kg/day (LOAEL)
- Exposure duration: 10-day value
 - Short term exposure is more consistent with expected exposure pattern
 - No lifetime or carcinogenic value derived

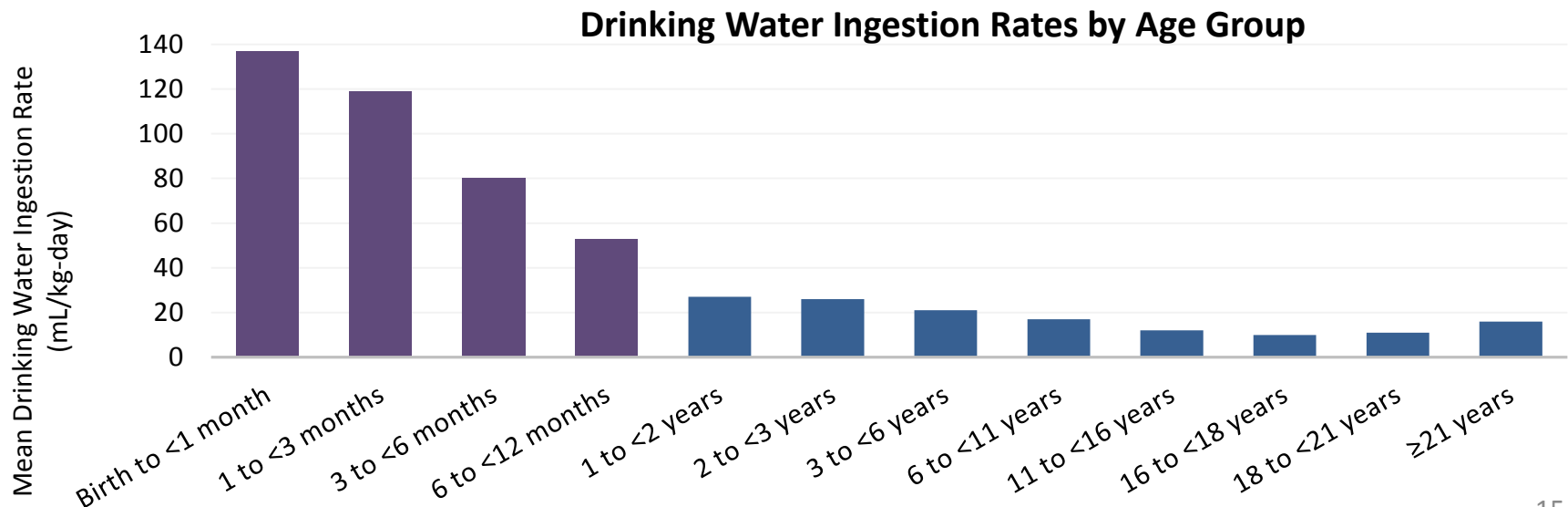
EPA Drinking Water HAs for Cylindrospermopsin

- Stressor: cylindrospermopsin
- Key Study Selected: Humpage and Falconer (2002, 2003); 11 weeks drinking water study in mice
- Exposure pathway: oral ingestion of drinking water (by gavage)
- Most sensitive endpoint: kidney damage
 - Increased weight of kidney and decreased urinary protein
- Exposure duration: 10-day value
 - No lifetime or carcinogenic value
- POD: 30 µg/kg/day (NOAEL)
- Exposed life stage and population: infants and adults
- Exposure duration: 10-day value
 - Short term exposure is more consistent with expected exposure pattern
 - No lifetime or carcinogenic value derived

