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Cyanobacterial Toxins : Risk Management for Environmental and Health Protection

Geoffrey A. Codd, Louise F. Morrison and James S. Metcalf
Division of Environmental and Applied Biology, School of Life Sciences, University of Dundee, U.K.

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ABSTRACT

Risk management is required to protect water resources, aquatic biota, human and animal health from the harmful effects of cyanobacterial populations and cyanobacterial toxins. This approach is necessary because of: the high toxicity of cyanobacterial toxins to mammals; global occurrences of toxigenic cyanobacteria in waterbodies; widespread examples of associated animal poisonings and emerging human health problems; and the presence of cyanobacterial toxins in water resources used for drinking and recreation at concentrations above guidelines identified for health protection. Advances in understanding of the occurrence and significance of cyanobacterial toxins are presented. Adverse health outcomes, from mild to fatal, of human and animal exposure to cyanobacterial toxins, have occurred in several countries over recent years. In several such cases, e.g. in the UK, Australia and Brazil, these incidents arose when no structured, experience-based system was in place to manage the risks presented by the toxins. In some cases, cyanobacterial poisoning events and consequent disruption of water supply or other water-uses,have been rapidly followed by the development and implementation of risk management strategies. These strategies have continued to evolve and recent adaptations and needs are discussed. Risk management strategies, including hazard analysis of critical control points (HACCP) and action plans, may be useful as templates for adoption, with appropriate adaptation, in other countries where toxigenic cyanobacterial mass populations grow in waterbodies used as human resources.

Keywords : cyanobacterial toxins, eutrophication, water quality

1. INTRODUCTION

Cyanobacteria (blue-green algae) are natural, cosmopolitan inhabitants of fresh-, brackish- and marine waters, and terrestrial environments [1]. They fulfill key roles in the biogeochemical cycling of matter and in the structure, maintenance and biodiversity of microbial and higher organism communities. This benign view of the cyanobacteria from a human standpoint is being increasingly qualified by the realization that these Gram negative prokaryotes produce a wide range of potent toxins [2-4]. Toxigenic cyanobacteria are not listed among waterborne pathogens in the water industry, either with primary microbial pathogens such as *Salmonella* and *Shigella*, or with opportunistic pathogens e.g. *Aeromonas* and *Enterobacter* [5]. They appear to be unable to colonise, invade and grow in human or animal hosts to cause disease. Cyanobacterial toxins are produced by cyanobacterial popula-tions in the waterbody. Evidence is accumula-ting of adverse health effects on humans and animals, ranging from mild to fatal, associated with exposure to cyanobacterial cells and their toxins. These observations, with increasing data on the occurrence of potentially toxic cyanobacterial

mass populations in water-bodies needed for human use, and modern analyses of cyanobacterial toxin concentrations, were together reviewed at a major European workshop [6]. The meeting, "Europe Facing Toxic Cyanobacterial Blooms" produced the following unanimous statement on cyanobacterial toxin risk management:

"These findings indicate cyanotoxins (cyanobacterial toxins) to be a substantial hazard because they are among the most widespread and health-relevant chemicals in water used both for drinking-water abstraction and recreation."

Summaries of the occurrence and toxicity of cyanobacterial toxins are presented here, together the exposure routes and media involved in presenting risks to human health. The derivation of guideline values for the toxins in drinking water and of corresponding guidance levels for the cells in recreational water is also presented, with necessary qualifications regarding their use. Finally, an outline of the management strategies to mitigate the hazards presented by cyanobacterial toxins and cell populations, and their wider applicability, is discussed.

2. Hazard Identification, Recognition and Detection of Cyanobacterial Mass Populations and Toxins

In contrast to several other water-borne microbial health hazards, cyanobacteria are often readily apparent to the human eye, and sometimes to the nose. This is due to the ability of cyanobacterial to discolour the water and accumulate as readily observable mass populations.

These include: **(i) blooms** of planktonic species. These may be positioned throughout the water column due to their buoyancy-regulating ability, or to waterbody-mixing processes; **(ii) scums** of planktonic species. These accumulate at the water surface due to a rapid increase in cyanobacterial buoyancy, followed by calm weather which does not favour water mixing or scum resuspension; **(iii) mats** and **biofilms of** benthic and littoral species. These may grow on the surface of the sediment in shallow water or on rocks at the water margin. Given appropriate awareness-raising (e.g. by leaflets, posters and handbooks), the gross appearance of cyanobacterial blooms, scums and mats enables water-users and water-workers with no, or little, scientific training to recognise that a cyanobacterial health hazard exists in a waterbody.

