Chapter 35: Risk Assessment Workgroup Report

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Introduction

Risk assessment is a four–stage process used in evaluating the impact of contaminants on the well being of individuals, populations and/or the physical environment. As defined by the National Academy of Sciences (1983), the four components are as follows: hazard identification, dose–response assessment, exposure assessment and risk characterization.

The goal of a risk assessment is to utilize existing information coupled with site specific data to quantitatively characterize the potential risk of a stressor to an identified receptor(s). Quantitative, risk–based estimates of dose–response relationships integrated with exposure scenarios and information on environmental conditions often become the basis for regulatory measures or management policies to protect the population or physical environment from harm. The precision of the guideline value is impacted by the quantity and quality of scientific data available because uncertainty factors are applied in its derivation to compensate for deficiencies in the database. The more comprehensive the database, the lower the uncertainty in the risk assessment and the more precise the value generated.

Risk assessments are one tool used by risk managers when choosing between various options for protecting human health and the environment. They play a significant role in risk management decisions. However, the physical and societal environment is complex. It includes a multitude of

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receptors, each of which may be impacted by any risk management decision. Management decisions almost always involve considerations of a variety of risk factors, competing priorities, societal value systems, and resource limitations. In addition, the decision process may need to consider balancing risks.

The Risk Assessment Work Group was given the overall charge to identify the research needs for both cyanobacteria and their toxins. In order to provide context and focus to their deliberations, the work group addressed the following six charge questions:

- What data are available to derive health–based guideline values (TDI's, RfD's) for cyanobacterial harmful algal blooms (CHABs)?
- What research is needed to reduce uncertainty in health based guidelines?
- What research is needed to minimize the cost and maximize the benefits of various regulatory approaches?
- What are the exposure pathways for the receptors of concern?
- What are the ecosystem–services we want to protect?
- How can regulators best devise a framework for making risk management determinations that incorporates consideration of the characteristics of CHABs, the risk to human health and ecosystem sustainability, and the costs and benefits of CHABs detection and management?

The report that follows will address each of the stated charge questions in sequence culminating with a management framework that integrates concerns for human health protection with those for environmental ecosystems.

Regulatory Context

Cyanobacteria produce toxins that have adverse effects on the health of humans, domestic animals and wild life. These effects range from mild cases of dermatitis to death. Overgrowth of cyanobacteria in surface waters can produce unsightly conditions along the shoreline and in open waters making them unsuitable for recreation (e.g., swimming, fishing, boating). Affected surface waters that are the source for drinking water lead to concern that the toxins may gain access to public drinking water supplies. These are the situations that give rise to the need to consider possible regu-

latory controls for the cyanobacteria and their toxins under the US Safe Drinking Water Act (SDWA) and Clean Water Act (CWA) statutes. Offensive taste and odors associated with cyanobacteria can also make water unsuitable for drinking.

Contaminant Candidate List (CCL) and National Primary Drinking Water Regulations (NPDWRs)

The SDWA, as amended in 1996, required the US Environmental Protection Agency (U.S. EPA) to establish a list of contaminants to aid the Agency in regulatory priority setting for the drinking water program and to reconstitute that list every five years. EPA published the first Contaminant Candidate List (CCL) on March 2, 1998 (63 FR 10273, U.S. EPA, 1998). The second CCL was published as final February 24, 2005 (70 FR:9071, US EPA 2005). Cyanobacteria and their toxins were included on the first CCL and carried over to CCL2.

The SDWA requires EPA to make regulatory determinations for no fewer than five contaminants from the CCL list within three years of its publication. The criteria established by the SDWA for a positive regulatory determination are as follows:

1. The contaminant may have an adverse effect on the health of persons.
2. The contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern.
3. In the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

Positive findings for all three criteria must be met in order to make a determination on whether to regulate. A decision not to regulate is considered a final Agency action and is subject to judicial review.

The inclusion of cyanobacteria and their toxins on the first and second CCL is one factor that fuels the need for research. As indicated by the decision criteria, regulatory determination for contaminants requires the EPA to evaluate the health impact of the contaminants and quantify the dose–response relationship through a formal health risk assessment process. Monitoring data from public water systems must also be available along with effective treatment technologies.

There are major data deficiencies and barriers that prevent the US EPA from making regulatory determinations for the cyanobacterial toxins at this

time. At present there are insufficient health effects data for many of the cyanobacterial toxins (although from a European standpoint, it could be argued that there are sufficient data to warrant a precautionary approach in the absence of comprehensive data). Analytical methods with the sensitivity to detect many of the contaminants at concentrations of possible health concern and suitable for national monitoring of public water systems in the US have yet to be developed. Accordingly, these data gaps and others have been highlighted as research needs for the SDWA.

The data on occurrence in drinking water are gathered through Unregulated Contaminant Monitoring Rules (UCMR). The SDWA grants the US EPA the authority to require large (serving >10,000) National Pubic Drinking Water Systems (NPDWS) and a representative sample of small systems to monitor for no more than 30 unregulated contaminants over a one year period. Samples are collected quarterly for surface water systems and semiannually for ground water systems. The monitoring results are reported to the EPA in the National Contaminant Database. Methods development and inclusion of a contaminant in the UCMR are closely coordinated with the CCL. EPA can issue a new list of contaminants for UCMR monitoring every 5 years. Methods development problems have thus far prevented inclusion of cyanobacterial toxins in the UCMR.

In cases where EPA determines under the CCL program that a regulation is necessary, the regulation should be proposed within 24 months of the regulatory determination and finalized within eighteen months of the proposal. As required by the SDWA, a decision to regulate commits the EPA to publication of a Maximum Contaminant Level Goal (MCLG), Maximum Contaminant Level (MCL), and promulgation of a National Primary Drinking Water Regulation (NPDWR) for that contaminant. EPA can also determine that there is no need for a regulation when a contaminant fails to meet one of the statutory criteria.

In addition to health effects studies and analytical method development, data needs that underlie the development of the NPDWR include suitable treatment technologies for large and small systems and the economic data required for cost–benefit assessments. While there are technologies available for treatment, data gaps exist in both the treatment technologies and cost–benefit areas as they apply to cyanobacteria and their toxins.

Clean Water Act Requirements for Ambient Waters

The objective of the US Clean Water Act (CWA) is to restore, maintain and protect the chemical, physical and biological integrity of the nation's waters. The nation's waters include navigable rivers, streams, lakes, natu-

ral ponds, wetlands, and marine waters. Under this statute, the US EPA sets water quality criteria and technology–based effluent guidelines to protect water quality. States set specific water quality–based standards. The standards provide a means for achieving the goals of the CWA.

There are 3 components of a state's water quality standards: uses, criteria, and an anti–degradation policy. States determine use designations for the protection and propagation of fish, shellfish and wildlife, recreation, drinking water, agricultural and industrial uses, as well as other uses such as navigation, special habitats such as coral reef protection, oceanographic research, aquifer protection, marinas, and hydroelectric power. Uses are determined through a use attainability analysis that involves a water–body survey, waste load allocation, and economic analysis.

Water quality criteria establish a limit on a pollutant or on a condition of a water body. The criteria are intended to protect the designated use of that water and will trigger a management action if exceeded. There are two types of water quality criteria: numeric and narrative. The numeric criteria are developed for specific chemicals or microbial agents. The narrative criteria are set for contaminants that are more difficult to quantify. For example, "surface water shall be free from floating, non–petroleum oils of vegetable or animal origin."

The types of criteria include:

- Aquatic life criteria for the protection of aquatic plants and animals
- Human health criteria protective for water and fish consumption
- Biological threshold or guideline levels describing the desired biological integrity of waters
- Sediment criteria to assess material that may pose a threat to human or ecological health.

An anti–degradation policy is designed to protect existing uses, describes water quality characteristics, and includes implementation measures to protect designated uses.

Existing Regulatory Guidelines

Presently there are no US regulations or guidelines that apply to cyanobacterial toxins under the SDWA or CWA. Several US States have implemented standards or guidelines that apply to recreational water uses. The World Health Organization has issued a guideline that applies to microcystin LR and guidelines or standards have been established by a number

of countries around the globe. Relevant standards and guidelines are discussed below.

U.S. EPA Secondary Standards

The US EPA has established secondary Maximum Contaminant Levels (SMCLs) for Drinking Water Contaminants that apply to factors such as color, taste and odor which may be considered relevant to cyanobacteria. SMCLs are not regulatory; however, some may be adopted as regulations by individual states. Existing SMCLs for color and odor may have some utility as mechanisms to stimulate action by states in situations where cyanobacteria affect the color or odor of drinking water.

The SMCL for color is 15 color units (CUs). A CU is defined as a color that is objectionable to a significant number of users. For comparison, a CU of 5 represents color that can be detected in a bathtub and a CU of 30 can be detected by all users and is considered objectionable. The SMCL of 15 CU has been set to prevent the majority of consumer complaints regarding color.

The SMCL for odor is 3 threshold odor numbers (TON). A TON of water is the dilution factor required before the odor is minimally perceptible. A TON of 1 indicates odor–free water, while a TON of 3 indicates that a volume of the test water would have to be diluted to 3–times its volume before the odor became minimally perceptible. Some sources cause odors that may be considered by consumers to be less tolerable than others of equal intensity, and some affect taste as well as odor. Water that is relatively odor–free helps to maintain consumer confidence. The decay of algae in water can cause a disagreeable musty odor in the water. Oxidation and activated carbon are two treatment methods for controlling odors in drinking water.

State Guidelines

In the absence of U.S. EPA guidance values regarding cyanotoxins, most states have looked to the World Health Organization (WHO) and the latest research in Australia for suggested drinking and recreational water use guidelines. Water and algal testing, health alerts, and subsequent beach and lake closures involving cyanobacteria bloom waters have increased in recent years with widely publicized dog deaths in waters of New York, Nebraska, Wisconsin and Minnesota. States such as Maryland and Virginia have used WHO guidelines for cyanobacteria and microcystins in support of beach closures. Nebraska and Iowa have implemented 15 ppb microcystin guideline values for issuing recreational use health alerts on lakes

with blooms. The Vermont State Health Department has set a standard of 6 ppb microcystin for reopening a beach after a toxic bloom event. Cyanobacteria derived food supplements are big business but no national guidance exists for acceptable contaminant levels such as microcystins in these food supplements. The Oregon Health Department has adopted a 1ppm maximum acceptable concentration.

World Health Organization (WHO)

There are insufficient data to determine health–based guidelines or standards for even a representative selection of the toxins. The best studied is microcystin LR, although uncertainties exist, particularly with regard to its tumour promoting capability. WHO proposed a provisional guideline value in 1998 for microcystin LR, based on the data generated by the United Kingdom (UK) National Research Programme.

