Cyanotoxin Action Levels for Humans and Domestic Animals

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Office of Environmental Health Hazard Assessment
California Environmental Protection Agency
TOXICOLOGICAL SUMMARY AND SUGGESTED ACTION LEVELS TO REDUCE POTENTIAL ADVERSE HEALTH EFFECTS OF SIX CYANOTOXINS

May 2012

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Office of Environmental Health Hazard Assessment
California Environmental Protection Agency
Highlights of the Report

- **Cyanotoxins considered**: anatoxin-a, cylindrospermopsin, microcystin-LR, -RR, -YR and -LA
- **Reference doses** developed for humans and animals
- **Exposure scenarios** estimated for humans and animals
- **Action levels** derived for humans and animals in several types of exposure media
Overview of the Process

Reference Dose
Maximum recommended dose

Exposure
Amount of media consumed (e.g., water)

Action Level
Health-protective chemical concentration in media (e.g., mg/L)
Reference Dose

The Reference Dose (RfD): level of exposure over a given time period that is not expected to cause any adverse effects

1. Identify the best dose-response study
2. Identify a dose that effects very few test animals
3. Translate that animal dose to humans and domestic animals using Uncertainty Factors
RfD Exposure Durations

- **Acute**: <24 hrs
- **Short-term**: up to 30 days
- **Subchronic**: up to 10 percent of lifetime
- **Chronic**: more than 10 percent of lifetime
## Reference Dose Studies

### Test Animal and Endpoint

<table>
<thead>
<tr>
<th>Type RfD</th>
<th>MCs</th>
<th>ANA-a</th>
<th>CYN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Human</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>Rat Liver Tox</td>
<td>Mouse Neurotox</td>
<td></td>
</tr>
<tr>
<td>Sub-chronic</td>
<td>Rat Liver Tox</td>
<td>Rat Neurotox</td>
<td>Mouse Kidney Tox</td>
</tr>
<tr>
<td>Chronic</td>
<td>Mouse Histo</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Domestic Animal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>Sheep Lethality</td>
<td>Mouse Lethality</td>
<td>Rat Lethality</td>
</tr>
<tr>
<td>Sub-chronic</td>
<td>Rat Liver Tox</td>
<td>Mouse Lethality</td>
<td>Mouse Kidney Tox</td>
</tr>
</tbody>
</table>
Human RfD Uncertainty Factors

Cumulative UF of 1000

- 10 - the average human could be more sensitive than the laboratory animals
- 10 - the most sensitive human could be more sensitive than the average human
- 10 - complete toxicology profiles are not available particularly with regard to effects in children
Domestic Animal RfD UF

**Acute:** Cumulative UF of 100
- 10 - the average domestic animal could be more sensitive than the test animals
- 10 - complete toxicology profiles are not available and the endpoint is severe

**Subchronic:** Cumulative UF of 10
- 10 - the average domestic animal could be more sensitive than the test animals and complete toxicology profiles are not available
\[ \text{"No Effect Level"} \div \text{UF} = \text{RfD} \]

<table>
<thead>
<tr>
<th></th>
<th>Type RfD</th>
<th>MCs</th>
<th>ANA-a</th>
<th>CYN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Human (mg/kg-d)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td></td>
<td>0.0064 0.0000064</td>
<td>2.5</td>
<td>0.0025</td>
</tr>
<tr>
<td>Sub-chronic</td>
<td></td>
<td>0.0064 0.0000064</td>
<td>0.5</td>
<td>0.0005 0.000033</td>
</tr>
<tr>
<td>Chronic</td>
<td></td>
<td>0.003 0.000003</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Domestic Animal (mg/kg-d)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td></td>
<td>3.7 0.037</td>
<td>2.5</td>
<td>4.0 0.04</td>
</tr>
<tr>
<td>Sub-chronic</td>
<td></td>
<td>0.0064 0.00064</td>
<td>Use Acute</td>
<td>0.033 0.0033</td>
</tr>
</tbody>
</table>
Exposure to Cyanotoxins

- Humans swimming
- Human consumption of sport fish and shellfish
- \textit{Did not estimate exposure through drinking water for humans}
- Cattle drinking from natural/impounded waters
- Dogs drinking from natural/impounded waters
- Cattle consumption of crusts or mats
- Dog consumption of crusts of mats
Exposure from Recreational Waters

7-10 year old swimmers receive the highest exposure per body weight

They inadvertently drink 0.25 liters of water and inhale 5 cubic meters of air during 5 hours of swimming

Information about these 7-10 year old swimmers was used to establish a mathematical relationship between swimmer dose and water concentration
### Exposure Pathways & Dose Ratios

Ratios of Swimming Water Concentration over Swimmer Dose \((\text{mg/L})/(\text{mg/kg-d})\)

<table>
<thead>
<tr>
<th>Exposure Routes Considered</th>
<th>Ingestion</th>
<th>Inhalation</th>
<th>Dermal</th>
<th>Total&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCs</td>
<td>√</td>
<td></td>
<td></td>
<td>121</td>
</tr>
<tr>
<td>CYN</td>
<td>√</td>
<td></td>
<td></td>
<td>121</td>
</tr>
<tr>
<td>ANA-a</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>37.2</td>
</tr>
</tbody>
</table>

<sup>a</sup>\[\text{Total} = \frac{1}{\text{Ingestion} + \text{Inhalation} + \text{Dermal}}\]