Cyanobacterial toxicity appears to occur globally (Table 1). Toxicoses associated with, and in some cases attributable to, cyanobacterial cell populations and their toxins have included wild and domestic mammals, birds, amphibians and fish, with human cases ranging from mild to fatal (for reviews, see [2-4,7-13]). Human health effects are diverse: gastroente-ritis, nausea, vomiting, fevers, flu-like symptoms, sore throat, blistered mouth, ear and eye irritation, rashes, myalgia, abdominal pains including painful hepatomegaly, pulmonary consolidation, visual disturbances, kidney damage and liver damage. Increased incidence of primary liver cancer has been associated with exposure to cyanobacteria in raw drinking water in China, and deaths in Brazil have been attributed to exposure to cyanobacterial hepatotoxins (microcystins) via haemodialysis water [7,10,13].

Bloom-forming genera with toxin-producing members include *Microcystis*, *Anabaena*, *Anabaenopsis*, *Planktothrix*, *Aphanizomenon*, *Cylindrospermopsis*, *Raphidiopsis* and *Nodularia*. Scum production is particularly common with *Microcystis*, *Anabaenopsis*, *Planktothrix* and *Aphanizomenon* and less so with the remaining genera. Mat- and biofilm-forming genera with toxigenic members include *Phormidium*, *Oscillatoria* and *Lyngbya*. Light microscopy has traditionally been used in water monitoring for cyanobacterial taxa and their abundance, and this continues to be widely relied upon. However, there are increasing needs to detect the increase in cyanobacterial populations, and ideally of toxigenic cells, at an early stage. Flow cytometry, with autofluorescence/immunofluorescence, is an increasingly valuable technique for the detection and enumeration of water

Table 1. Geographical reports of toxic cyanobacterial blooms, scums or mats.

Europe	Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Netherlands, Norway, Poland, Portugal, Russia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Ukraine, United Kingdom
Americas	Argentina, Bermuda, Brazil, Canada, Chile, Mexico, USA (at least 27 States), Venezuela
Middle East and Asia	Bangladesh, India, Israel, Japan, Jordan, Malaysia, Nepal, Peoples' Republic of China, Philippines, Saudi Arabia, Sri Lanka, South Korea, Thailand, Turkey, Vietnam
Australasia	Australia (New South Wales, Queensland, South Australia, Tasmania, Victoria, Western Australia), New Caledonia, New Zealand
Africa	Botswana, Egypt, Ethiopia, Kenya, Morocco, South Africa, Zimbabwe
Marine	Atlantic Ocean, Baltic Sea, Caribbean Sea, Indian Ocean
Antarctica	McMurdo Ice Shelf

Source : Updated from Codd *et al.* [4]

pathogens at low numbers. However, this method may be limited for the toxic cyanobacteria since the latter commonly form colonies, coiled filaments or bundles of filaments. Submersible spectrofluorimetry with specificity for cyanobacterial pigments, is being applied to monitor vertical cyanobacterial abundance [14]. When coupled with real-time data transmission to the laboratory, this technique can be expected to fulfill a useful role in bloom early warning systems. Fluorescent *in situ* hybridization (FISH), already used in wastewater and food microbiology, has been shown to be a promising method for cyanobacterial detection using labelled cyanobacterial DNA markers [15]. FISH may be further applicable for the use of specific DNA sequences to detect single cells containing genes for cyanobacterial toxin synthesis, e.g. of the microcystin synthetase complex [16].

