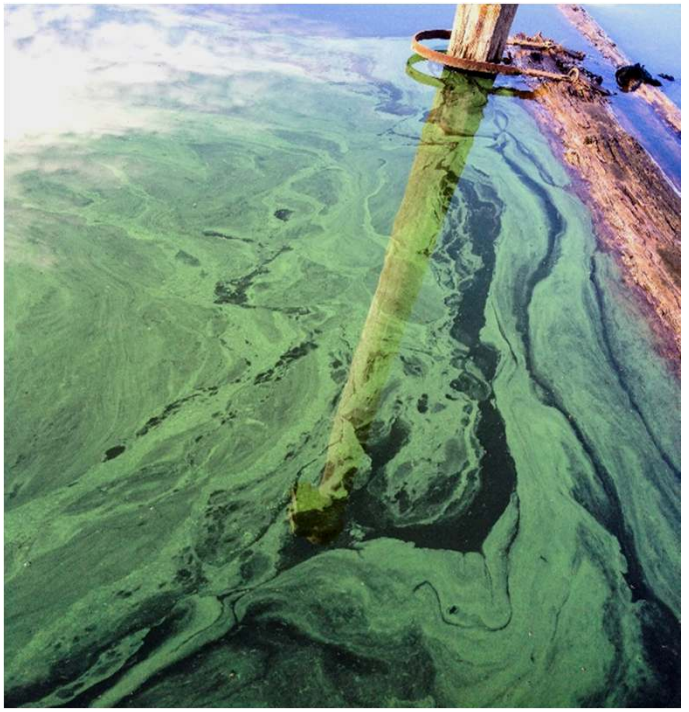
# EPA's Drinking Water Health Advisories and Recreational Criteria for Cyanotoxins



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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 µg/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 | Cylindrospermopsin | 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<br>1.6 µg/L school-age children and adults | 0.7 µg/L bottle-fed infants and pre-school age children<br>3 µg/L school-age children and adults | 20 µg/L | 0.2 µg/L |
| Oregon | 0.3 µg/L<br>age 5 and younger<br>1.6 µg/L<br>age 6 and older | 0.7 µg/L<br>age 5 and younger<br>3 µg/L<br>age 6 and older | 0.7 µg/L<br>age 5 and younger<br>3 µg/L<br>age 6 and older | 0.3 µg/L<br>age 5 and younger<br>1.6 µg/L<br>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