Children's Exposure to Cyanotoxins



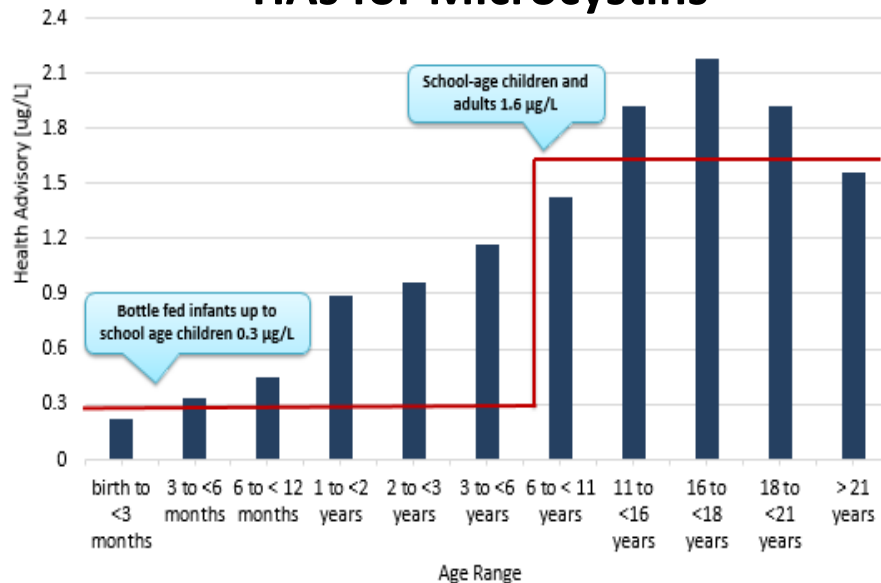
- Bottle-fed infants consume large amounts of drinking water compared to their body weight.
- Exposure to children < 12 months is 5 times higher than for adults > 21 years old, on a body-weight basis.
- At 6 years and older, exposure on a body-weight basis is similar to that of an adult.
- Infant-specific exposure factors are available from U.S. EPA's Exposure Factors Handbook (2011).



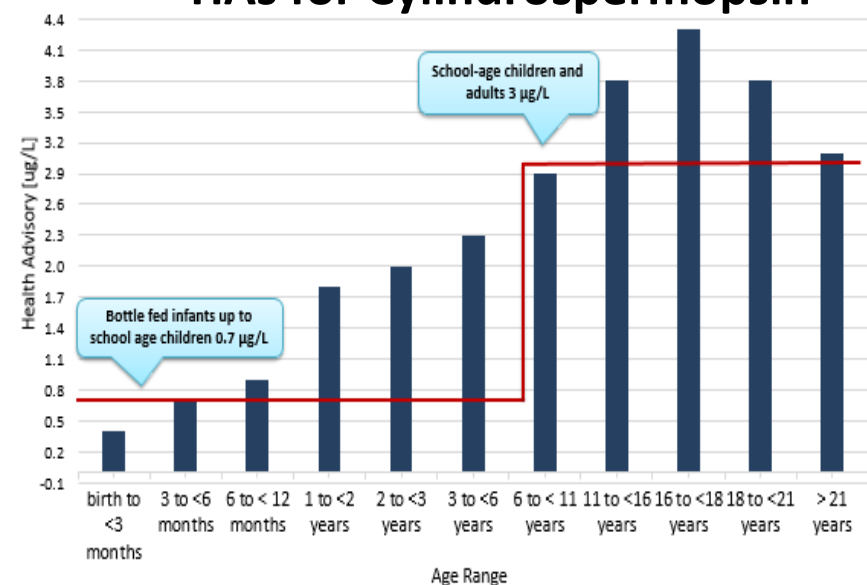
HAs for MCs and CYL by Age Group

Toxin	10-day Health Advisory	
	Bottle-fed infants and pre-school children	School-age children and adults
Microcystins	0.3 µg/L	1.6 µg/L
Cylindrospermopsin	0.7 µg/L	3 µg/L

HAs for Microcystins



HAs for Cylindrospermopsin



Difference among EPA and WHO GV for MCs

	Principal Study	Duration /Route	Dose (µg/kg-d)	Endpoint	Point of Departure (µg/kg-d)	Uncertainty Factors	TDI (µg/kg-d)	Guideline Value
WHO (1999) Provisional GV for MC-LR	Fawell et al. (1994)	13 weeks; gavage; MC-LR	0, 40, 200, and 1000	Minimal/ light chronic inflammation; increased serum enzymes	NOAEL= 40	10- interspecies 10- intraspecies 3-LOAEL to NOAEL 10- database Total = 1000	0.04	1 µg/L provisional for MC-LR Applies to a Lifetime Exposure *WHO applied an allocation factor of 0.80 to account for the proportion of daily exposure arising from drinking water
U.S.EPA GV for MCs	Heinze, 1999	28 day; drinking water; purified extract MC-LR	0, 50, 150 µg/kg-d	Increased liver weight, increased serum enzymes; degenerative and necrotic hepatocytes with hemorrhage	LOAEL = 50	10- interspecies 10- intraspecies 3-LOAEL to NOAEL 3-database Total = 1000	0.05	0.3 µg/L for infants and 1.6 µg/L for adults for MCs Applies to Short-term (10-day) Exposures