The WHO will develop additional guidelines for other toxins when there are adequate data, but the production of guideline values for an increasing list of toxins is seen as potentially counter–productive. The WHO (WHO, 2003) paragraph in Volume 1 of the revised Guidelines reads as follows:

> Cyanobacteria occur widely in lakes, reservoirs, ponds and slow flowing rivers. Many species are known to produce toxins, a number of which are of concern for health. There are many cyanotoxins, which vary in structure and may be found within cells or released into water. There is wide variation in the toxicity of recognised toxins (including amongst different varieties of a single toxin, e.g., Microcystins) and it is likely that further toxins remain unrecognized.
>
> The health hazard is primarily associated with overgrowth, (bloom) events. Such blooms may develop rapidly and they may be of short duration. In most circumstances, but not all, they are seasonal.
>
> Analysis of these substances is also difficult although rapid methods are becoming available for a small number, e.g. microcystins, in addition analytical standards are frequently not available. The preferred approach is therefore, monitoring of source water for evidence of blooms, or bloom forming potential, and increased vigilance where such events occur.
>
> A variety of actions are available to decrease the probability of bloom occurrence and some effective treatments are available for removal of cyanobacteria or cyanotoxins. For these reasons, monitoring of cyanotoxins is not the preferred focus of routine monitoring and is primarily used in response to bloom events. Whilst guideline values are derived where sufficient data exist, they are intended to inform the interpretation of data from the above

monitoring and not to indicate that there is a requirement for routine monitoring by chemical analysis.

Australia and New Zealand

Cyanobacterial blooms are common problems in Australia and New Zealand. Accordingly, the Australian and New Zealand Governments have been leaders in establishing risk management policies for CHABS and guideline values for cyanobacterial toxins in recreational waters and drinking water (See Burch, this volume). Australia has a drinking water standard for total microcystins (1.3 μg L^{-1}) based on the toxicity of microcystin LR. New Zealand has a guideline for the presence of cyanobacteria in drinking water (less than 1 cyanobacterium per 10 ml of sample) and provisional values for several anatoxins (anatoxin = 6 μg L^{-1}, anatoxin–a = 1 μg L^{-1}, homoanatoxin = 2 μg L^{-1}) mycrocystin LR (1 μg L^{-1}), cylindrospermopsin (1 μg L^{-1}), nodularin (1 μg L^{-1}), and saxitoxin–equivalents (3 μg L^{-1}).

The Australian guidelines for recreational waters are based on total microcystins or cell counts. Beach closure is recommended if either of the two following conditions are met:

- **Condition 1**: total microcystins at a concentration of either 10 μg L^{-1} total microcystins or >50,000 cells mL^{-1} toxic M. aeruginosa or a biovolume equivalent of >4 mm^3 L^{-1} for the combined total of all cyanobacteria where a known toxin producer is dominant in the total biovolume.
- **Condition 2**: either the total biovolume of all cyanobacterial material exceeds 10 mm^3 L^{-1} or scums are consistently present.

United Kingdom

The water industry in England and Wales was privatized in 1989 and the Government's technical regulator for the industry is the Drinking Water Inspectorate (DWI). The Water Supply (Water Quality) Regulations (2000), which the DWI enforces, do not include algal toxins as a specific parameter. However, the Regulations require that no substance may be present in drinking waters at concentrations that would cause a risk to health. In this respect water utilities would be required to monitor for algal toxins, if a risk situation existed. In the UK, water utilities currently base that risk assessment on the potential for algal loadings to compromise treatment processes and contaminate supplies.

The current UK view is that setting a standard based on the few toxins for which there were adequate data could be construed as potentially misleading because the absence of a particular toxin does not indicate the absence of a problem. In addition the potential for changes in the presence and absence of toxins means that sampling to give an appropriate level of reassurance could be problematical. Prevention of bloom formation is the best way forward, although this may present some difficulties. Control of eutrophication is an important issue for the Environment Agency in the UK and at the European level. It will be an important consideration in the Implementation of the European Union's Water Framework Directive.

Other Countries

A number of countries have adopted the WHO drinking water guideline for microcystins (See Busch, this volume). Brazil also has guideline values for saxitoxin equivalents and cylindrospermopsin. Germany and the Netherlands have guidelines for recreational waters based on microcystin concentrations. France's guidelines for recreational waters follow the cell count approach recommended by the WHO (Level 1: <20,000 cells mL^{-1}, Level 2: 20,000 to 100,000 cells mL^{-1}, Level 3: Presence of scum). The risk to human health increases with the level.

Charge 1

What data are available to derive health–based guideline values (TDIs; RfDs) for Cyanobacterial Harmful Algal Blooms (CHABs)?

As discussed previously, dose–response assessment involves describing the quantitative relationship between the amount of exposure to a substance and the extent of toxic injury or disease. Data are derived from animal studies or, less frequently, from studies in exposed human populations. The risks of a substance cannot be described with any degree of confidence unless dose–response relations are quantified, even if the substance is known to be toxic.

Health–based guidelines are based on quantitative values that describe an estimate of the exposure to the human population (including susceptible subgroups) that is likely to be without an appreciable risk of adverse health effects over a lifetime. These values are generally derived from a statistical lower confidence limit on the benchmark dose (BMDL), a no–observed–adverse effect–level (NOAEL), a lowest–observed–adverse–effect level

(LOAEL), or another suitable point of departure, with uncertainty/variability factors applied to reflect limitations of the data used.

The data available for derivation of health–based guidelines for cyanobacterial toxins are very limited. Due to the stringent data quality requirements set forth by the US Information Quality Act for the derivation of quantitative values, many available toxicity studies are deemed inappropriate for consideration due to one or more data quality failures. Additionally, the US EPA follows published guidelines for quantitative dose–response assessment and much of the available toxicity data are inherently insufficient for guideline value determination. Many of the toxicity studies that have been conducted on cyanobacterial toxins utilized cell extract preparations with unquantified total toxin levels rather than employing known quantities of purified toxin. As most cell extracts contain more than one toxin and, at equivalent doses, have been shown to be more potent than purified toxin (most likely due to additive or synergistic effects), studies that employ cell extracts are deemed inappropriate for single–chemical quantitative dose–response assessment. The single–chemical toxicity data currently available for potential guideline values for oral exposure to anatoxin–a, cylindrospermopsin and microcystin LR are described in Table 1.

As discussed above, there are inherent limitations in establishing health–based guidelines for individual toxins. There is a wide variation in the toxicity of known toxins, multiple toxins are produced during a bloom event, and it is likely that previously unrecognized toxins will continue to be identified. It is important to recognize that the development of health–based guidelines for individual toxins is simply a first step in the overall risk assessment of CHABs. Further exploration into the potential use of approaches such as a Toxicity Equivalency Factor (TEF) or quantitative structure–activity relationship (QSAR) is warranted.

Table 1. Summary Results of Major Studies for Oral Exposure of Experimental Animals to Anatoxin–a, Cylindrospermopsin and Microcystin–LR

Species	Sex	Dose (µg kg^{-1}–day)	Exposure Duration	NOAEL (µg kg^{-1}–day)	LOAEL (µg kg^{-1}–day)	Responses	Comments	Reference
Anatoxin–a								
Short–term Exposure								
Mouse	M/F	1200, 2500, 6200, 12300	5 days	ND	ND	Mortality at doses of 6200 & 123000	Range–finding study for 28–day study (see below);No control group	Fawell and James, 1994; Fawell et al., 1999a
Mouse	M/F	0, 100, 500, 2500	28 days	100	500	Mortality; no other significant treatment–related effects	Treatment–related mortality can not be ruled out; true NOAEL may be 2500	Fawell and James, 1994; Fawell et al., 1999a
Subchronic Exposure								
Rat	F	0, 51, 510	7 weeks	510	ND		No changes in any monitored parameters were reported	Astrachan and Archer, 1981; Astrachan et al., 1980

Species	Sex	Dose (µg kg^{-1}–day)	Exposure Duration	NOAEL (µg kg^{-1}–day)	LOAEL (µg kg^{-1}–day)	Responses	Comments	Reference
Developmental Toxicity								
Mouse		0, 2500	GD 6–15	2500	ND			Fawell and James, 1994; Fawell et al., 1999a
Cylindrospermopsin								
Short–term Exposure								
Mouse	NR	NR	14 days	50	150	Lipid infiltration in liver	Report of study provides limited detail	Shaw et al., 2000, 2001
Subchronic Exposure								
Mouse	M	0, 30, 60,120, 240	11 weeks	30	60	Increased relative kidney weight		Humpage and Falconer, 2003
Microcystin–LR								
Short–term Exposure								
Rat	M	0, 50, 150	28 days	ND	50	Slight to moderate degenerative and necrotic hepato-cytes with hemor-rhages		Heinze, 1999

Species	Sex	Dose (µg kg^{-1}–day)	Exposure Duration	NOAEL (µg kg^{-1}–day)	LOAEL (µg kg^{-1}–day)	Responses	Comments	Reference
Subchronic Exposure								
Mouse	M/F	0, 40, 200, 1000	13 weeks	40	200	Minimal/slight chronic inflammation with haemosiderin deposits and single hepatocyte degeneration		Fawell et al., 1999b
Chronic Exposure								
Mouse	F	0, 3	18 months	3	ND	No effects on survival, body weight, hematology, serum biochemistry, organs, or histopathology	Minor changes in ALP and cholesterol deemed insignificant	Ueno et al, 1999
Mouse	NR	80	80–100x over 28 weeks	ND	ND	Light injuries to hepatocytes in the vicinity of the central vein	Only liver examined; only 3 control animals	Ito et al., 1997

Species	Sex	Dose (µg kg^{-1}–day)	Exposure Duration	NOAEL (µg kg^{-1}–day)	LOAEL (µg kg^{-1}–day)	Responses	Comments	Reference
Monkey	NR	20–80	47 weeks	ND	ND	No clinical signs or effects on hematology, serum biochemistry, histopathology	Report of study provides limited detail	Thiel , 1994

ND = Not determined
NR = Not reported

Charge 2

What research is needed to reduce uncertainty in health–based guidelines?

Hazard and Dose Response Data Needs

Hazard assessment is the characterization of the adverse effects on human health caused by oral, inhalation or dermal exposure. Effects can range from short–term reversible dermatitis to death from respiratory paralysis or cancer. Hazard identification is descriptive; dose–response assessment is quantitative. The hazard identification includes a description of all of the adverse health effects caused by a toxic substance, independent of the doses causing the effects. On the other hand, the dose–response assessment identifies whether or not effects are manifest at specific doses and the impact of an increase in the dose on the appearance and/or severity of the effects. It is rare for any single study to provide a complete picture of potential effects for any contaminant and the relationship of those effects to dose. Generally, a suite of studies is necessary to fully elucidate the potential for hazard and its relation to dose. At present there are numerous deficiencies in the database that impede a high confidence hazard and dose–response assessment for the cyanobacterial toxins (see Health Effects Work Group Report and Ecosystem Effects Work Group Report this volume). Accordingly, the Risk Assessment Work Group has focused on how filling critical data gaps in the hazard and dose–response database for the cyanobacterial toxins would reduce the uncertainty in the risk assessment (Table 2). This approach to research prioritization will help to improve the precision of the risk assessment, the efficiency of the research plan and the risk management costs.

After examining the available data on hazard, dose–response, and exposure pathways, the Work Group developed a matrix (Table 2) to illustrate how the execution of specific types of studies will contribute to reductions in uncertainty in the risk assessment. An "X" in a given cell designates the importance of the study to reducing uncertainty. A question mark in a cell suggests uncertainty in the need for the study at this time. Notes provide additional information on the type of study suggested and its contribution to the database needs.