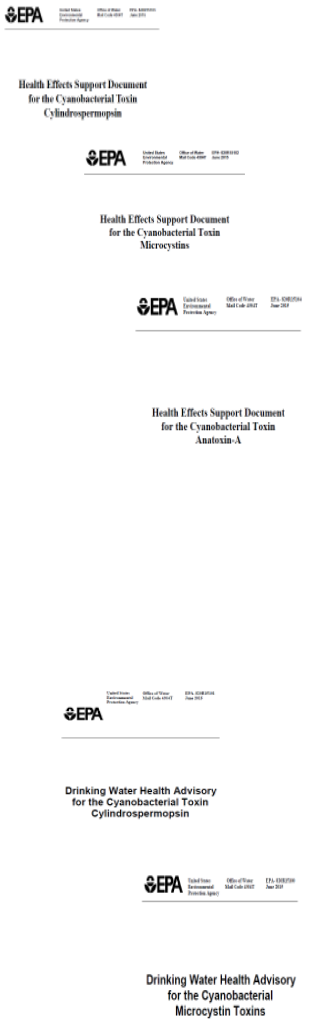
- Microcystins
- Cylindrospermopsin

# 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 90$^{th}$ 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.

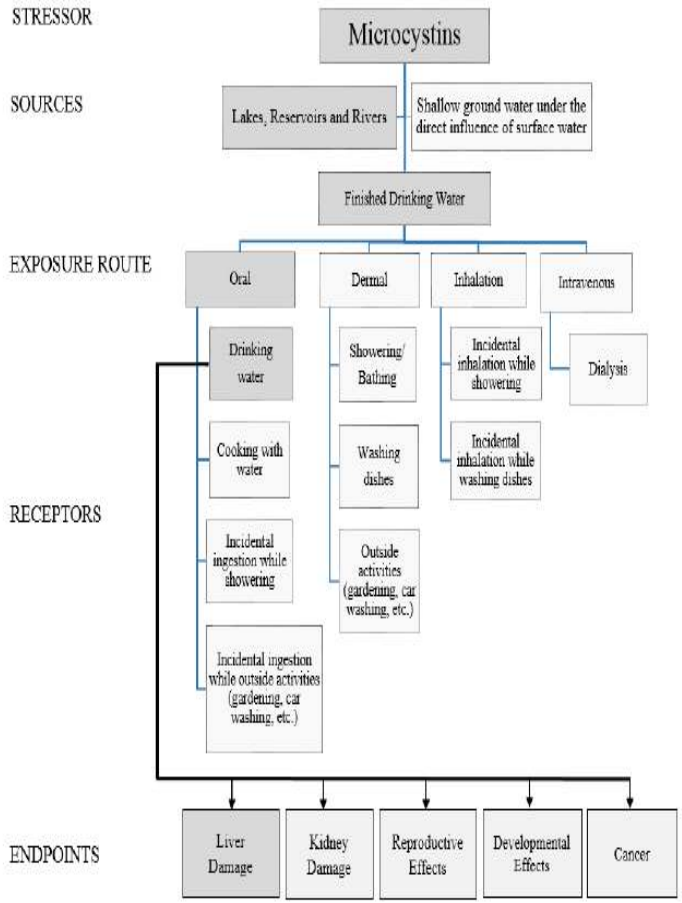
# Cyanotoxins Health Advisories Development

- 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



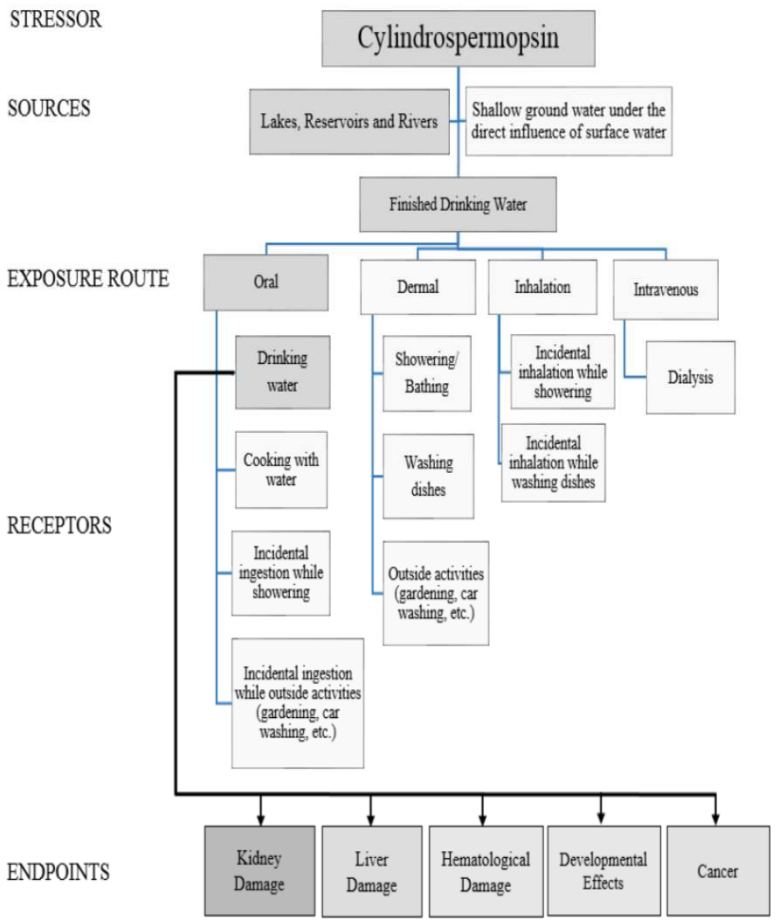
# EPA Drinking Water HAs for Microcystins