Concentration/Dose Ratio * RfD = Action Level
Water Skiing and Jet Boating

• A study was found in which water and a few air concentrations were measured at a lake

• The data was insufficient to establish an action level for water skiing

• The dose to a 7-10 year old swimmer would be 17,000 times greater than that of a water skier
Exposure in Fishers

Based on consumption of sportfish and shellfish by the general fishing population

\[ D_{\text{consume}} = \frac{C_F \times CR}{BW} \]

\[ C_F = \frac{RfD \times BW}{CR} \]

Set \( D_{\text{consume}} \) equal to RfD and solve for \( C_F \)

\( D_{\text{consume}} = \) Dose to fisher (should meet RfD)

\( C_F = \) Concentration in fish (Action Level)

\( CR = \) Consumption rate (1 meal/wk, 8oz fresh)

\( BW = \) Body weight of fisher (70 kg Adult)
Exposure in Cattle

• Based on small breed dairy cows, ~ 450 kg (greatest exposure potential)

• **Water consumption**: 0.23 L/kg-d (based on NRC nutritional formulas)

• **Crust consumption**: 2.6 g crust/kg-d (based on spontaneous meal size reported by NRC)
Exposure in Dogs

- Based on 20 kg dog

- **Water consumption**: 0.084 L/kg-d
  - Drinking intake: 0.01 L/kg following an hour of exercise in warm temperatures
  - Grooming intake: 0.074 L/kg estimates the amount of toxin that may remain on a saturated coat

- **Crust consumption**: 25 g crust/kg-d (based on energy requirements while exercising)
Uncertainty in Animal Exposure

- Advised by peer reviewers to address:
  - Preferential consumption of cyanobacteria
  - Uncertainty in exposure via grooming

- Uncertainty factor of 3 was applied to each domestic animal exposure scenario
  - Consumption may be up to 3 times higher than estimated
  - Estimated intake * 3 = Final Exposure
Domestic Animals

\[ C_x = \frac{RfD \times BW}{IR \times UF} \]

- \( C_x \) = Concentration of cyanotoxin in water or crusts (Action Level)
- RfD = Reference dose (acute or subchronic)
- BW = Body weight (cattle or dog)
- IR = Intake rate (of water or crusts by cattle or dog)
- UF = Uncertainty factor of 3
Action Level

Health-protective chemical concentrations in the environmental media that are designed to prevent an organism from receiving exposures above the RfDs

- Risk management tool
- Not criteria or regulation
- Not applicable to human drinking water exposures
Overview of the Process

Reference Dose
Maximum recommended dose

Exposure
Amount of media consumed (e.g., water)

Action Level
Health-protective chemical concentration in media (e.g., mg/L)
### Action Levels for Humans Subchronic Exposure

<table>
<thead>
<tr>
<th>Media (units)</th>
<th>MCs(^1)</th>
<th>ANA-a</th>
<th>CYN</th>
<th>Water (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recreational Uses(^2)</strong></td>
<td>0.8</td>
<td>90</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td><strong>Sport Fish Consumption</strong></td>
<td>10</td>
<td>5000</td>
<td>70</td>
<td>Fish (ng/g) ww(^3)</td>
</tr>
</tbody>
</table>

\(^1\) Includes microcystins LA, LR, RR, and YR  
\(^2\) Not for drinking water  
\(^3\) Wet weight or fresh weight
## Action Levels for Dogs
### Subchronic and **Acute** Exposure

<table>
<thead>
<tr>
<th></th>
<th>MCs(^1)</th>
<th>ANA-a</th>
<th>CYN</th>
<th>Media (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drinking</strong></td>
<td>2</td>
<td>100</td>
<td>10</td>
<td>Water (µg/L)</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>100</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td><strong>Eating Crusts and Mats</strong></td>
<td>0.01</td>
<td>0.3</td>
<td>0.04</td>
<td>Crusts and Mats (mg/kg) dw(^2)</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>0.3</td>
<td>0.5</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) Includes microcystins LA, LR, RR, and YR

\(^2\) Dry sample weight
## Action Levels for Cattle Subchronic and **Acute** Exposure

<table>
<thead>
<tr>
<th></th>
<th>MCs&lt;sup&gt;1&lt;/sup&gt;</th>
<th>ANA-a</th>
<th>CYN</th>
<th>Media (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drinking</strong></td>
<td>0.9</td>
<td>40</td>
<td>5</td>
<td>Water (µg/L)</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>40</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td><strong>Eating Crusts and Mats</strong></td>
<td>0.1</td>
<td>3</td>
<td>0.4</td>
<td>Crusts and Mats (mg/kg) &lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> Includes microcystins LA, LR, RR, and YR

<sup>2</sup> Dry sample weight
## Limiting Subchronic Action Levels for Recreational Waters

<table>
<thead>
<tr>
<th></th>
<th>MCs(^1)</th>
<th>ANA-a</th>
<th>CYN</th>
<th>Media (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Swimming</td>
<td>0.8</td>
<td>90</td>
<td>4</td>
<td>Water (µg/L)</td>
</tr>
<tr>
<td>Cattle Drinking</td>
<td>0.9</td>
<td>40</td>
<td>5</td>
<td>Water (µg/L)</td>
</tr>
</tbody>
</table>

\(^1\) Includes microcystins LA, LR, RR, and YR