Cyanobacterial toxins are grouped according to the physiological systems, organs, tissues or cells which are primarily affected. They include: **(i) neurotoxins**: anatoxin-a and homoanatoxin-a are postsynaptic, cholinergic neuromuscular blocking agents, and are alkaloids. Anatoxinn-a(s) is a guanidine methyl phosphate ester which inhibits acteylcholinesterase. The saxitoxins, of which about 20 structural variants are known in cyabobacteria, are carbamate alkaloids which block sodium channels; **(ii) hepatotoxins**: these have been most often implicated in cyanobacterial toxicoses. They include the cyclic heptapeptide microcystins, of which over 70 structural variants are recorded, and the cyclic pentapeptide nodularins, of which about 6 variants are known. These peptides inhibit protein phosphatases, cause changes in membrane integrity and conductance, and are tumour promoters, in addition to causing major liver damage. Nodularin is also a carcinogen; **(iii) cytotoxins**: cylindrospermopsin is a guanidine alkaloid inhibitor of protein synthesis which causes widespread necrotic injury in mammals

(liver, kidneys, lungs, spleen, intestine). It is also genotoxic, and can cause chromosome loss and DNA strand breakage [17-18]; **(iv) irritants and gastrointestinal toxins**: aplysiatoxin, debromoaplysiatoxin and lyngbyatoxin, produced by marine cyanobacteria cause skin irritation and are tumour promoters. Lipopolysaccharide endotoxins (LPS), widely produced by cyanobacteria, may contribute to inflammatory and gastrointestinal incidents.

Sources of the toxins principally implicated in, or associated with human or animal poisoning incidents, and their acute toxicities by intraperitoneal administration (i.p.) to the mouse, are summarised in Table 2. Observations of toxicoses and toxin analyses have typically been made initially with cyanobacterial blooms, scums and mats. Monocyanobacterial laboratory cultures of isolates which continue to produce the toxins are available in almost all cases, indicating the cyanobacterial origin of the toxins, but these do not exclude the possibility that associated heterotrophic bacteria may have a role in toxin production. Several gaps still exist in the confirmation of the cyanobacterial origin of the toxins by detection of toxin production by bacteria-free isolates (Table 2). FISH, using labelled antibodies to the toxins and DNA sequences for the genes for toxin biosynthesis, and PCR using primers for the latter, may help to assign cyanobacterial toxin origins in cases where culturable, axenic strains of cyanobacteria are not available.

Methods for the detection and analysis of cyanobacterial toxins, particularly for drinking water and recreational water are reviewed elsewhere [19-20].

3. Hazard Characterization of Cyanobacterial Toxins and Cells

The investigated cases of human illness and deaths after exposure to cyanobacterial cells and toxins vary widely in depth. Data on the concentrations of cells and/or toxins to which the subjects were exposed, and on the doses actually received, are almost always lacking. Characterization of the hazards to humans therefore relies heavily on animal studies, from which quantitative estimates of the hazards to humans must be extrapolated.

3.1 Cyanobacterial Toxins

For drinking water, a start has been made in estimating the tolerable daily intake (TDI) of some cyano-bacterial toxins [13,21-22]. The requirement for quantitative animal oral dosing data, with follow up over extended periods (ideally over the lifetime of the test animal), to estimate a no-observable-adverse-effect level (NOAEL), or at least a lowest-observable-adverse-effect-level (LOAEL) has only been satisfied for microcystins, anatoxin-a and cylindrosper-mopsin so far. Consistent with standard TDI determination practice, TDIs for cyanobac-terial toxins are only appropriate if a threshold in the relationship between dose and response is probable, e.g. with anatoxin-a. In the case of genotoxic carcinogens, it is likely that no threshold exists below which the toxin fails to initiate carcinogenesis.

For drinking water, the TDI can be estimated as:

$$TDI = \frac{\text{NOAEL or LOAEL}}{UF} \quad \text{Equn. 1}$$

where TDI is in units of mg/kg body wt/day, or mg/kg body wt/day and UF = the product of uncertainty factors (10 for intraspecies variation; 10 for interspecies variation; 10 for a less-than-lifetime study; 5 for a LOAEL; 3 for tumour promotion).

A guideline value (GV; mg/ litre water), to be used in formulating risk management strategies to ensure drinking water safety throughout lifetime consumption [21], can be calculated as:

$$GV = \frac{TDI \times \text{body wt} \times AF}{C} \quad \text{Equn. 2}$$

where body wt is assumed to be 60kg for a human adult

and AF = allocation factor: the proportion of the TDI via drinking water. Since some oral exposure may be via food or dietary

Table 2. Sources and acute toxicities of cyanobacterial toxins.