- 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



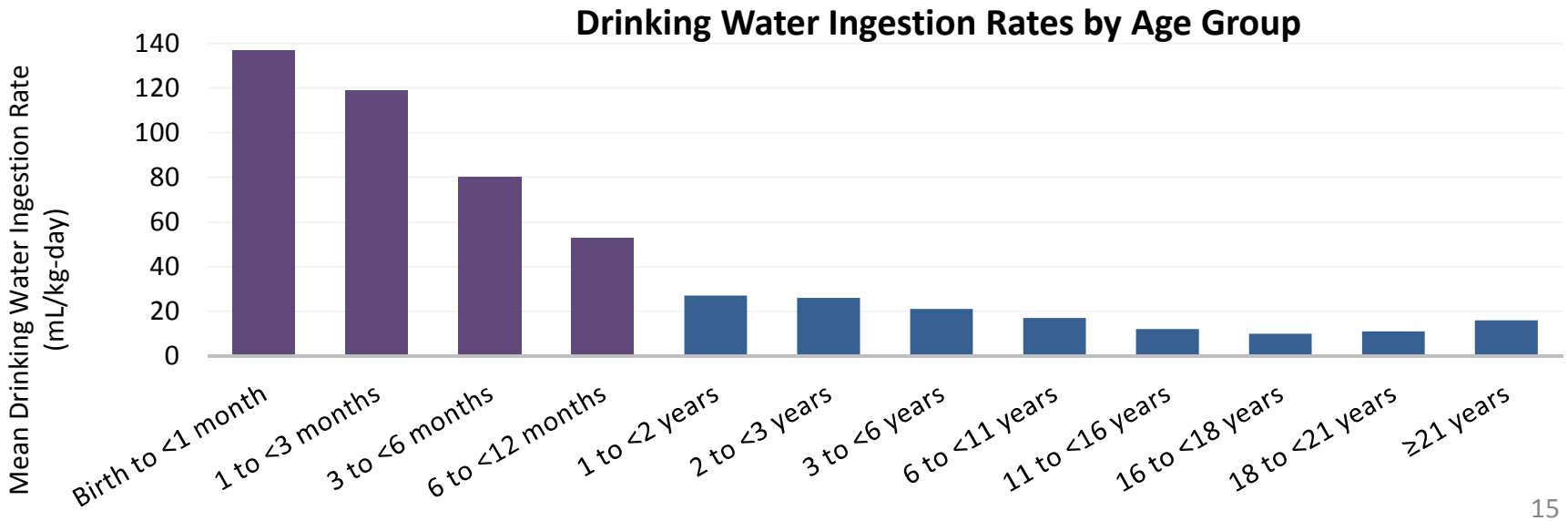
# EPA Drinking Water HAs for Cylindrospermopsin

- 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
- No lifetime or carcinogenic value derived