Table 2. Cyanobacterial Toxins: Research Needs Categorized Based on Reducing Uncertainty in the Risk Assessment

Related Uncertainty Factor (UF)	**Intra– and Interspecies Factors**		**Duration Uncertainty**		**Data Deficiencies Uncertainty**	**Notes**
Toxin	***Kinetics***	***Dynamics***	***Acute Toxicity***	***Subchronic/ Chronic Toxicity***	***Developmental/ Reproductive/ Other Toxicity***	
Reduction in UF	*3→1*	*3→1*	*NA*	*10→3→1*	*10→3→1*	*Reduction in some UFs can be achieved in increments*
Microcystins	X	X		X	X	–Absorption, Distribution, Metabolism, and Excretion (ADME) studies needed. Only if data are adequate to model tissue dose for the target organ(s) will it be possible to reduce the toxicokinetic UF for inter– and/or intraspecies adjustments. –Data are needed regarding the kinetic and dynamic differences among individual microcystins (e.g. LA,RR,LI, RI, YR) –A cancer bioassay is needed –There are some developmental toxicity data. There are no reproductive toxicity studies

Related Uncertainty Factor (UF)	Intra– and Interspecies Factors		Duration Uncertainty		Data Deficiencies Uncertainty	Notes
Toxin	***Kinetics***	***Dynamics***	***Acute Toxicity***	***Subchronic/ Chronic Toxicity***	***Developmental/ Reproductive/ Other Toxicity***	
Reduction in UF	*3→1*	*3→1*	*NA*	*10→3→1*	*10→3→1*	*Reduction in some UFs can be achieved in increments*
Anatoxin A	X	X	X	X	X	– ADME Studies needed. Only if data are adequate to model tissue dose for the target organ(s) will it be possible to reduce the toxicokinetic UF for inter– and intraspecies adjustments. –A subchronic study is needed. For longer–term and lifetime risk values –The acute toxicity data are marginally adequate for a short term value. Identify whether the dog is a good model for acute toxicity.
Anatoxin A(s)	X					–Risk assessments, at least for short term effects can utilize data on organophoaphates and QSAR. ADME data would be helpful in utilizing the QSAR application to risk assessment

Related Uncertainty Factor (UF)	Intra– and Interspecies Factors		Duration Uncertainty		Data Deficiencies Uncertainty	Notes
Toxin	***Kinetics***	***Dynamics***	***Acute Toxicity***	***Subchronic/ Chronic Toxicity***	***Developmental/ Reproductive/ Other Toxicity***	
Reduction in UF	*3→1*	*3→1*	*NA*	*10→3→1*	*10→3→1*	*Reduction in some UFs can be achieved in increments*
Cylindrospermopsin	X			X	X	–ADME Studies needed. Only if the data are adequate to model tissue dose for the target organ(s) will it be possible to reduce the toxicokinetic UF for inter– and intraspecies adjustments –Based on mutagenicity, a chronic bioassay is needed –Developmental data could help reduce the short term data uncertainty. –A reproductive toxicity study will allow for an additional decrease in database uncertainty
Saxitoxin	?	?	X	X	X	In general, data are limited making it difficult to conduct a risk assessment. While there are human intoxication data from marine exposures, a complete battery of studies is suggested.

Related Uncertainty Factor (UF)	Intra– and Interspecies Factors		Duration Uncertainty		Data Deficiencies Uncertainty	Notes
Toxin	***Kinetics***	***Dynamics***	***Acute Toxicity***	***Subchronic/ Chronic Toxicity***	***Developmental/ Reproductive/ Other Toxicity***	
Reduction in UF	*3→1*	*3→1*	*NA*	*10→3→1*	*10→3→1*	*Reduction in some UFs can be achieved in increments*
BMAA						Is important to study fate during drinking water treatment before investing in additional toxicological research

An "X" in a cell indicates that filling the indicated data need would have a strong potential to reduce uncertainty in the risk assessment. An "?" in a cell indicates that the impact of filling the indicated data deficiency on uncertainty cannot be determined at this time.

In the case of microcystin–LR, the chronic and reproductive toxicity studies will have the most significant impact on reducing uncertainty because between the two, they have the potential to reduce the overall uncertainty by a factor of 10. To the extent that studies on the dynamics of the toxicity were incorporated in the chronic and reproductive toxicity studies, additional reductions in uncertainty might be obtained. In the case of the other microcystin congeners the most productive research relative to reductions in uncertainty will be that supporting quantitative measures of toxic equivalence to microcystin–LR including kinetic and dynamic parameters, because the total data base for the other microcystin congeners is very limited compared to that for microcystin–LR (Dietrich et al. this volume).

Subchronic and developmental toxicity studies are those likely to have the most immediate impact on reducing the uncertainty for anatoxin A. There are several moderately informative studies of the acute neurotoxicity of this compound but studies that evaluate a more comprehensive set of health endpoints following moderate duration exposures will make a significant addition to the database. Anatoxin A(s)'s toxic activity appears to be qualitatively and quantitatively comparable to organophosphate cholinesterase inhibitors. Accordingly, the development of a QSAR model based on analysis of the structure and functional groups of organophosphate pesticides, would be a useful approach to predicting hazard and dose–response properties for this toxin.

Cylindrospermopsin tested positive for mutagenicity in several studies. Thus, completion of a long term cancer bioassay combined with analysis for other long term toxic effects is a definitive data need for this compound. Such a study has the potential to reduce a chronic duration uncertainty factor from a 10 to a 1. A reproductive study with integrated evaluation of developmental endpoints could produce an additional three–or ten–fold reduction in uncertainty.

The Work Group felt that the saxitoxins and beta–methylamino–L–alanine (BMAA) were presently of low priority for research on cyanotoxins. Regulatory and action limits for PSP toxins are well established in the international community (Anderson et al. 2001). The supporting work has been based primarily on shellfish poisoning concerns from estuarine and marine dinoflagellates producing chemicals of the saxitoxin family. However, freshwater cyanobacteria have been recognized to produce saxitoxin as well (e.g., Cylindrospermopsin, Aphanizomenon, Lyngbya). Because the database on fresh water saxitoxins is very limited, to single out one particular study type that would have the greatest impact of reducing uncertainty in the risk assessment is difficult. However, the use of state–of–the–art analytical methodology allows quantitation of saxitoxins and neos-

axitoxins in the freshwater environment and thus the comparison with levels of concern for the marine environment. In the case of BMAA, its identification as a cyanobacterial toxin is quite recent (Cox et al. 2005). Thus, much more must be learned about its environmental fate and transport before singling out any particular type of study that would have the greatest impact on uncertainty reduction in the risk assessment process. However, most recent information does suggest BMAA may be contained in copious quantities in cyanobacteria food supplements, i.e. *Spirulina sp.* And *Aphanizaomenon flos–aquae* based products (Dietrich et al. this volume), thus suggesting that the prioritization of BMAA with regard to research efforts may have to be revisited if these findings are confirmed by other work groups.

One cross cutting problem in conducting toxicological research for all of the cyanotoxins in Table 2, is the difficulty and expense of obtaining sufficient pure toxin for use in short or long term animal studies. Both chronic and reproductive toxicity studies require as an absolute minimum 20 animals of each sex per dose group and sufficient toxin to dose the animals for up to two years. In addition, although chronic and reproductive studies with single toxins may improve the database on the single toxins species, they do not resolve the problems of potential additive or synergistic toxicity. Indeed, as pointed out in Dietrich et al. (this volume) exposure to multiple toxins in bloom events appears more likely the norm rather than the exception. Consequently, and in support of WHOs' stance on additional guideline values, frequent monitoring and vigilance with regard to blooms and presence of toxins may be a better approach for most risk scenarios (e.g. recreational or drinking water). However, because guideline values present authorities with possibilities of legal enforcement, lack thereof and substitution with monitoring and vigilance may not suffice for human health protection. This may be exemplified by cases where cyanobacterial toxin exposure of humans occurs via contaminated food and food supplements.

Contrary to the direct exposure of humans to cyanobacterial toxins via contaminated water, the risk situation involving exposure via food and food supplements is much more complex. Worst–case exposures can be interpolated from assumed daily or weekly consumption of specific food sources (e.g. fish, crayfish, shellfish, vegetables, salads, etc.) for the general populace as well as for populations at high risk (e.g. indigenous tribes predominantly existing on a specific food source) (Dietrich and Hoeger 2005). However, the potential human toxin exposure via food that provides the basis for risk calculations is also largely determined by the degree of toxin contamination of a given food source as well as by the bioavailability of the toxin from the food type. Furthermore, bioaccumulation of

cyanotoxins in the food chain, as is the case with BMAA, may provide for an additional element of risk (Cox et al. 2005). The occurrence of multiple toxins within the same food chain and the potential for additive or synergistic effects complicates hazard identification. The lack of appropriate guidance by authorities (e.g. WHO or federal or state laws) will prohibit local authorities from implementation and enforcement of measures intended to reduce human health risks.

Analytical Methods Research Needs

The challenges posed by cyanotoxins in water are in many respects different from those posed by other chemical toxins. Whether the toxin is present in the source water or generated during treatment, occurrence of a concentration posing an acute risk is unlikely, unless a contamination event has occurred. Furthermore, once seasonal effects and the influence of treatment processes have been characterized, variations in the concentrations of many chemical toxins are reasonably predictable.

The cyanotoxins are possibly unique among chemical toxins in that they can cause serious illness or death rapidly at concentrations that occur naturally in the environment. Although their presence can be anticipated through surveys of algal populations, cyanotoxin concentrations in water are unpredictable and may change quickly.

Two distinct analytical requirements can be distinguished: (i) methods to characterize the concentrations of specific cyanotoxins or their congeners and (ii) methods to detect the toxins at levels to support assessment of a risk to health. These requirements coincide if there is only one cyanotoxin present. However, different cyanotoxins, or congeners of the same cyanotoxin type may be present and the risk posed by the different toxins or their congeners may be different. Furthermore, where mixtures of toxins are involved, an assessment of the overall risk to health may be of more immediate interest (toxic equivalency concept) than quantification of individual compounds.

Requirement (i) applies in studies of removal or inactivation of cyanotoxins in water treatment processes, in surveys of concentrations in environmental waters, or in checking compliance against guidelines or standards for specific cyanotoxins. Quantitative analysis for cyanotoxins has been an active branch of analytical chemistry since the mid 1980s. In Australia and the UK, compendiums of standard methods have now been published (Anon, 1998; Brenon and Burch, 2001) and an output from the European Union's Framework Research Programmes includes a mono-

graph on monitoring and analysis (Meriluoto and Codd, 2005). Nevertheless, the extent of validation of methods of analysis varies.

Although the performance of methods for microcystins, nodularins, cylindrospermopsin and saxitoxins have been demonstrated in inter–laboratory studies, there is a need for better characterization of the performance of methods for anatoxins and BMAA. Confidence in analytical methods would be further improved by the application of standard protocols to assess the performance characteristics of the methods.

Requirement (ii) is more likely to be of interest when exposure to cyanotoxins through recreational use of water or through consumption of fish and shellfish is being considered. If water treatment processes are absent or have been compromised in some way, there may be a concern for health risks.