Data Gaps Identified

- The toxicity of microcystins to the male reproductive system after sub-acute to chronic oral exposure.
- The toxicity of microcystins to the female reproductive tissues and those of offspring following oral exposure.
- The relative potencies of other microcystin congeners when compared to microcystin-LR.
- The adverse effects of inhalation and/or dermal exposures to cyanotoxins.
- The carcinogenic potential of cyanotoxins.
- Potential health risks from exposure to mixtures of cyanotoxins.
- Bioconcentration and bioaccumulation of cyanotoxins in aquatic food webs.

EPA Recreational Ambient Water Quality Criteria for Cyanotoxins

- Microcystins
- Cylindrospermopsin



Guidelines and Regulations for Recreational Water

- No federal regulations for cyanobacteria or cyanotoxins in recreational water in the U.S.
- World Health Organization (WHO) Guidelines:

Relative Probability of Acute Health Effects	Cyanobacteria (cells/mL)	Microcystin-LR (µg/L)
Low	< 20,000	<10
Moderate	20,000-100,000	10-20
High	100,000-10,000,000	20-2,000
Very High	> 10,000,000	>2,000

- Guidance values for recreational water have been adopted by many countries and some states based on WHO guidelines.

Recreational Water (RW) Guidelines for Cyanotoxins

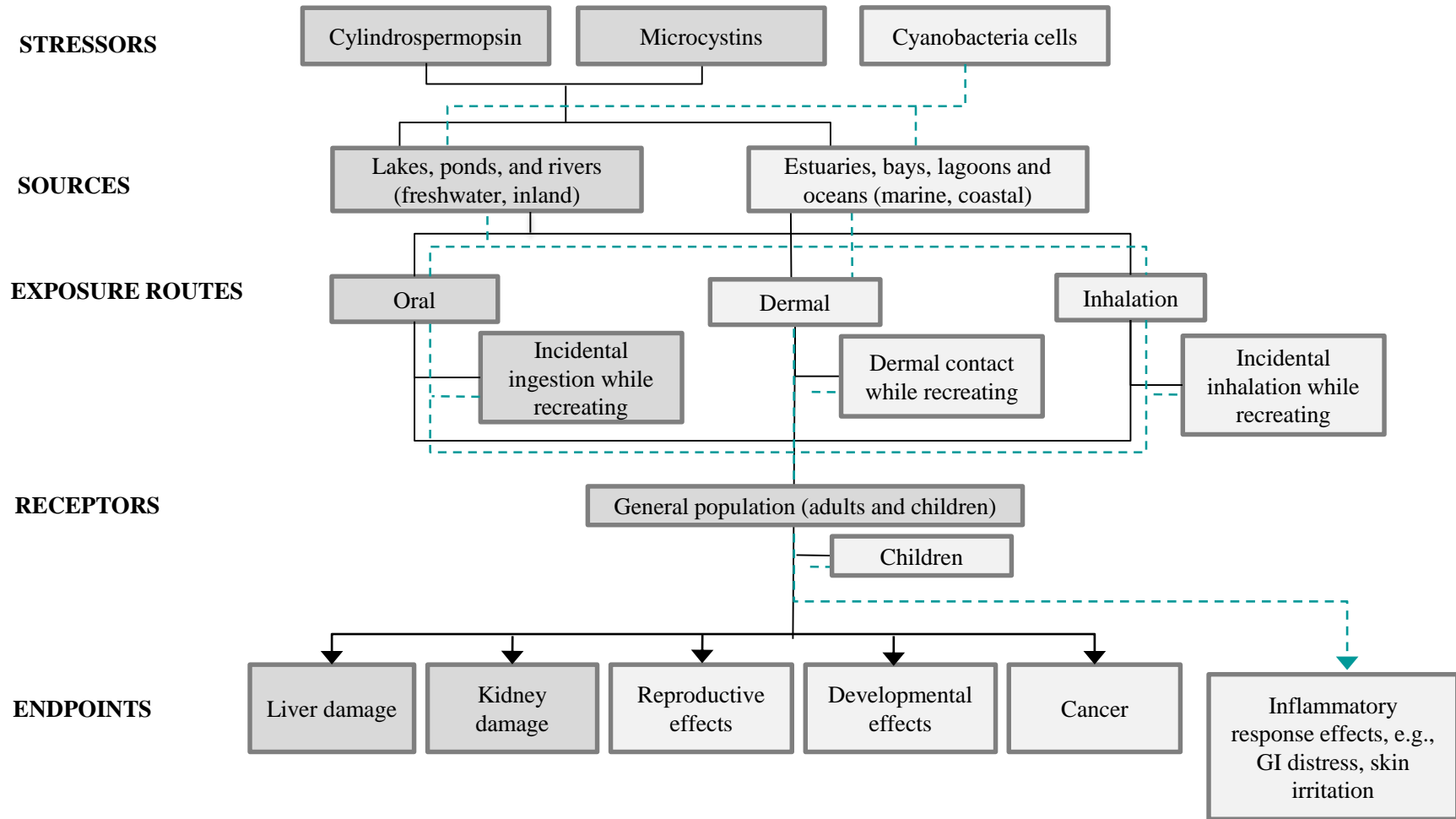
Authority/State	Recreational Water Guidance/Action Level			
WHO	Relative Probability of Acute Health Effects	Cyanobacteria (cells/mL)	Microcystin-LR (µg/L)	Chlorophyll-a (µg/L)
	Low	< 20,000	<10	<10
	Moderate	20,000-100,000	10-20	10-50
	High	100,000-10,000,000	20-2,000	50-5,000