# Children's Exposure to Cyanotoxins

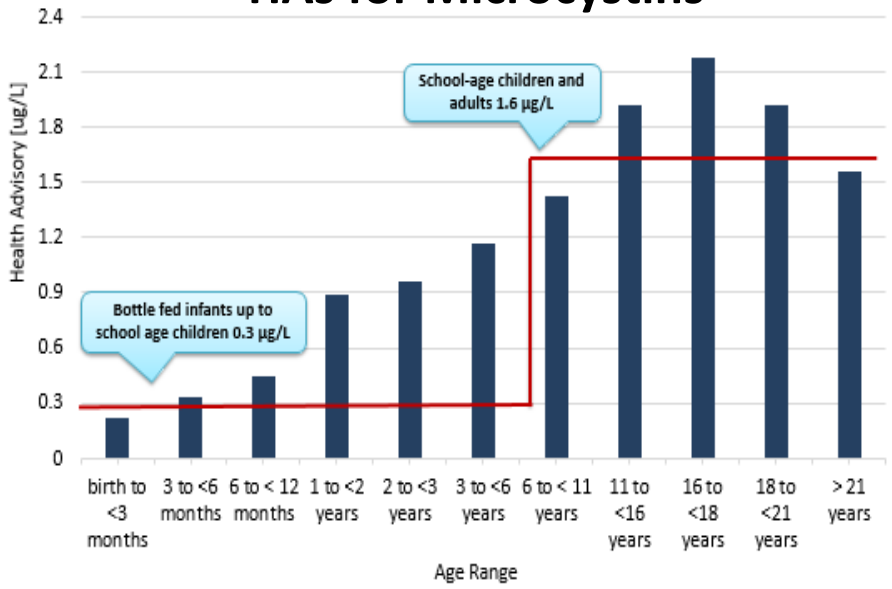
- Bottle-fed infants consume large amounts of drinking water compared to their body weight.
- Exposure to children < 12 months is 5 times higher than for adults > 21 years old, on a body-weight basis.
- At 6 years and older, exposure on a body-weight basis is similar to that of an adult.
- Infant-specific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



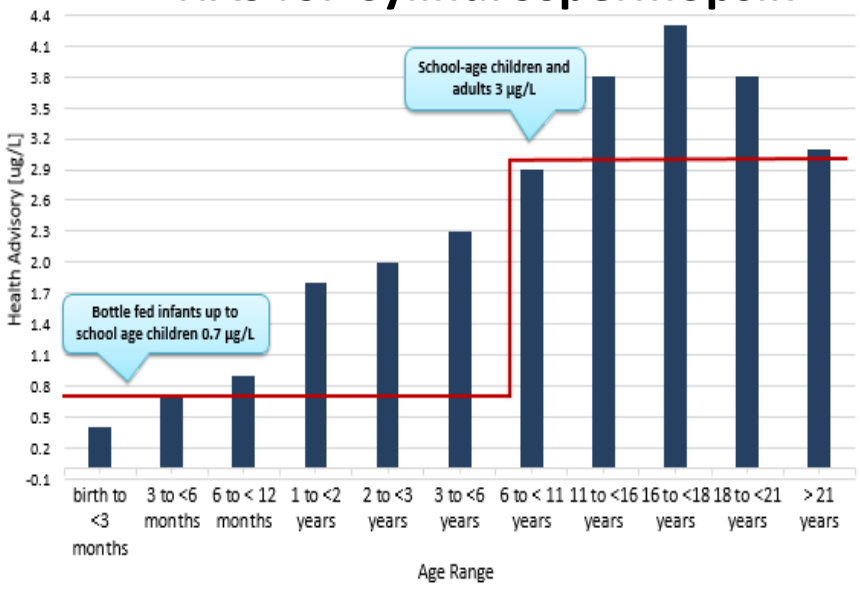
# HAs for MCs and CYL by Age Group

| 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<br>10-intraspecies<br>3-LOAEL to NOAEL<br>10-database<br><br>Total = 1000 | 0.04 | 1 µg/L provisional for MC-LR<br><br>Applies to a Lifetime Exposure<br><br>*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<br>10-intraspecies<br>3-LOAEL to NOAEL<br>3-database<br><br>Total = 1000 | 0.05 | 0.3 µg/L for infants and 1.6 µg/L for adults for MCs<br><br>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.

