



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

November, 2012

Regina Linville, Ph.D.

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

Ned Butler, Ph.D.

Jim Carlisle, D.V.M., M.Sc.

Regina Linville, Ph.D.



**Office of Environmental Health Hazard Assessment
California Environmental Protection Agency**

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 convulsions 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*, *Raphidiopsis*, *Anabaena*

*Literature through 2008 reviewed with few exceptions

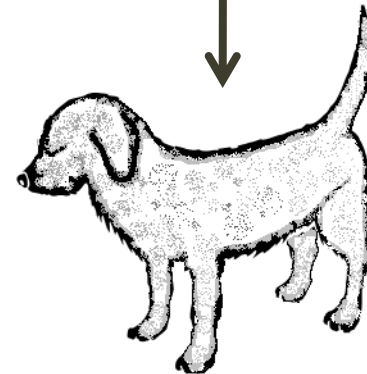
Overview of the Process

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

$$\text{RfD} = \text{“No Effect Level”} \div \text{UF}$$

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:

$$\frac{\text{Rec. water conc. (mg/L)} *}{\text{Swimmer dose (mg/kg} \cdot \text{d)}} \times \text{RfD (mg/kg} \cdot \text{d)} = \text{Action level (mg/L)}$$

**Set equal to 1 to solve*

- Risk management tool; Not criteria or regulation

Action Levels for Humans

Subchronic Exposure

	MCs ¹	ANA-a	CYN	Media (units)
Recreational Uses ²	0.8	90	4	Water (µg/L)
Sport Fish Consumption	10	5000	70	Fish (ng/g) ww ³

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

	MCs ¹	ANA-a	CYN	Media (units)
Dogs Water Intake	2	100	10	Water (µg/L)
	100	100	200	
Cattle Water Intake	0.9	40	5	Water (µg/L)
	50	40	60	
Dogs Crusts & Mats	0.01	0.3	0.04	Crusts/Mats (mg/kg) dw ²
	0.5	0.3	0.5	
Cattle Crusts & Mats	0.1	3	0.4	Crusts/Mats (mg/kg) dw ²
	5	3	5	

¹ Includes MCs LA, LR, RR, and YR; ² Dry sample weight

Limiting Subchronic Action Levels for Recreational Waters

	MCs ¹	ANA-a	CYN	Media (units)
Human Swimming	0.8	90	4	Water (µg/L)
Dog Drinking	2	100	10	Water (µg/L)
Cattle Drinking	0.9	40	5	Water (µg/L)

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