Toxin	LD_{50} (i.p.mouse, μg/kg body wt)	Source		
		Natural populations, dominant genera	Monocyanobacterial cultures, not bacteria-free	Monocyanobacterial cultures, bacteria-free
Anatoxin-a	250	*Ana, Osc, Aph, Cylmum, Plank*	*Ana, Osc, Plank*	*Ana*
Homoanatoxin-a	250	*Plank*	*Plank*	
Anatoxin-a(s)	40	*Ana*	*Ana*	
Saxitoxins	10 to 30	*Aph, Plank, Ana, Cylsis, Lyng*	*Aph, Ana, Lyng*	
Microcystins	25 to ~1000	*Mic, Ana, Nos, Plank, Anasis, Hapalo*	*Mic, Ana, Nos, Plank, Hapalo*	*Mic, Ana, Plank*
Nodularins	30 to 50	*Nod*	*Nod*	*Nod*
Cylindrospermopsin	200 - 2100	*Cylsis, Aph, Raph, Umez*	*Cylsis, Aph, Raph*	

Ana, Anabaena; Osc, Oscillatoria; Aph, Aphanizomenon; Cylmum, Cylindrospermum; Plank, Planktothrix; Lyng, Lyngbya; Cylsis, Cylindrospermopsis; Mic, Microcystis; Nos, Nostoc; Anasis, Anabaenopsis; Hapalo, Hapalosiphon; Nod, Nodularia; Raph, Raphidiopsis; Umez, Umezakia.

Table 3. Estimations of tolerable daily intake (TDI) and guideline values (GV) for cyanobacterial toxins in drinking water.

Toxin	Oral toxicity test; μg/kg body wt/day	UF[a]					TDI (μg/kg body wt/day)	GV[b] (μg/litre water)	Comments/ references
		intra	Inter	llt	LOA	tum			
Microcystin	NOAEL (mouse, 13 weeks); 40	10	10	10	-	-	0.040	0.96	Toxicity test, Fawell *et al.* [23]
		10	10	10	-	3	0.013	0.31	Includes UF for tumour promotion
	LOAEL (pig, 44 days); 100	10	3	10	5	-	0.067	1.61	Falconer *et al.* [21,24] UF inter 3, due to physiological proximity of pigs and humans
Anatoxin-a	NOAEL (mouse, 4 weeks); 100								Database considered insufficient [21]
	NOAEL (mouse, 7 weeks); 510	10	10	10	-	-	0.51	12.24	Astrachan *et al.* [26]; Duy *et al.* [13] Toxicity test; Falconer and Humpage [22]
Cylindrospermopsin	NOAEL (mouse, 11 weeks); 30	10	10	10	-	-	0.03	0.72	
		10	10	10	-	-	0.03	0.95	As above, but with AF of 0.9 and 70 kg body wt.

[a] UF, uncertainty factors: intra, intraspecific; inter, interspecific; llt, less than lifetime test; LOA, LOAEL; tum, tumour promotion.
[b] unless stated otherwise, all GV estimations made by assuming a human body wt of 60 kg; allocation factor, AF, of 0.8 and daily drinking water consumption, C, of 2 litres.
TDI and GV values calculated according to Equn. 1 and 2.

supplements [11], an AF of 0.8 (80% of total intake) is assumed for drinking water

and C = drinking water consumption per day; assumed to be 2 litres for an adult.

As shown in Table 3, similar TDIs for microcystin were obtained (0.040 vs. 0.067) from oral dosing trials with mice with pure toxin, versus with pigs using freeze-thawed *Microcystis* cells containing quantified microcystins. These give similar GVs (0.96 vs. 1.61). For additional safety, the World Health Organization (WHO) has adopted the lower value for its provisional GV for microcystin in drinking water for adults, rounded to 1 mg/litre [21]. The above derivations do not take into account the tumour promoting actions of microcystins and with an additional UF of 3 for this hazard, a GV of about 0.3 mg/litre emerges (Table 3). Microcystins are largely retained within the producer-cells during growth, but are released in bulk into the water when the cells lyse naturally, or are broken or permeabilised during water treatment. These GVs should therefore apply to the sum of the intracellular and extracellular microcystin pools.

Data to enable TDI and GV estimation for anatoxin-a are not so abundant. A WHO working party did not consider the toxicological database sufficient for TDI estimation [21]. An alternate attempt based on an earlier mouse oral trial [25], yields a GV of about 12mg/litre [13] (Table 3), although this estimate should also be regarded as provisional and requiring more research.