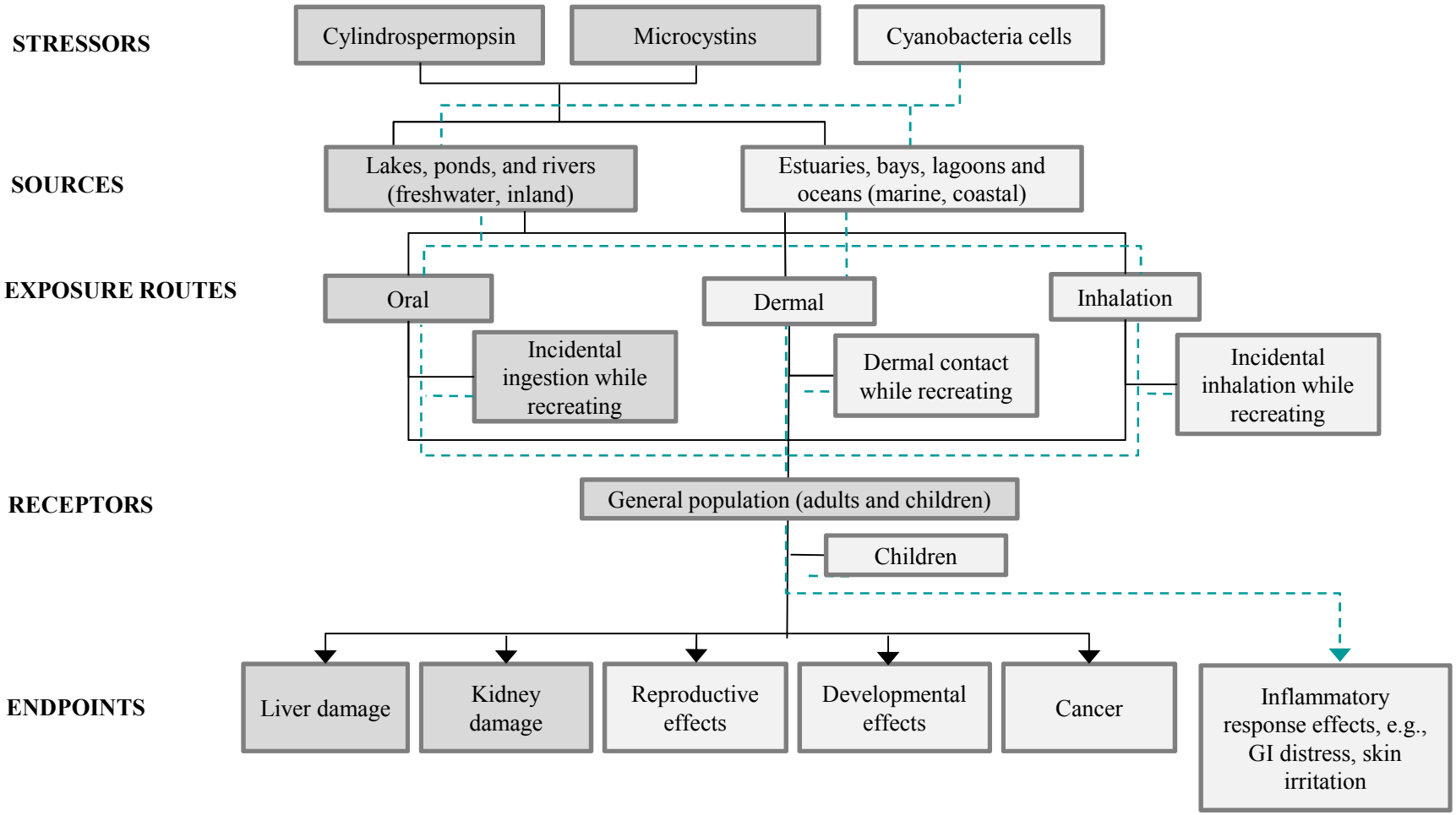
# Recreational Water (RW) Guidelines for Cyanotoxins

| 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 | | | |
| **Illinois** | Microcystin-LR concentration results approach or exceed 10 µg/L | | | |
| **Indiana** | Level 1: very low/no risk < 4 µg/L microcystin-LR<br>Level 2: low to moderate risk 4 to 20 µg/L microcystin-LR<br>Level 3: serious risk > 20 µg/L microcystin-LR<br>Warning Level: Cylindrospermopsin: 5 ppb | | | |
| **Ohio** | Microcystin-LR: PHA: 6 µg/L; NCA: 20 µg/L<br>Cylindrospermopsin: PHA: 5 µg/L; NCA: 20 µg/L<br>Anatoxin-a: PHA: 80 µg/L; NCA: 300 µg/L<br>Saxitoxin: PHA: 0.8 µg/L; NCA: 3 µg/L | | | |
| **Wisconsin** | > 100,000 cells/mL or scum layer | | | |