The HPLC and MS based methods that have been developed for individual cyanotoxins and their isomers are characterized by low daily throughput. The rate determining steps are the sample transport time from remote locations and the time needed to prepare extracts of samples for analysis. The timescale between commissioning the taking of a sample and receiving the results of analysis is typically days to weeks. This may be unacceptable if health risks are involved and especially so if the result could determine whether restriction of access to water or sale of food is necessary. The problems of poor speed of response are compounded if there is change in the toxicity characteristics of algal blooms, for example, the species(s) of algae predominating in the bloom and consequently the type(s) of toxin(s) present change over relatively short periods of time.

Where a rapid speed of response is essential, analysis will need to be carried out onsite, or in an adjacent location where facilities may fall far short of what is expected in a laboratory environment. This creates a demand for simple to use kits for specific cyanotoxins, or the entity that confers toxicity (e.g. the alanine, aspartate, alanine, aspartate (ADAD) amino acid components of microcystins and nodularins) (Fischer et al. 2001; Zeck et al. 2001). Other possibilities include *in vitro* systems such as the acetylcholine esterase or protein phosphatase inhibition assays. A promising format for rapid screening tests would appear to be broad spectrum Enzyme–Linked Immunosorbent Assay (ELISA) techniques with universal cross–reactivity to the numerous toxin congeners. ELISA test kits are already available for Microcystins and for toxins causing Amnesic Shellfish Poisoning.

There is a need for research to support development of a wider range of rapid test systems to provide the data necessary for managing exposure to cyanotoxins. Managers will need to be confident about the consistency and comparability of data generated by different operators in different loca-

tions. This implies the need for independent assessment of the performance of test kits using recognised test protocols and for the results of these assessments to be placed in the public domain.

In order to evaluate the performance of test kits it will also be necessary to develop stable standards suitable for distribution in performance studies.

Research Prioritization to Reduce Uncertainty in Health–Based Guidelines

The Work Group recognized that the prioritization of research needs is as important as their identification. Accordingly the group further characterized the hazard, dose–response, analytical method, and treatment technology needs identified above according to whether they should be targeted for immediate study or classified as longer term research needs. The Work Group suggestions are summarized below.

The Work Group suggestions were selected with the objective of obtaining the maximum research output with the smallest monitary investment by answering those questions, on exposure and toxicity that, at the moment appear to be the most pressing. Each study suggested will provide some answers and undoubtedly also raise new questions. Accordingly, the suggestions must be revised and reordered as additional data become available.

Near-term Research Priorities

- Microcystins
  - Kinetic and Dynamic equivalences between congeners
  - Certified analytical methods for monitoring
  - Monitoring of finished drinking water
- Anatoxins
  - Subchronic study for Anatoxin a
  - QSAR for Anatoxin A(s) based on organophosphate data
  - Impact of treatment technologies on removal
- Cylindrospermopsin
  - Occurrence data for ambient and drinking water
  - Developmental effects

- General
  - Kinetic studies
  - Suitability of extract studies for Clean Water Act guidelines

Long-term Research Priorities

- Microcystins
  - Preparation of enough pure material to conduct a long term study
  - Chronic cancer bioassay
- Anatoxins
  - Evaluation of dogs as an appropriate model for human toxicity
  - Long term effects of A(s) variant
- Cylindrospermopsin
  - Preparation of enough pure material to conduct a long tern study
  - Chronic cancer bioassay
  - Bioconcentration studies
- General
  - Toxin interactions in mixtures
  - Factorial design studies

Charge 3

What research is needed to minimize the costs and maximize the benefits of the various regulatory approaches?

The costs and benefits of preventing cyanobacterial blooms is very dependant on the nature of the water body and its uses. It is therefore difficult to generalize (See Steffenson this volume). However, the efficacy of watershed management techniques have been demonstrated (See Piehler this volume).

The cost of engineering works to control or prevent blooms, while site specific, is generally the easiest component to assess. Assessing the impact of blooms on aesthetic and environmental aspects and the value of controlling or preventing those impacts is the most difficult area. The impacts may affect a wide range of activities including tourism, fishing and agriculture. Further research is required to quantify these costs and benefits. There are also less tangible aspects such as the value one places on maintaining natural ecosystems. The willingness of the community to pay for the preventative measures may be the best guide of the value of preventing cyanobacterial blooms.

When comparing the relative costs and benefits of alternative control measures, the outcome will be influenced by how broadly the assessment is made. Increasingly there will be an expectation that the cost benefit analysis includes the broader social and environmental aspects and consideration of the sustainability of the options. Issues such as energy use and green house gas production may become more important in the future and may make some of the engineering options less attractive.

Charge 4

What are the exposure pathways for the receptors of concern?

In addressing this question, the workgroup felt it was important to first articulate what constitutes a bloom as a way of providing context for various exposure pathways (see also Fig. 2a and 2b).

What is a bloom?

There have been continuing efforts to develop a definition for what designates an algal bloom. A bloom as an ecological phenomenon has characteristics of magnitude (biomass and abundance), duration, frequency, spatial extent, and composition. Blooms collectively represent part of a trophodynamic process with regional, seasonal and species–specific issues (Smayda 1997). In a traditional sense of the plankton science, 'bloom' has reflected the historical focus of marine phytoplankton ecologists on the annual, high biomass, diatom dominated spring (upwelling) abundances or biomass (Smayda 1997). 'Harmful Algal Bloom' can refer to "blooms of toxic and non–toxic algae that discolor the water, as well as to blooms which are not sufficiently dense to change water color but which are dangerous because of the algal toxins they contain or the physical damage they cause to other biota." (Anderson et al. 2001). This definition reflects the diversity of phytoplankton now recognized for harmful effects and focuses on population phenomena being observed. We can extend the concept to include cyanobacteria as Falconer (1998) noted that when the body of water is visibly colored by cyanobacteria, then is it considered a bloom and cyanobacteria probably number more than 10,000 cells/ml.

While the discussion and debate continues on an all–encompassing definition for bloom, we can functionally apply suggested guidance values available or being developed for the species of interest. With specificity toward species, habitats, regions, population and trophodynamics involved,

and no one definition yet suitable to all bloom conditions, we increasingly find the use of abundance (cell density) and toxin thresholds reflected in natural resource management programs. Cell counts and toxin concentrations for cyanobacteria linked with no effect, sub–chronic, chronic and lethal thresholds are of interest in managing waterways for protecting human health. Potential impacts are increasingly being defined with respect to counts that trigger toxin testing in shellfish, restricting recreational activity or limiting agricultural uses such as cattle watering. Cyanotoxin thresholds are increasingly desired or available for guidance with drinking water, fish or shellfish harvest and their consumption.

Threshold definitions are most frequently developed for the protection for human health. Definitions of thresholds protecting ecosystem integrity and services, however, further challenge our research needs. Notable consequences of blooms have included wildlife, fish, shellfish and human health effects both sublethal and lethal. Indirect effects of blooms are many such as reductions in water clarity that impact light to submerged aquatic vegetation, effects on the dissolved oxygen dynamics that can lead to fish kills in shallow water zones, organic matter sinking and leading to hypoxic or anoxic conditions developing in deep water, biogeochemical changes in nutrient pathways, and synergistic or allelopathic effects of toxins. Gastrich and Wazniak (2002) provide an example and potential model of categorizing bloom effects on natural resources without human health implications for the golden–brown algae *Aureoccous anophagefferens* (Table 3). Species, toxins and effects pathways within the ecosystem continue to be evaluated. Linkage with risk assessment research is likely to provide additional guidance for threshold developments in ecosystem management.

Table 3. Brown Tide Bloom Index

Category	Cell Count cells/ml	Impact
1	<35,000	No observed impact
2	≥ 35,000 to < 200,000	Reduction in growth of juvenile hard clams, (Mercenaria mercenaria). Reduced feeding rates in adult hard clams; Growth reduction in mussels (Mytilus edulis) and bay scallops (Argopecten irradians).

Category	Cell Count cells/ml	Impact
3	≥ 200,000	Water becomes discolored yellow–brown; Feeding rates of mussels severely reduced; Recruitment failures of bay scallops; No significant growth of juvenile hard clams; Negative impacts to eelgrass due to algal shading; Copepod production reduced and negative impacts to protozoa.

Ingestion Pathway

Cyanobacterial–supplements

Food supplements made from cyanobacteria (blue–green alga supplements; BGAS) can concentrate toxins and result in human exposure (See Dietrich et al. this volume). The levels of algal toxins in food supplements are unregulated at the Federal level in the United States because they fall outside the purview of the US Food and Drug Administration. However, Oregon has set limits on microcystins in food supplements.

Regulatory approaches to BGAS products based on toxicity have not yet been developed and limit the management options for insuring safety. BGAS are generally produced from three cyanobacteria species: Spirulina maxima, Spirulina platensis or Aphanizomenon flos–aquae. Analysis of BGAS for the presence of toxins is not wide spread, but low levels of anatoxins, microcystins, and/or saxitoxins have been found in some BGAS samples (See Dietrich et al. this volume). There is also the possibility that BGAS supplements may contain the neurotoxic amino acid BMAA (See Dietrich et al. this volume). Since supplements can contain one or more of the toxins produced by the species used, issues of potential additivity and synergy must be considered in the risk assessment for BGAS products.

Drinking Water

At present there are no monitoring data from public water systems in the United States for individual cyanobacterial toxins. The lack of data is due, in part, to the absence of standardized analytical methods for individual toxins that can be utilized in a national monitoring program. Problems with cyanobacterial toxins in drinking water, including some human deaths have been reported in the United States, Australia, South America, China, and other countries, but are infrequent (Hitzfeld et al. 2000). In one incident, several dozen individuals died as a result of dialysis with contami-

nated water (Jochimsen et al. 1998). Although blooms in source water cannot always be detected visually, they may be detected through inspection of filters at water treatment facilities. Such detections indicate that the source water may be contaminated with algal toxins. Water treatment processes can be initiated to eliminate the toxins from finished water. However, the efficacy of treatment processes is dependent upon many factors (see Causes, Prevention, and Mitigation Work Group Report this volume). Successful treatment may be dependent upon the identification of toxin type and data on the efficacy of treatment techniques for the toxins identified. Research is needed to better describe the efficacy of treatment techniques by toxin type.

Fish and Shellfish Consumption

Consumption of CHABs through contaminated shellfish and fish can lead to impacts on the liver and the nervous system. Microcystins affect the liver and can promote tumor growth. Cylindrospermopsin also produces liver toxins. Anatoxins produced by *Anabaena* and *Oscillatoria spp* are acutely neurotoxic through interaction with cholinergic mechanisms. Saxitoxins, the cause of Paralytic shellfish poisoning (PSP) are also neurotoxic. Freshwater CHABs such as *Lyngbya wollei* and *Aphanizomenon flos–aquae* produce neurotoxins similar to saxitoxins. For further information on poisonings related to contaminated fish and shellfish consumption see Carmichael et al. (1997), Carmichael (2001); and Van Dolah et al. (2001).