	Very High	> 10,000,000	>2,000	>5,000
California	Microcystin: 0.8 µg/L; Anatoxin-a: 90 µg/L; Cylindrospermopsin: 4 µg/L			
Iowa, Nebraska, Oklahoma, Texas	Microcystin ≥ 20 µg/L			
Idaho	Surface scum visible and associated with toxigenic taxa* Sum of all potentially toxigenic taxa ≥100,000 cells/mL The density of Microcystis or Planktothrix >40,000 cells/mL <small>*Toxigenic taxa include Anabaena, Microcystis, Planktothrix, Nostoc, Coelosphaerium, Anabaenopsis, Aphanizomenon, Gloeotrichia, Woronichinia, Oscillatoria, and Lyngbya. Additional taxa are known to be potentially toxic and may be added to the list.</small>			
Ohio	Microcystin-LR: PHA: 6 µg/L; NCA: 20 µg/L; Anatoxin-a: PHA: 80 µg/L; NCA: 300 µg/L Saxitoxin: PHA: 0.8 µg/L; NCA: 3 µg/L; Cylindrospermopsin: PHA: 5 µg/L; NCA: 20 µg/L			
Oregon	Microcystin: 10 µg/L; Anatoxin-a: 20 µg/L; Cylindrospermopsin: 20µg/L; Saxitoxin: 10 µg/L			
Washington	Microcystin-LR: 6 µg/L; Anatoxin-a: 1 µg/L; Cylindrospermopsin: 4.5 µg/L; Saxitoxin: 75 µg/L			
Wisconsin	> 100,000 cells/mL or scum layer			

EPA's Ambient Water Quality Criteria (AWQC) Development for Recreational Exposures

- EPA is developing Clean Water Act §304(a) recreational Ambient Water Quality Criteria (AWQC) to ensure safety for recreational exposures to cyanobacteria and the cyanotoxins microcystin and cylindrospermopsin.
- Focus on a recreational scenario where immersion and incidental ingestion of ambient water are likely.
- Consumption of fish and shellfish will **not** be considered in the assessments.