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

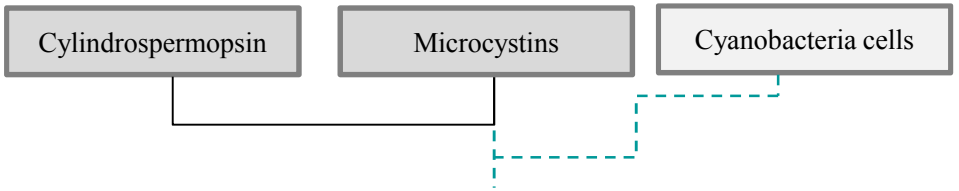
- EPA is developing Clean Water Act §304(a) recreational Ambient Water Quality Criteria (AWQC) to ensure safety for recreational exposures to cyanobacteria and the cyanotoxins microcystin and cylindrospermopsin.
- Focus on a recreational scenario where immersion and incidental ingestion of ambient water 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



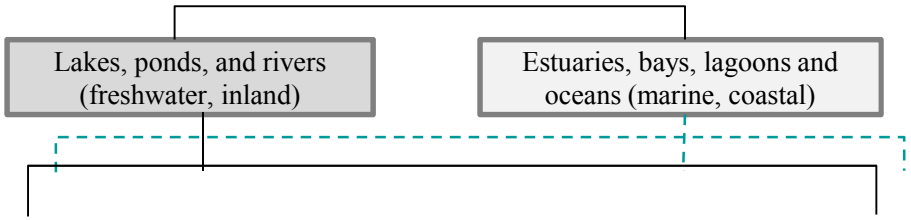
# Rationale of Factors Considered in the Conceptual Model

## 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.

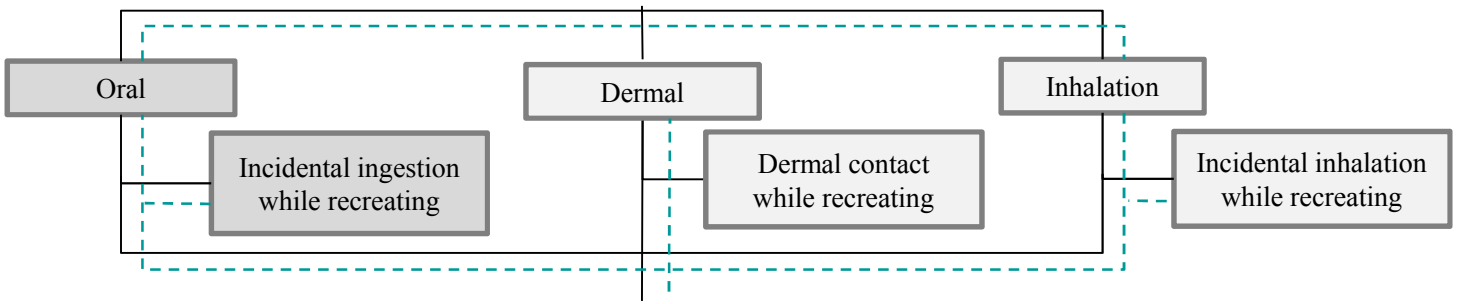
## SOURCES: where is the stressor coming from?




- 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.

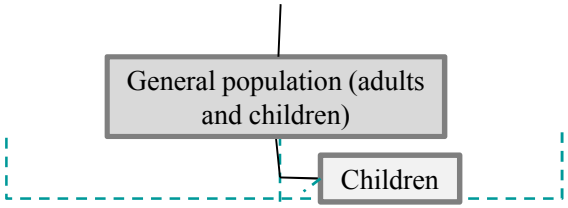
# Rationale of Factors Considered in the Conceptual Model

## 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 Waters 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

# Contact Information

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EPA's CyanoHABs Website
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