Cyanotoxin Action Levels for Humans and Domestic Animals

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California Environmental Protection Agency

TOXICOLOGICAL SUMMARY AND SUGGESTED ACTION LEVELS TO REDUCE POTENTIAL ADVERSE HEALTH EFFECTS OF SIX CYANOTOXINS

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Highlights of the Report

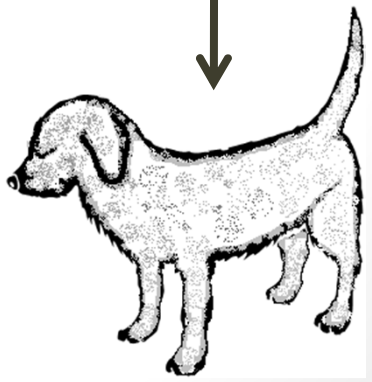
- **Cyanotoxins considered**: anatoxin-a, cylindrospermopsin, microcystin-LR, -RR, -YR and -LA
- **Reference doses** developed for humans and animals
- **Exposure scenarios** estimated for humans and animals
- **Action levels** derived for humans and animals in several types of exposure media

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

	Type RfD	MCs	ANA-a	CYN
Human	Acute	Rat Liver Tox	Mouse Neurotox	
	Sub-chronic	Rat Liver Tox	Rat Neurotox	Mouse Kidney Tox
	Chronic	Mouse Histo		
Domestic Animal	Acute	Sheep Lethality	Mouse Lethality	Rat Lethality
	Sub-chronic	Rat Liver Tox	Mouse Lethality	Mouse Kidney Tox

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 UFs

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

“No Effect Level” ÷ UF = RfD

	Type RfD	MCs	ANA-a	CYN
Human (mg/kg-d)	Acute	0.0064 0.0000064	2.5 0.0025	
	Sub-chronic	0.0064 0.0000064	0.5 0.0005	0.033 0.000033
	Chronic	0.003 0.000003		
Domestic Animal (mg/kg-d)	Acute	3.7 0.037	2.5 0.025	4.0 0.04
	Sub-chronic	0.0064 0.00064	*Use Acute*	0.033 0.0033

Exposure to Cyanotoxins

- Humans swimming
- Human consumption of sport fish and shellfish
- ***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 (mg/L)/(mg/kg-d)

	Exposure Routes Considered			
	Ingestion	Inhalation	Dermal	Total[a]
MCs	√			121
CYN	√			121
ANA-a	√	√	√	37.2

$$^{a}\text{Total} = \frac{1}{\text{Ingestion} + \text{Inhalation} + \text{Dermal}}$$

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

$$D_{consume} = \frac{C_F \times CR}{BW} \qquad C_F = \frac{RfD \; x \; BW}{CR}$$

Set $D_{consume}$ equal to RfD and solve for C_F

$D_{consume}$ = 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

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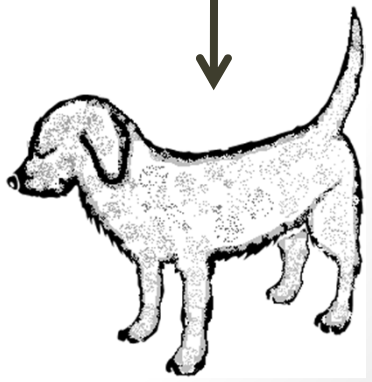

Action Levels for Humans
Subchronic Exposure

	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
Subchronic and Acute Exposure

	MCs[1]	ANA-a	CYN	Media (units)
Drinking	2 100	100 100	10 200	Water (µg/L)
Eating Crusts and Mats	0.01 0.5	0.3 0.3	0.04 0.5	Crusts and Mats (mg/kg) dw[2]

[1] Includes microcystins LA, LR, RR, and YR

[2] Dry sample weight

Action Levels for Cattle
Subchronic and Acute Exposure

	MCs[1]	ANA-a	CYN	Media (units)
Drinking	0.9 50	40 40	5 60	Water (µg/L)
Eating Crusts and Mats	0.1 5	3 3	0.4 5	Crusts and Mats (mg/kg) dw[2]

[1] Includes microcystins 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)
Cattle Drinking	0.9	**40**	5	Water (µg/L)

[1] Includes microcystins LA, LR, RR, and YR