Dermal Contact

Dermal contact with cyanobacteria and their toxins can occur through a variety of water–related recreational activities, most notably swimming at CHAB impacted beaches (salt or fresh water). There have been case reports of skin rashes and dermal or ocular irritation from recreational exposures (Queensland Health 2001; WHO 2003), but controlled toxicity studies of dermal and ocular responses are largely lacking.

Showering and bathing

The use of treated water for showering or bathing minimizes concern for contact with the cyanobacteria because most treatment processes would remove or reduce cyanobacteria in the filtration process, although dense blooms may overwhelm filtration units allowing cells or cell fragments to pass through. However, the toxins could still be present in treated water

allowing for exposure through dermal uptake and inhalation of aerosol during showering. To the extent that cells were carried through the treatment process, heating of the water for bathing and showering would lyse the cells, releasing the toxins.

The use of untreated water for showering or bathing increases the risk for toxin exposure since higher levels of cells and toxin are likely to be present. In one case, after the use of cyanobacteria–contaminated water for a sauna in Finland, 48 people developed gastrointestinal, dermal and neurological symptoms that could have been related to toxin exposure (Hoppu et al. 2002 as cited in Dietrich et al. this volume)

Direct contact with ambient water

Water–sports (e.g. swimming, boating, fishing, etc.) in fresh, estuarine, and ocean water are popular recreational activities. When water bodies are impacted by CHABs, water–sports can be an important exposure route. For swimming and boating, the peak season for these activities tends to parallel that for the cyanobacterial blooms, increasing the risk of exposure. Enjoyment of recreational water sports tends to be a series of episodes that vary in frequency; causing concern for both higher level acute and lower level repeated exposures.

Most case reports of dermal irritation (contact dermatitis, eye irritation) due to cyanobacteria are related to swimming exposures. It has been suggested that the toxins responsible for skin and eye irritation are lipopolysaccharides, endotoxins, the blue–green pigment of the cyanotoxins (phycosyanin) and dermal toxins produced by Lyngbya and Planktothrix species (Queensland Health 2001). There are differences in sensitivity to these toxins; some individuals respond to very low concentrations while others are much more tolerant to exposures from swimming in CHAB impacted waters. Sensitive individuals can experience symptoms ranging from mild contact dermatitis to blistering and peeling of the skin (Queensland Health 2001). Prolonged contact through wet bathing suits increases the risk for dermal effects.

Charge 5

What are the ecosystem–services we want to protect?

Ecosystem services are processes by which the environment produces resources. Such services and their related resources may be affected by cyanobacteria abundance and biomass as well as toxins. Significant ecosystem services may therefore be protected through guidance values regarding cyanobacterial abundance and toxin levels in the environment. The following is a discussion of some of the ecosystem services potentially affected by cyanobacterial blooms.

Nutrient cycling

High biomass cyanoblooms can drive short and long term fluctuations in dissolved oxygen resources. Dissolved oxygen availability plays a critical role in nutrient cycling in the water column and the sediments where aerobic conditions favor biogeochemistry that will sequester phosphorus; anaerobic conditions promote liberation and greater availability of phosphorus. Phosphorus availability is frequently the critical limiting nutrient affecting bloom development, magnitude and persistence. Other nutrients, however, such as nitrogen can also play a concomitant critical role with bloom dynamics often determining whether cyanobacteria with heterocysts for fixing nitrogen or those without heterocysts predominate in a bloom. Bloom conditions can further lead to increases in pH affecting conditions that vary the nutrient cycling pathways, particularly with respect to phosphorus dynamics. High pH promotes dissociation of bound phosphorus, again altering source–sink dynamics of a system and making the phosphorous available and to perpetuating the longevity of blooms. Limiting cyanobacteria blooms can be one factor promoting environmental conditions more suitable to effective nutrient processing in the ecosystem.

Hydrologic cycle effects– Contamination of water sources.

While groundwater is frequently the source of public water supplies, surface water sources are usually those that serve the largest populations and are slated for additional development in some regions affected by blooms. Cyanobacteria can impart unfavorable taste and odors to tap water but additional risks are present from a diversity of cyanotoxins. Preventing blooms in surface waters also has beneficial implications for livestock,

pets and aquatic dependent wildlife including plants. Research is needed to assess the ability of cyanotoxins to accumulate in ground water.

Energy conversion

Production of safe food

The accumulation of cyanobacteria biomass promotes the risk that toxins could be concentrated and bioavailable. Controlling blooms protects the service of uncontaminated surface water used for agricultural irrigation, watering livestock, and/or growing fish in aquaculture. The accumulation of cyanotoxins in the food web could impact subsistence and recreational harvest of fish and shellfish but is poorly characterized at this time. For example, microcystins can accumulate readily in the liver and significantly less in the muscle. Saxitoxin in shellfish is known to persist but there appears to be little evidence so far for issues of cyanobacterially–derived saxitoxin being problematic in freshwater environments. Additionally, there are reports of fish tasting musty when harvested from cyanobloom waters, reducing their desirability as a food source.

Trophic transfer of energy through the ecosystem

Cyanobacteria are not frequently considered favorable primary producers toward passing energy efficiently through the food web. Microzooplankton for instance may track *Microcystis* populations; however, under the same environmental conditions, larval and juvenile fish growth rates feeding on microzooplankton can be reduced over fish feeding on mesozooplankton due to energy density per food item consumed. Such effects on energetic pathways affect growth and survival of organisms throughout the food web, year class strength of populations and therefore community dynamics in the ecosystem. Such effects may ultimately have implications in the availability of harvestable fish.

Maintenance of ecological diversity and integrity

Extensive bloom conditions effectively block light needed to support survival of submerged aquatic vegetation. Some toxins or chemicals associated with the blooms may also act to inhibit growth of submerged aquatic vegetation. Thus ecosystem integrity is impacted by species specific toxins and species nonspecific shading factors. Indirect effects of cyanoblooms on habitat complexity (light limitation to submerged aquatic vegetation or

dissolved oxygen conditions stressful or lethal to aquatic life) can affect spatial and temporal distribution of refuges that affect predatory–prey relationships. Aquatic community composition or the protection of threatened and endangered fauna can be impacted. Many disease fighting drugs available and under development have been mined from the available diversity. Conditions that promote lower diversity on a local to global scale would be expected to further limit the possibilities of culturally valuable mining of natural resources for their disease treatment and other properties.

Disease vectoring

Disease prevalence has been correlated with quantities of clean water available for personal and domestic hygiene (Chorus and Bartram 1999). Controlling blooms and their toxicity can therefore provide ecosystem services that aid in regulating disease and mortality. For example, human skin irritations are common through cyanobloom water contact. Skin irritations, related allergic reactions, skin, eye and ear infections compromise natural defense mechanisms of animals and humans. Bloom affected waters have promoted conditions for increased prevalence of such health impairments (Chorus and Bartram 1999).

Disease effects may also impact the condition of natural resources via indirect pathways. Biomass of cyanobacteria can accumulate along the windward shorelines of a waterbody. Decomposition of this organic–rich biomass can produce indirect effects of hypoxic (low oxygen) and anoxic (no oxygen or anaerobic) environments. Such environments typically occur in mid–late summer with temperatures favorable to germination of the *Clostridium botulinum* bacteria associated with botulinum toxins. The toxin can be inadvertently ingested by waterfowl leading to a potential botulism outbreak. Maggots feeding on a dead carcass in such an environment can accumulate the toxin and are ingested by other waterfowl and shorebirds promoting sickness and death in those populations. Hypoxic and anoxic environments lead to habitat impairments increasing stress on fish and shellfish compromising their immune defenses, and allowing access of disease vectors into the organism and population.

Transmission of cyanotoxins through the food web is a concern to natural resource and human health management agencies. There is a long history of livestock and pet deaths associated with consumption of bloom waters containing cyanotoxins (Chorus and Bartram 1999). Necropsies of Great Blue Herons (*Ardea herodias*) from a waterbird kill in a Chesapeake Bay–related event showed they exhibited a condition known as steatitis, excessive fat production (Driscoll et al. 2002). A leading hypothesis is that microcystin toxicosis may be a precursor to the development of this condi-

tion. It was determined in the analyses of liver tissue that microcystin levels were sufficient to account for the observed toxicosis (W. Carmichael pers. comm.). Understanding the transmission of such toxins through the food web and their potential to impact the expression of other disease conditions is poorly understood.

Health and wellness through leisure services provided by the ecosystem

Cyanobacteria bloom impacts can reduce the effectiveness of leisure services provided by the ecosystem that contributes to human wellbeing and quality of life. “Healthy” refers not only to physical well–being but also to the status of a number of related processes (Heintzman 1999). It involves a holistic integration of the physical, emotional, spiritual, intellectual, and social dimensions of people's lives (Bensley 1991; Crompton 1998; Ellison 1983; Ellison and Smith 1991). As an integrative component of holistic wellness, spiritual wellness needs to be an important consideration in leisure services that can enhance the quality of life for persons who have disabilities or who are devalued (Heintzman 1999).

Although coastal counties (excluding Alaska) account for only 11% of the land area in the United States, they are home to 53% of the population (Hunter 2001). Populations in proximity to coastal water resources as well as inland water bodies increase the demand for outdoor experiences dependent upon water quality. Unfortunately, many waterbodies are increasingly eutrophic and can be suitable for cyanobacteria bloom conditions. Chorus and Bartram (1999) cite a 1990’s survey that showed large percentages of lakes already classified as eutrophic (Asia Pacific region (54%), Europe (53%), Africa (28%), North America (48%) and South America (41%). Bloom conditions for example have increasingly led to beach closures (Chorus and Bartram 1999) affecting recreational opportunities we frequently associate with leisure activities. In 2001, more than 82 million U.S. residents fished, hunted and watched wildlife (USDI et al. 2002). These activities bring recreationalists into contact with waterways that are or can be directly and indirectly affected by bloom waters. Guidelines that may be translated into water quality standards would aid the protection of such leisure services valuable to individual and social well–being.

Charge 6

How can regulators best devise a framework for making risk management determinations that incorporates consideration of the characteristics of CHABs, the risk for human health and ecosystem sustainability, and the costs and benefits of CHABs detection and management.

Cyanobacterial harmful algal blooms lead to a broad spectrum of public health, environmental protection and economic concerns. Stressors associated with these blooms can pollute drinking water supplies, degrade ecological services, and decrease agricultural productivity. Effective management of CHABs and the problems they create will require a comprehensive decision–support framework that addresses all facets of bloom occurrence, ecological and human health risks, and the control options for prevention and mitigation of those risks. This framework can be used to inform development of guidelines and standards for human exposure to cyanotoxins, to understand and control environmental impacts, and to support evaluation of the relative benefits and costs of alternative risk management options.

To maximize its utility, the decision–support framework must be able to accommodate the range of considerations relevant to bloom formation and occurrence, the causal pathways and mechanisms leading from blooms to ecological and human health effects, management actions to prevent blooms and minimize their impacts, and the costs associated with bloom occurrence and management. It should reflect the current state of knowledge regarding cyanobacteria ecology, the hazards of the cyanobacteria present, and the technologies available to address those hazards. Ideally, the framework also should be flexible with respect to incorporating new knowledge and technologies as these are developed.