The results of oral dosing with cylindrospermopsin were recently reported [22], which yield a TDI of 0.03, based on the NOAEL (Table 3). Using the "standard" adult body wt of 60 kg and a 0.8 AF, a GV of 0.71 is obtained. Falconer and Humpage [22] have taken the larger average Australian physique into account: for a 70 kg adult and AF of 0.9 rather than 0.8, a GV of 0.95 emerges (Table 3) suggesting a GV for cylindrospermopsin of 1 mg/litre.

In identifying GVs for cyanobacterial toxins in drinking water, it is important that the aims and functions of the GVs are clearly understood. In this case, the GVs should be used and interpreted in the sense of WHO guidelines for drinking water quality. They represent current estimates of the concentrations of the toxins which would not result in a significant risk to consumer health over a lifetime of consumption. The cyanobacterial toxin GVs are: **(i)** not mandatory, but advisory; **(ii)** provisional, to be responsive to advances in research and future experience; **(iii)** recommended for use in the development of risk management strategies to take into account practicality and feasibility in addition to the protection of health; **(iv)** not to be used as a recommended level to which water can be allowed to degrade. For further details of the aims and correct uses of the GVs, see WHO [26-27] and Falconer *et al.* [21].

3.2 Cyanobacterial Cells

Hazard characterization of cyanobacterial cells is useful to contribute to the monitoring and control of drinking waters, and is necessary for the risk management of recreational waters which support cyanobacterial growth. This is also needed for occupational risk management for e.g. water workers, boatmen, and environ-mental scientists. Recreational activities involv-ing direct contact with water (swimming, sailboarding, canoeing, paddling, and to a lesser extent boating and angling) may result in incidental or accidental ingestion, aspira-tion/inhalation or skin contact with cyanobac-terial cells [11-12]. Quantitative dose-response relationships for recreational and occupational exposure to cyanobacterial cells are typically lacking. However, cases of animal deaths and human illness after contact with-, and inges-tion/aspiration of cyanobacterial cells, consis-tent with cyanobacterial toxicoses, are available [8-11]. The approach taken to derive guidelines for recreational exposure includes: **(i)** estima-tion of the risk of adverse health outcomes, of increasing severity, from acute and long-term severe to mild; **(ii)** assumption that exposure

to microcystins is the most likely scenario; **(iii)** a *Microcystis* cell may contain about 0.2 pg of microcystin, that of *Planktothrix* may be higher. The presence of scums, or detached accumulations of mat fragments, in bathing or paddling areas would present the highest risk (Table 4). Guidance levels (GL) to reduce the medium and low probability of adverse health effects (from subacute to mild) are estimated to be 100,000 and 20,000 cells per ml, respectively. The corresponding chlorophyll *a* concentrations are based on the mean cell quota for the pigment, and for microcystins during laboratory culture of *Microcystis*. As with the drinking water GVs, the recreational water GLs are provisional and require to be assessed for their suitability for local/regional circumstances. Whilst uncer-tainty exists regarding the health significance of allergenic and irritatory effects of cyanobacterial cell components (e.g. [28]), it is beyond doubt that cyanobacterial scums and accumulated detached mat fragments present a high risk of adverse health effects and that these materials and the water close-by should be avoided during recreation.

4. HUMAN EXPOSURE ROUTES AND MEDIA

The recognised routes of exposure of humans to cyanobacterial cells and toxins and relevant exposure media are summarised in Table 5. Water is the major perceived medium at present, accounting for the high AF (e.g. 0.8, 0.9) used in TDI estimation (Equn.1) for drinking water assessment. Examples exist of cyanobacterial toxin concentrations in raw and treated drinking waters, in each case both below and above the provisional GVs. It is necessary to take local practices into account in assessing the relative importance of exposure routes and media and to be alert to additional possibilities. Nodularin accumulation in edible blue mussels (*Mytilus edulis*; [29]) and microcystins in edible catfish (*Ictalurus punctatus*; [30]) have been found. Microcystins and *Microcystis* cells have occurred in spray irrigation water and in sprayed-irrigated salad lettuce intended for human consumption, but withdrawn from sale [31]. It is possible that dairy cows might secrete cyanobacterial toxins in their milk after oral exposure. However tests todate after administration of microcystins to

Table 4. Guideline levels (GL) for cyanobacterial cells in bathing waters.

