Summary of findings from toxicological report and suggested action levels; public health perspective; critical data needs

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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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Cyanotoxins Reviewed*

- **Microcystins** –LR (–RR, –YR and –LA)
  - **Liver toxin:** causes liver damage/failure.
    - Human cases: 76 mortalities from i.v. exposure
    - Animal cases: high mortality from oral exposure
    - MC-LR is a possible tumor promoter in humans
    - Stable in the environment
  - **Produced by:** cyanobacterial species of several genera, e.g., *Microcystis*, *Anabaena*, and *Planktothrix* (*Oscillatoria*)

*Literature through 2008 reviewed with few exceptions*
Cyanotoxins Reviewed*

- **Anatoxin-a**

- **Neurotoxin**: causes convolutions and rapid death by respiratory paralysis.
  - Human cases: not documented
  - Animal cases: high mortality from oral exposure
  - Relatively stable in the environment

- **Produced by**: cyanobacterial species of several genera, e.g., *Anabaena*, *Planktothrix (Oscillatoria)*, *Aphanizomenon*

*Literature through 2008 reviewed with few exceptions*
Cyanotoxins Reviewed*

• **Cylindrospermopsin**

  • **Liver and kidney toxin:** causes liver and kidney damage/failure.
    • Human cases: poisonings from drinking water
    • Animal cases: mortality from oral exposure
    • Stable in the environment

  • **Produced by:** cyanobacterial species of several genera, e.g., *Cylindrospermopsis, Aphanizomenon, Rhaphidiopsis, Anabaena*

*Literature through 2008 reviewed with few exceptions*
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
Uncertainty Factors

RfD = “No Effect Level” ÷ UF

**Human cumulative UF** of 1000: “mouse to man” (10); sensitive people (10); incomplete data (10)

**Domestic Animal UF** of 100 (acute) to 10 (subchronic): interspecies extrapolation; incomplete data; severity of endpoint (acute)

**Domestic Animal exposure UF** of 3 was also applied due to the preferential consumption of cyanobacteria. In this case, estimated exposure was multiplied by 3
Exposure Scenarios

- Humans swimming
  - *Does not apply to drinking water*
- Human consumption of sport fish and shellfish
- Dogs & cattle drinking from natural/impounded waters
- Dogs & cattle consumption of crusts or mats
Action Levels

Health-protective chemical concentrations in the exposure media that should result in chemical intake below or equal to the RfDs.

• Algebraic relationship between concentration in exposure media and chemical dose, for example:

\[
\text{Rec. water conc. (mg/L) } \times \text{ RfD (mg/kg } \cdot \text{d) = Action level (mg/L)}
\]

*Set equal to 1 to solve

• Risk management tool; Not criteria or regulation
## Action Levels for Humans Subchronic 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>Recreational Uses$^2$</strong></td>
<td>0.8</td>
<td>90</td>
<td>4</td>
<td>Water (µg/L)</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 & 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>Dogs Water Intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dogs Water Intake</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>Cattle Water Intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cattle Water Intake</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>Dogs Crusts &amp; Mats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dogs Crusts &amp; Mats</td>
<td>0.01</td>
<td>0.3</td>
<td>0.04</td>
<td>Crusts/Mats (mg/kg) &lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>0.3</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td><strong>Cattle Crusts &amp; Mats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cattle Crusts &amp; Mats</td>
<td>0.1</td>
<td>3</td>
<td>0.4</td>
<td>Crusts/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 MCs 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><strong>Human Swimming</strong></td>
<td>0.8</td>
<td>90</td>
<td>4</td>
<td>Water (µg/L)</td>
</tr>
<tr>
<td><strong>Dog Drinking</strong></td>
<td>2</td>
<td>100</td>
<td>10</td>
<td>Water (µg/L)</td>
</tr>
<tr>
<td><strong>Cattle Drinking</strong></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
Public Health Perspective

• Who can the public contact for clear answers?

• Effective risk communication

• Protection of animals (highest exposure group)

• Address practice of pumping bloom water for use in farming and ranching

• Non-contact water recreational scenarios

• Drinking water

• Educate doctors/vets of signs and symptoms
Critical Data Needs

- Toxicological data on other cyanotoxins, e.g., saxitoxin, anatoxin-a(s), MC analogs, lyngbyatoxin
- Exposure data for non-contact water recreation
- MC concentrations in sportfish and shellfish
- Measurement standards for cyanotoxins
- Database of California poisonings (dogs, livestock, wildlife)
- Effects on aquatic species and wildlife