Risk assessment has been adopted internationally as an important decision–support tool informing policy and the management of stressors affecting human health and ecological vitality. Because CHABs can pose risks simultaneously to a wide variety of assessment endpoints (valued components of the combined ecological–human–socioeconomic system potentially impacted by CHABs), and those risks likely are interconnected, an integrated approach to risk assessment (Suter et al. 2003; See Orme–Zavaleta and Munns this volume) is an attractive alternative to separate human health and ecological risk assessments. Furthermore, as multiple toxin exposures during CHABs are highly likely, an integrated risk assessment could provide additional information. When deployed with other

technologies, such as multi–criteria decision analysis and benefit–cost analysis, and used in conjunction with approaches proven to be effective for managing CHAB risks, integrated risk assessment provides a logical cornerstone for an effective CHAB decision–support framework.

The workgroup recommends an overall decision–support framework with six basic elements (Fig. 1). The first two of these focus on integrated conceptual models that relate CHAB formation and occurrence to environmental and human health risks generically and comprehensively (Element 1), and on a site and situation–specific basis (Element 2). Reflected in the conceptual models are options for CHAB prevention and mitigation, and the socioeconomic costs of CHAB impacts. Element 3 utilizes these models to plan and perform risk assessments. It is important to understand the likelihood of adverse effects of CHABs on assessment endpoints relevant the specific problem at hand, be it development of national guidelines for cyanotoxins in drinking water, or prevention of blooms in livestock tanks. The concepts and approaches of multi–criteria decision analysis are used in Element 4 to help evaluate the attractiveness of alternatives for managing the risks characterized for the specific problem. Element 5 uses the collective information from the previous elements to construct management plans to control site and situation–specific risks. These plans identify control options, methods to monitor the effectiveness of controls, and the costs and benefits of options to assist in real–time decision–making. Finally, Element 6 evaluates the effectiveness of the overall framework for CHAB detection and management. Each of these elements is outlined below, together with the research and development activities needed to implement that element and the overall framework.

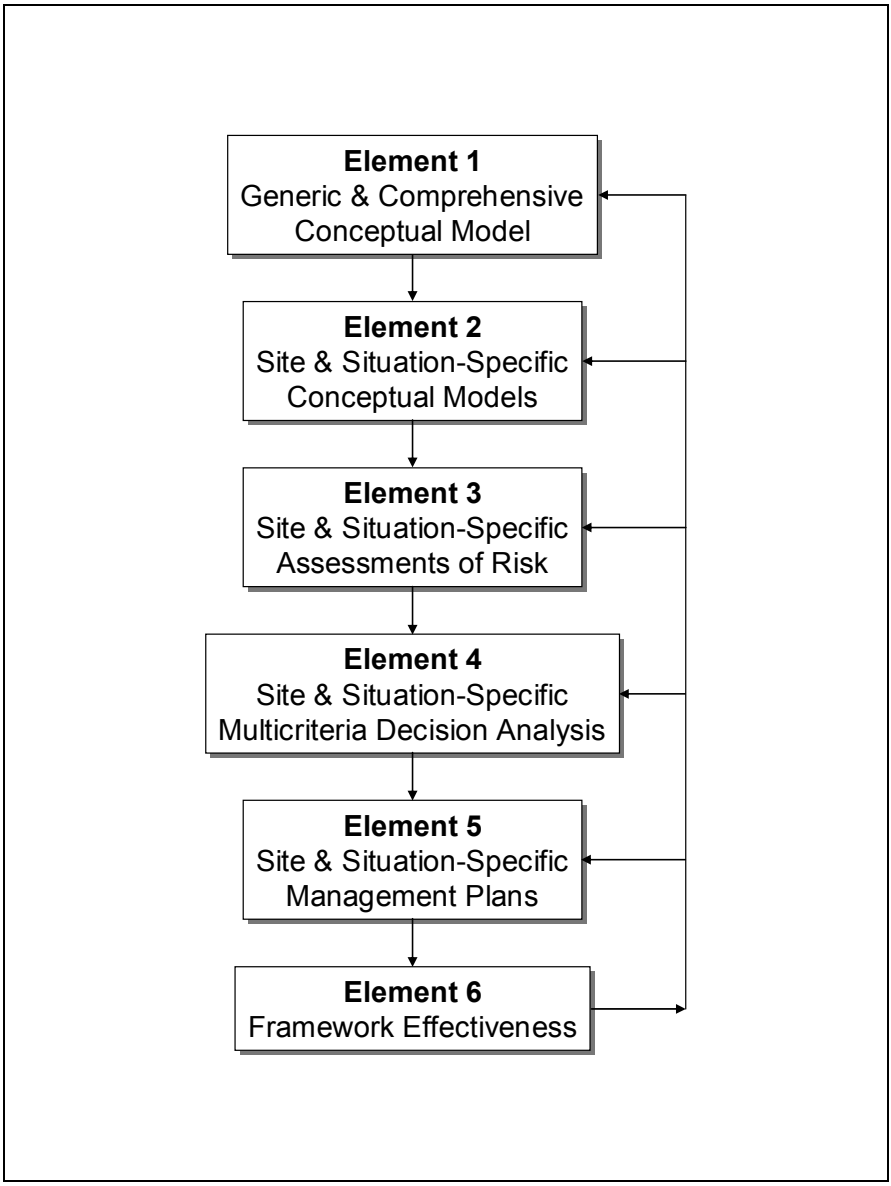

Fig. 1. Multidecision Framework

Generic and Comprehensive Conceptual Model

As evidenced during the symposium, the environmental factors influencing formation of cyanobacterial HABs are complex and incompletely under-

stood. Similarly, the risks posed by CHABs to humans and valued ecological receptors and services are diverse, resulting from interconnected exposure pathways, environmental processes, and mechanisms of effect. Effective identification of hazards and assessment of risk requires a system–wide conceptualization of the environmental factors, processes, and social behaviors that influence the occurrence and possible outcomes of cyanobacteria blooms. This conceptual model should be comprehensive with respect to the state of knowledge, reflecting current technical understanding as a series of working hypotheses that describe formation of blooms, pathways of exposure to human and ecological receptors for stressors associated with blooms (toxins, biomass, etc.), biological and ecological effects resulting from those exposures, the factors that amplify or moderate these effects (e.g., presence of other stressors, conditions that affect receptor susceptibility), and relationships among system elements that directly or indirectly influence risks to important assessment endpoints. The generic conceptual model also should identify the costs incurred by CHABs and the various management actions that can be taken to prevent or mitigate the effects of blooms.

An initial construct for the generic conceptual model is illustrated in Fig. 2a and 2b. This model attempts to capture current understanding of CHAB occurrence, and the exposure media and pathways through which human and ecological receptors come into contact with stressors associated with CHABs (e.g., ingestion of toxins in drinking water). It also reflects key interactions among system components and the factors that modify the nature and intensity of effects, and ultimately risk. To facilitate its development and use, the generic conceptual model is organized into sub–models, each describing an important component of the overall CHAB problem or an expected pathway leading to risk. Thus, an Occurrence Sub–model encompasses the important environmental factors and processes, including human activity in the landscape, as they affect CHAB development and persistence. A Toxin Effects Sub–model describes exposure pathways relevant to human and ecological receptors, and begins to lay out the nature of effects that could be experienced as a result of exposure to cyanotoxins. A Cost Sub–model identifies in a cursory way the many effects that CHAB occurrence, prevention and mitigation have on social and economic systems. These can range from lost revenues and opportunities for recreation and tourism, to the emotional costs associated with loss of pets and even livelihoods.

The generic conceptual model communicated in Fig. 2a and 2b is incomplete with respect to important effects sub–models and specific descriptions of causal pathways and mechanisms associated with exposure and effect. For this reason, an Algal Biomass Effects Sub–model is in-

cluded solely as a placeholder to indicate the need to describe fully the multitude of issues associated with the CHAB problem. Further, salient details that relate, for example, to costs associated with prevention or mitigation of cyanobacteria blooms, an element of the Cost Sub–model, and to potential control points in the Occurrence Sub–model are omitted due to ignorance of those relationships, as well as to preserve the communication value of Fig. 2a and 2b. An important development activity with respect to the implementing the decision–support framework will be to complete this model to the extent current understanding permits. The deliberations of the other workgroups in this symposium can contribute to the model's completion.

Although informal guidance is available for development of conceptual models (e.g., U.S. EPA 1998; Harwell and Gentile 2000), their construction is as much an art as it is a science. To be fully supportive of CHAB risk management needs, the conceptual model is best developed in a group exercise that involves diverse disciplines, vocations and stakeholders. Members of this group should include scientists and public health specialists, regulatory analysts and managers, water distribution and treatment specialists, environmental economists, and representatives of key stakeholder groups. This group would focus on the realism, accuracy and completeness of the generic conceptual model as a system–wide representation of the CHAB problem. Its deliberations would be critical to identification of assessment endpoints against which risks are to be assessed, considering the myriad regulatory, economic, ecological and social factors associated with CHABs. To help ensure its credibility, the model should be independently reviewed by similar experts. Further, the model should be revisited periodically and refined with new technical understanding and the lessons learned from its application in management of CHAB issues.

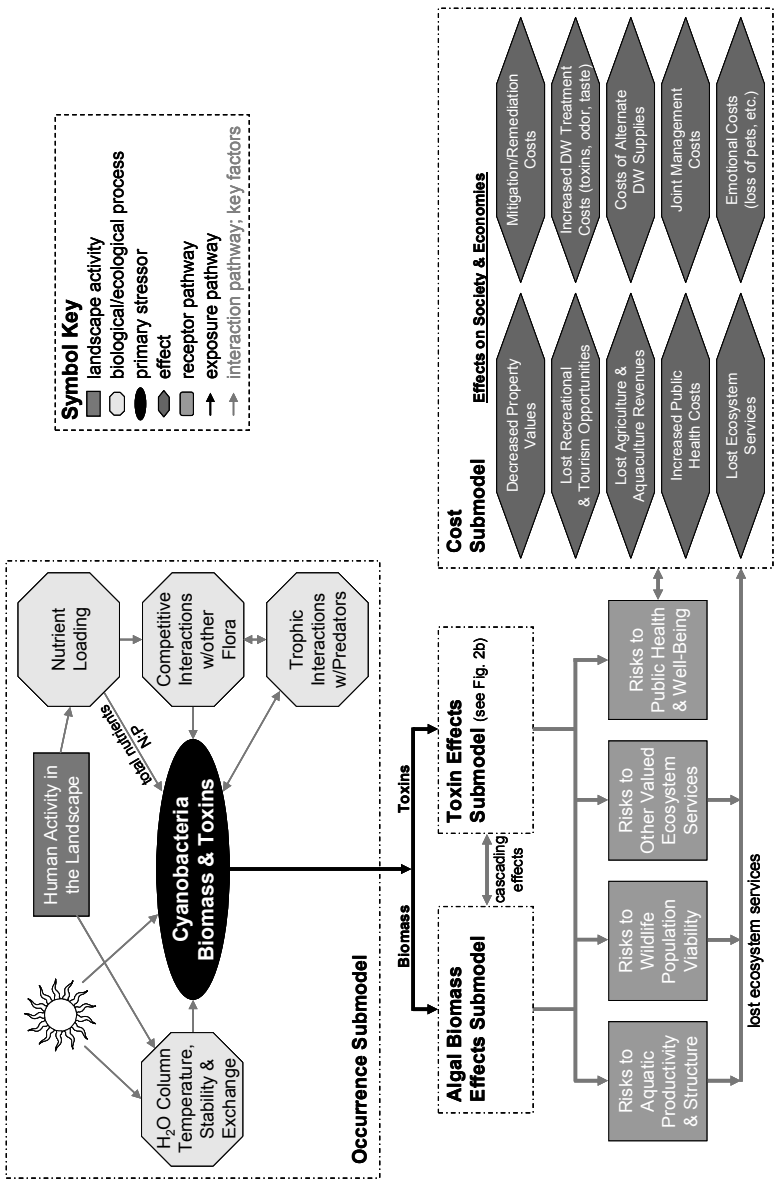

Fig. 2a. Conceptual model of cyanobacteria integrated risk: overall model;