Risk	Potential for adverse health outcomes[a]	Basis for Derivation	GL		Potential microcystin conc.[c]
			cells/ml	μg chl *a*/litre[b]	
HIGH	AP, LTI, STMI	Human case histories; oral animal poisonings	Scums, detached mats		> 1 mg/litre
MEDIUM	LTI, STMI	Provisional GV for microcystins in drinking water and related data	100,000	50	10-20 μg/litre (up to 50 possible)[d]
LOW	STMI	Human epidemiological study[e]	20,000	10	2-4 μg/litre (up to 10 possible)[d]

[a] AP, acute poisoning; LTI, long-term illness, e.g. liver and pulmonary damage; STMI, short-term and mild illness e.g. gastrointestinal, skin irritations. [b] chlorophyll *a* conc. with cyanobacteria being dominant. [c] calculated from typical microcystin conc. per cell. [d] lower range likely if *Microcystis*, *Anabaena* dominant, uppermost number possible if *Planktothrix* dominant. [e] Pilotto *et al.* [32]

lactating cows by gavage have not resulted in microcystin detection in the milk (e.g. [33]).

5. RISK MANAGEMENT STRATEGIES FOR CYANOBACTERIAL TOXINS AND CELLS

The need for a risk management strategy to mitigate problems presented by cyanobacterial toxins and cells in potable and recreational waters has been recognized several times in different countries over recent years. Cyanobacterial mass populations and toxins in water resources are clearly not recent phenomena [4]. A lack of recognition of the health hazards presented has been, and still is, an important factor in accounting for the late and patchy development of risk management strategies. In developing countries, this situation may be compounded by a shortage of scientific and technical expertise and facilities. In some developed countries, risk management strategies for cyanobacterial populations and toxins have only been devised and applied after associated health incidents, affecting animals and/or humans, have occurred. Experiences in e.g. the UK, Australia, USA and Brazil have amply shown the importance of preparedness and contingency plans, to include reactive and proactive measures.

An outline of the sequence of actions necessary to develop and implement an appropriate risk management strategy is given in Figure 1: **(i) situation assessment**: this should include identification of the waterbodies with cyanobacterial mass populations and toxins, and of those with the potential for cell population toxin production; assessment of historical/current problems; assessment of past and current management measures (if any). Emergency actions and, ideally, contingency plans should ideally be implemented at this stage if necessary; **ii) assess priorities for action**: if the number of waterbodies affected, or at risk, overly extends resources, or if adverse health outcomes have already occurred, it would be necessary to set priorities. For example, drinking water sources would be of higher priority than recreational waterbodies, which would in turn be of higher priority than waterbodies used only for navigation or

Table 5. Human exposure routes and exposure media for cyanobacterial toxins.

Exposure route	Exposure medium
Oral (ingestion)	Drinking water, recreational water
	Food (shellfish, finfish if toxin accumulation has occurred during production; plant foods after irrigation with water containing cyanobacterial toxins)
	Dietary supplements (pills, capsules) if containing dried cyanobacterial cells with toxins
Pulmonary (inhalation; aspiration)	Water: aerosols, spray during recreation, work, showering
Dermal (skin, mucosal contact)	Water during recreation, work, showering
Haemodialysis	Water used for haemodialysis

Source : Summarised and updated from Codd *et al.* [4]