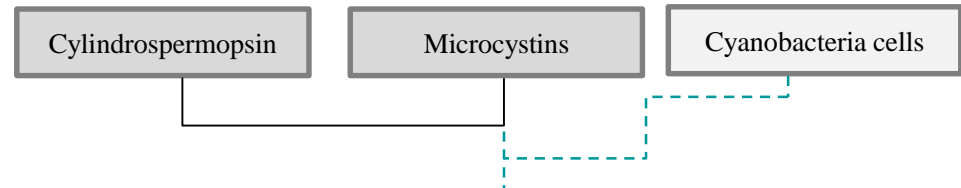


Conceptual Model of Exposure Pathways to Cyanobacteria and Cyanotoxins in Recreational Water



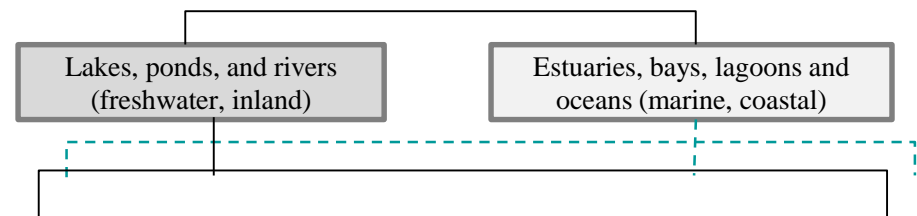
Rationale of Factors Considered in the Conceptual Model

STRESSORS: agents that cause an effect



- Considering both the cyanotoxins and cyanobacterial cells.
- Both have shown adverse health effects:
 - Cyanotoxins: Liver (microcystin) and Kidney (cylindrospermopsin)
 - Cyanobacterial cells: inflammatory responses such as gastrointestinal (GI), dermatologic, eye/ear, and respiratory.

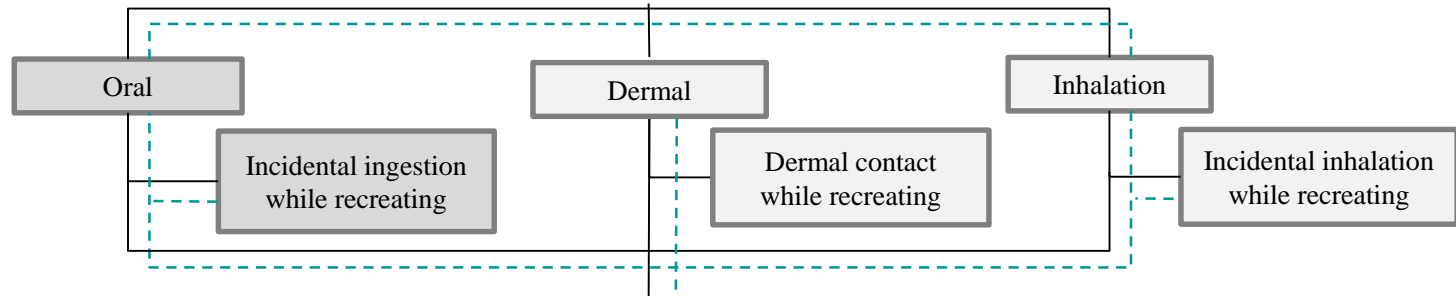
SOURCES: where is the stressor coming from?



- Focusing on freshwater occurrence of HABs producing microcystin and cylindrospermopsin.
- Evaluating reports of upstream fresh water HAB events affecting the downstream interface with estuarine/marine waters.

Rationale of Factors Considered in the Conceptual Model

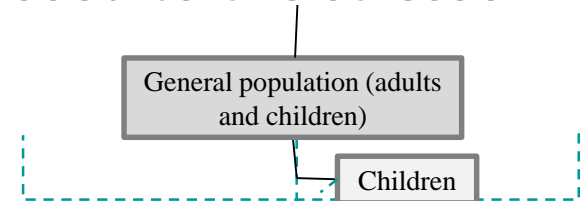
EXPOSURE ROUTES: how are recreators exposed?



- Focus on a recreational scenario where immersion and incidental ingestion of ambient water are likely.
- Dermal and inhalation exposures associated with primary contact recreation will be considered if data are sufficient.

RECEPTORS: populations and/or life stages exposed to the stressor

- EPA intends to derive criteria protective for a child who ingests water incidentally while swimming.
- Because:
 - Children incidentally ingest more water during recreational activities than adults.
 - Children spend more time swimming in fresh waters compared to adults.
 - Children can be exposed more frequently compared to adults.



Next Steps AWQC for Cyanotoxins

- EPA is planning to have a HAB-related session at the 2016 Recreational Water Conference in April.
- EPA is planning to hold additional webinars in 2016.
 - Engage with stakeholders
 - Communicate our progress
 - Provide a venue for feedback
 - Forum for information/data sharing
- Draft AWQC: Fall 2016



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