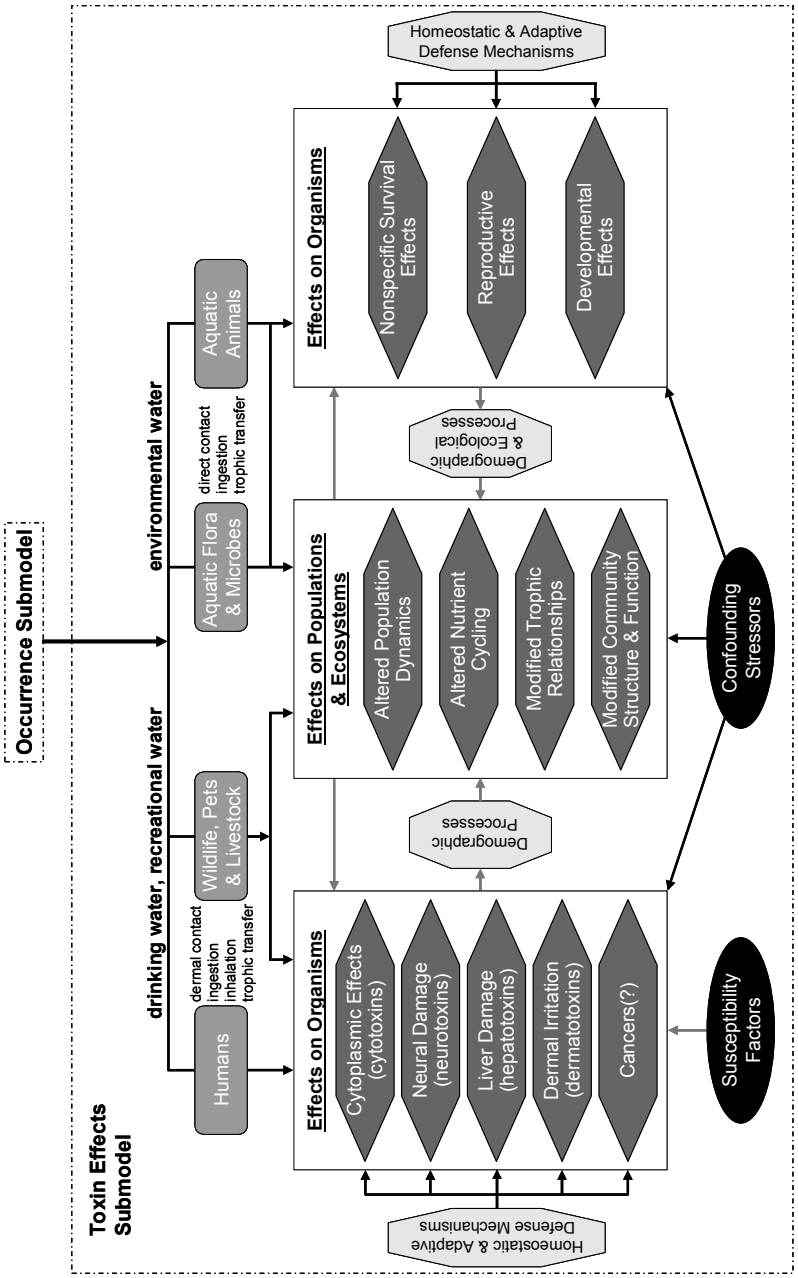

Fig. 2b. Expansion of the Toxins Effects Submodel shown in 2a.

An issue relevant to development of the generic conceptual model is the level of detail and complexity that it should reflect. Although a comprehensive model might seem overly complex and cumbersome, it does provide great value. First, it will support understanding of the full range of risks posed by CHABs, and therefore can help to inform regulatory and risk management actions through recognition of the connectivity of various system components. This will help to minimize unintended consequences associated with those actions. Second, it will facilitate recognition of critical prevention and mitigation control points and the evaluation of the effectiveness those controls through enhanced understanding of the relationships and factors influencing risks. Third, as a reflection of the state of knowledge, it can be used to identify critical research and information that are needed to manage CHAB risks effectively and efficiently. Fourth, it can serve as a useful tool for communicating the CHAB problem and its management to various stakeholder groups and the general public. And finally, it will facilitate development of the site and situation–specific conceptual models of Element 2 of the framework.

Site and Situation–Specific Conceptual Models

The issues associated with CHABs range from broad problems that are national in scope to localized ones, with characteristics that depend on context, scale, location and specific circumstances. Although comprehensive, the conceptual model of Element 1 is generic in its description of assessment endpoints, environmental circumstances, relevant stressors, and so on. Management action to address almost all CHAB problems will require additional specificity in defining the problem to be effective. To meet this need, Element 2 involves refinement of the generic, conceptual model on a site and situation–specific basis.

The conceptual models developed in this element would reflect the specific circumstances and factors relevant to particular CHAB prevention and management problems. Using a generalized case of drinking water distribution in South Australia to illustrate, the model would account for local factors affecting the occurrence of species of cyanobacteria within the source reservoir. Because the combination of species and the environmental factors that contribute to their bloom dynamics are somewhat unique to this situation, the conceptual model would focus specifically on those species and factors. The model would need to describe the relevant exposure pathways leading from source water to tap, identifying various control options that might be employed to detect and minimize drinking water contamination. It would account for possible effects linked to indi-

vidual cyanotoxins (and their combinations) prevalent in South Australian species, reflecting the specific modifying factors (e.g., confounding stressors) operative at the site. Importantly, the model would identify those assessment endpoints important to local municipalities and stakeholders. Such a model might also describe inadvertent exposure of wildlife and domestic livestock to the source water and its consequences, if those issues are pertinent. Management options reflected in the model for detecting and controlling CHABs and their toxins would be those feasible for the particular water distribution system, and their associated costs would be grounded in the local economies. The conceptual model constructed for this South Australian drinking water illustration likely would differ in key aspects from one developed for, CHAB risks relevant to recreational uses of water bodies in Australia or another country. The degree of site specificity will also vary across models in Element 2. The conceptual model for a localized drinking water distribution system will contain much more detail about local conditions and factors than would one supporting establishment of national guidelines for cyanotoxins in drinking water.

The site and situation–specific conceptual models of Element 2 are refinements of the comprehensive model of Element 1. We recommend that they be developed by stripping away irrelevant or unimportant causal pathways and assessment endpoints from the comprehensive model, and adding detail relevant to the particular circumstances of the CHAB problem being addressed. Obviously, this requires in–depth understanding of circumstances and processes important to each problem, suggesting the need for additional information–gathering and research to fill key knowledge gaps. Once developed, the resulting site and situation–specific conceptual models will be important tools that help to focus the analytical activities of Elements 3 and 4, and creation of management plans (Element 5) that are responsive to the CHAB problem at hand.

Site and Situation–Specific Assessments of Risk

Element 3 of the decision–support framework utilizes the site and situation–specific conceptual model(s) to frame quantitative assessments of CHAB risks. The results of these risk assessments can be used to: 1) inform the development of protective guidelines and standards for cyanotoxin exposure in drinking water and recreational waters (reviewed by Burch, this volume); 2) understand the nature and magnitude of adverse ecological effects potentially resulting from CHABs; 3) diagnose potential causes of public health and ecological problems; and 4) facilitate evaluation of management alternatives and control options. For reasons outlined

elsewhere (See Orme–Zavaleta and Munns this volume), we recommend that the risk assessments supporting CHABs management be integrated.

Risk assessment as a technology is fairly well developed; its concepts and uses for supporting policy and management need not be detailed here. Yet, several research and developmental needs remain with respect to its application to specific CHABs management problems. Many of these are identified earlier in this chapter and elsewhere in this volume as they apply to key knowledge gaps in CHAB occurrence, exposure and effects. Application of an integrated approach for risk assessment also will require development and testing of system–wide modeling techniques that reflect the connectivity of system components and therefore risks (See Orme–Zavaleta and Munns this volume). This need is not unique to the CHABs problem, rather being one of integrated risk assessment in general. As applied to CHABs , methods for integrated risk assessment will need to account for the complex interactions that occur within ecological–human–socioeconomic systems that are potentially affected by the stressors associated with blooms. Also required is the ability to accommodate a multitude of assessment endpoints salient to public health, ecological sustainability and services, domestic production and human well being. Until the science of integrated risk assessment is fully developed, this element of the decision–support framework may need to rely on independent assessments of health and ecological risks.

It is likely that some CHAB management determinations can be made effectively in a context narrower than that afforded by integrated risk assessment. For instances where regulatory or other requirements focus singularly on some component or aspect of the overall problem (e.g., mitigating risk of livestock mortality caused by cyanobacteria in an isolated pond), reasonable decisions can be made relative to such requirements without the need to evaluate the overall problem comprehensively. Thus, the risk assessments of Element 3 can be performed with this singular aspect as their objective. While permitting implementation of the decision–support framework in advance of full development of integrated risk assessment methods, the decisions that result may fail to acknowledge the implicit tradeoffs involved.

The degree of conservatism in assumptions taken in the risk assessments of Element 3 will depend upon the management decisions supported. Application of the framework to national–scale issues, such as establishing protective guidelines for drinking water, likely will require use of uncertainty or safety factors to ensure protection of especially sensitive or susceptible receptors. For some localized issues, such as prevention of blooms in water bodies used primarily for recreation, lower levels of conservatism may be advantageous as the benefits of recreational use are

weighed against the costs of preventative measures. As with that for performing integrated risk assessments, the research needed to ensure appropriate conservatism in risk assessment is not unique to the CHAB problem, but this problem provides a distinct context within which to conduct that research.

Site and Situation–Specific Multi–criteria Decision Analysis

As described during this symposium and reflected in the comprehensive conceptual model of Element 1, the ecological–human–socioeconomic systems potentially affected by CHABs are complex. The information used to evaluate these systems is diverse, as often are the stakeholders affected by decisions made to manage CHAB risks. Because of this, it might be argued that policy and decision making can only be accomplished by partitioning the problem into more tractable subsets. To do so, however, may reduce the effectiveness of management determinations through failure to recognize the tradeoffs inherent to those decisions and the unintended consequences that may result. In Element 4, we recommend applying the concepts and methods of multi–criteria decision analysis (Belton and Steward, 2002) to facilitate informed decision making in the complex context of CHABs problems.