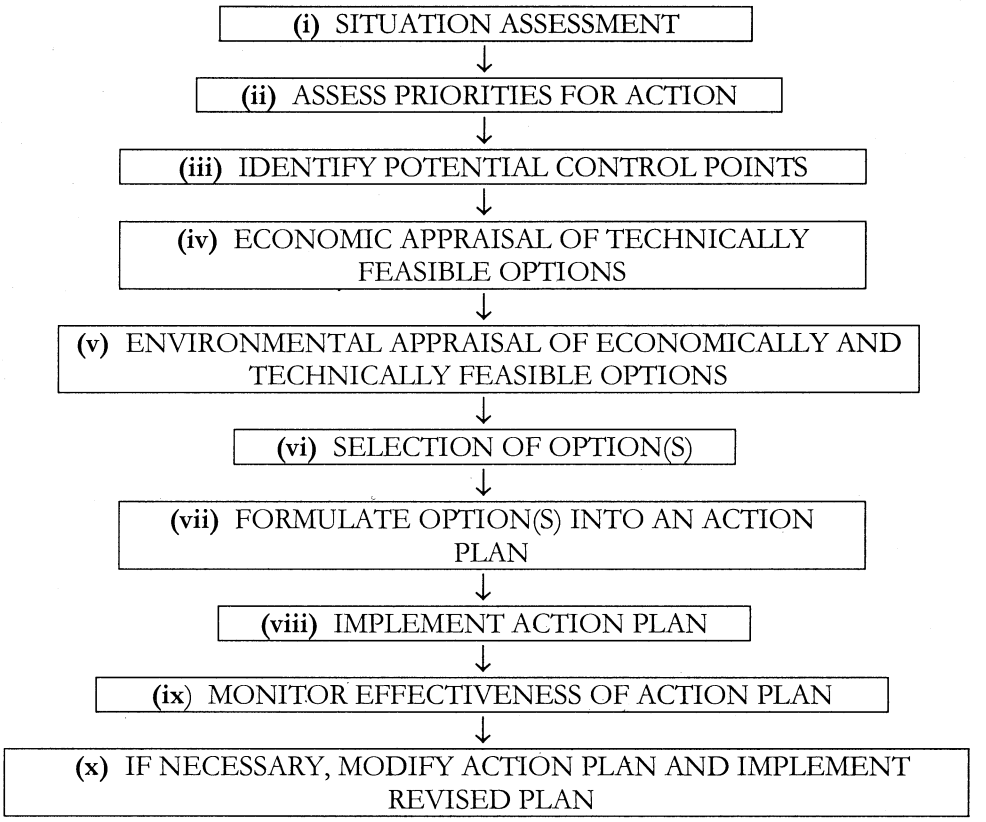

Figure 1. Development and implementation of a strategy for the risk management of cyanobacterial toxins and cells in waterbodies.

general amenity; **(iii) identify potential control options**: this should include short- and long-term control options. Possible control options should be considered and incorporated into a structured decision-making scheme. This should include short- and long-term controls, ranging from e.g. (temporary) interventions to bar water-use and improve water treatment, to in-reservoir controls, and catchment management; **(iv) economic appraisal of technically feasible options**: essential for decision-making according to the scale of the problem, costs of options and costs of inaction; **(v) environmental appraisal of technically feasible options**: some options, e.g. algicides or ferric-dosing for in-reservoir phosphate-precipitation, may have adverse environmental effects; **(vi and vii) select option(s)** and **incorporate into action plan**: the Hazard Assessment Critical Control Point (HACCP) system has been successfully applied in the food industry for 30 years to assess health hazards and provide quality assurance for food safety. There are potential benefits of the HACCP system for the production and distribution of safe drinking water [34]. The HACCP system is also useful in identifying critical control options and following through to their implementation and verification of effectiveness for cyanobacterial cell and toxin control. Limits for control of critical points, e.g. toxin and cell concentrations with reference to provisional GVs and GLs, and phosphorus concentration in the waterbody need to be established; **(viii) implement action plan**: monitoring, analysis, documentation and reporting are key components;**(ix and x) monitor effectiveness of action plan** and **if necessary, modify and implement revised plan**: procedures are needed to determine whether the plan is achieving defined

objectives. Short-term objective attainment, e.g. reduction of toxin concentration in a treated drinking water to below GV, may need to be assessed within hours or days. Long-term objectives e.g. reduction in reservoir nutrient loading, may require assessment over months and from year to year.

Effective risk management for cyanobacterial cell and toxin control requires input by experts in multiple fields (e.g. biology, chemistry, toxicology, medicine, public health, water engineering) and by stakeholder officials (e.g. waterbody owners, water suppliers, environment agencies, land management sector; [3]). Examples of the successful use of short-term controls (e.g. [35-36]) and the findings of a WHO working group [37] may serve as models for wider application, with adjustments to meet local/national needs. It is important that the controls and standards are responsive to experience and advances in research and that they are subjected to periodic review, with modification if necessary (e.g. [38]).

Finally, the eight-hundred year-old proverb "Prevention is better than cure" is entirely appropriate to the long-term risk management of cyanobacterial populations and toxins in drinking and recreational waters. Catchment management, up to basin level, is being developed to reduce eutrophication (e.g. [39-40]). This offers prospects of long-term control to reduce cyanobacterial population development, and toxin production to acceptable levels in waterbodies required for human use.

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