Multi–criteria decision analysis is designed to support selection among alternatives in situations involving potentially conflicting objectives or decision criteria. Approaching such problems in a systematic fashion, multi–criteria decision analysis involves the key steps of: 1) structuring decision making goals in terms of defined hierarchies of criteria; 2) evaluating decision alternatives in terms of the extent to which they satisfy each of the identified criteria; and 3) aggregating across criteria to measure the extent to which each alternative satisfies the overall goals represented by the criteria. The result of its application is an ordered ranking of decision alternatives that communicates the best option while considering a number of factors (e.g., risk, benefits, costs, option effectiveness, stakeholder values, etc.).

Multi–criteria decision analysis is an evolving technology, receiving increasing attention for managing complex environmental problems. Examples of multicriteria–decision analysis used by Federal Agencies are available (Kiker et al. 2005). Multi–criteria decision analysis would utilize the assessments of risk from the previous element, together with an understanding of the alternatives for management action, estimates of associated costs, and the values expressed by stakeholders, to provide a decision–support framework for addressing the site and situation–specific CHAB issue. There are numerous specific methods available to accomplish the

three key steps of multi–criteria decision analysis (Belton and Steward, 2002 and See Linkov and Steevens this volume). Finding no examples of their application to CHABs, a substantial research need for the framework will be to explore and refine approaches for multi–criteria decision analysis for use with the types of problems and issues associated with CHABs. This approach will facilitate decision making in the face of the seemingly overwhelming complexity of some CHAB problems, thus supporting development of management plans to address those problems.

Site and Situation–Specific Management Plans

In general, managers can exert a greater influence on physical rather than chemical factors controlling CHABs. Many of the actions are directly related to watershed management alternatives (Fig. 3). For example, water resource managers may be able to alter water flow and thus decrease residence time in a reservoir, or affect vertical mixing in the water column by controlling water intake. Similarly, the ability to release water from different depths behind dams could affect algal blooms by changing the temperature profile of water downstream. Consistent forceful mixing prevents algae from maintaining optimal water depth, slowing their growth. Additionally, shear disrupts the filaments which hold together heterocysts, the nitrogen–fixing cells formed by some cyanobacteria. Although mixing the water in a reservoir may not be a practical option for many managers, other options may be available such as controlled downstream releases to reduce cell and toxin concentrations or dredging to lower nutrient and trace metal concentrations. Our literature review indicates that even though managers may be able to influence multiple factors associated with algal blooms, little work has been done to study the actual impact of water management options on CHABs and subsequent toxin production.

Armed with an understanding of the risks posed by CHABs in specific situations, and of effective alternatives for managing those risks, Element 5 of the decision–support framework consists of management plans for controlling risks on a prospective and real–time basis. These plans would focus on CHAB prevention, detection, response and mitigation as appropriate to the situational context, all as reflected in the relevant conceptual model. Various versions of such plans currently are being used, particularly in Australia. The recommendations for management plans in Element 5 rely heavily on the best–practice experiences gained through their use.

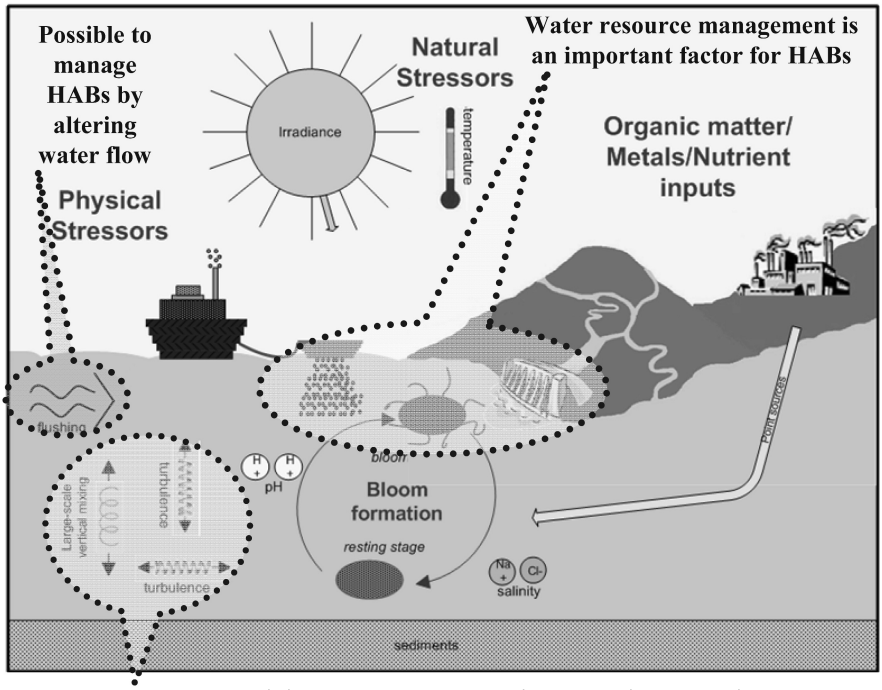

Fig. 3. HABs and water resource management actions.

Each management plan would identify the particular actions to be taken to manage aspects of CHAB risk. An outline of a management plan for prevention of CHABs in a hydrological system providing water to a municipal water supply is provided in Fig. 3 as an illustration. Identified in this outline are the:

- "Critical Control Points" for management action within the system (e.g., catchment, rivers, etc. Fig. 3). These identify where, and perhaps when, management action is to be taken to control some factor or environmental process contributing to risk.
- Environmental factors or processes to be managed and approaches for their management ("Management Control"). Targets and controls for nitrogen and phosphorous loading into the catchment would be specified in the relevant critical control point example reflected in Fig. 4.
- Protocols to provide the data both to monitor the effectiveness of controls and to identify the data elements that act as triggers for further

action ("Monitoring Strategy"). For example, protocols would be specified to assess nutrient loading into the catchment.

- Graded "Alert Level Frameworks" to direct action if triggers are exceeded. Frameworks currently are in use in South Australia for human drinking water, recreational water and livestock drinking water that define levels of alert based on cell counts, and recommend actions to be taken at each level.
- Characterizations of the "Costs" associated with each element of the plan, based on available technologies and local economies.
- Characterizations (to the extent possible) of the "Benefits" gained by each element of the plan, including benefits not directly related to CHAB management (e.g., improved aesthetics as an ecological service).

Aspects of management plan development would be informed by the multi–criteria decision analyses of Element 5. Current understanding of the environmental and social context of the situation, plus transfer of best–practice knowledge gained from local experience, are critical to effective plans. In addition to the research identified elsewhere in this volume, site–specific understanding of local hydrologic cycles, sources of nutrient input, cyanobacteria dynamics, social behaviors, and other factors may be needed on a site and situation–specific basis to tailor the management plans to specific problems. The site and situation–specific conceptual models of Element 2 can be used to guide investments in this research, focusing on their largest uncertainties.

Critical Control Point	Management Control	Monitoring Strategy	Alert Level Framework	Costs	Benefits
1. Catchment	nitrogen & phosphorus	nutrient loading	Alert Level 1 • triggers • actions Alert Level 2 • triggers • actions etc.	A$	A$, improved aesthetics
2. Rivers	flow	stratification, cell counts	Alert Level 1 • triggers • actions Alert Level 2 • triggers • actions etc.	A$	A$, improved productivity
3. Reservoir	nitrogen & phosphorous, stratification	nutrient concentrations, stratification, cell counts	Alert Level 1 • triggers • actions Alert Level 2 • triggers • actions etc.	A$	A$, reduced livestock risks

Treat after extraction is a further control point:

Critical control point	Management control	Monitoring strategy	Alert level framework	Cost	Benefits
Treatment plant	cyanobacterial cell and metabolites	Removal of cells and metabolites		$	$ reduced human health risk

Fig. 4. Example of Critical Control Point

The details and uses of management plans likely will vary across CHAB problems. While the example outlined above has obvious application for municipal and private authorities providing drinking water, a management plan appropriate for national implementation of a guideline would take a very different form, one likely grounded in the established regulatory and compliance structure of that country (or other authority). A research need for the decision–support framework therefore relates to optimizing the nature of the management plans for various CHAB issues.

Framework Effectiveness

Effective decision–making requires an explicit structure for jointly considering the environmental, ecological, technological, economic, and socio–political factors relevant to evaluating alternatives and making a decision. Integrating this heterogeneous information with respect to human aspirations and technical applications demands a systematic and understandable framework to organize the people, processes, and tools for making a structured and defensible decision.

For further information on MCDA see Appendix A of this report (Linkov and Steevens this volume).

Summary and Conclusions

The Risk Assessment Work Group focused on six charge questions related to CHABS, cyanobacteria and their toxins. The charge questions covered the following topics:

- Research needed to reduce uncertainty in establishing health based guidelines
- Research that minimize the cost and maximize the benefits of various regulatory approaches
- Exposure pathways for receptors of concern
- Data available to support the derivation of health–based guideline values for harmful cyanobacterial algal blooms
- Ecological services that guidelines or regulations should protect?
- A framework for making risk management determinations that incorporates consideration of the characteristics of CHABs, the risk for human health, ecosystem viability, and the costs and benefits of CHABs detection and management?

The Work Group concluded that there is a considerable amount of human case-study data and information from animal studies to demonstrate that cyanobacterial toxins pose a hazard to humans, domestic animals, wildlife, and the ecosystem. However, the data on dose–response are limited and confounded by a lack of sufficient pure toxin to conduct most of the toxicological studies that will be needed in order to answer remaining questions on risk, and to provide the data for quantitative dose–response analysis. The Work Group recommended that research on purification or

synthesis of pure toxin must be accomplished before the large scale studies to establish dose–response relationships will be possible. As the necessary–pure toxins become available, the Work Group recommended that studies be prioritized by the impact that they will have on reducing the uncertainty in the risk assessment in order to minimize the research costs and maximize the risk assessment benefits. Use of quantitative structure activity relationships (QSAR) and toxicity equivalency factor studies are also recommended as approaches for filling dose–response data gaps.

The Work Group recognized that CHABs rarely introduce single toxins into the water supply. Under CHAB conditions, affected water is likely to contain a variety of toxins in varying concentrations that may change over the duration of the bloom. Accordingly, research on cyanotoxin interactions is needed, along with the development of risk assessment approaches for CHAB mixtures.

The development of simple, accurate analytical methods that can be utilized by most analytical laboratories or used in the field was recognized as a major data need for establishing exposure potential and monitoring bloom conditions. Most currently available methods are time–consuming and/or costly.

Human exposure to cyanobacterial toxins can occur through ingestion of contaminated drinking water, plus dermal contact and/or inhalation of aerosols while bathing and showering in tap water. Treatment can reduce the concentrations of both the toxins and the bacteria in the treated water but there is still much to be learned about the effectiveness of most treatment technologies on cyanobacteria and toxin removal.

Human exposure to cyanobacteria and their toxins also occurs through incidental ingestion, dermal contact, and inhalation of aerosols during recreational use of surface waters, ingestion of contaminated fish and other foods of aquatic origin, and/or BGAS supplements. Establishing intakes and duration parameters for these exposure scenarios will facilitate the application of risk assessment approaches to these situations.

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