An adaptive, comprehensive monitoring strategy for chemicals of emerging concern (CECs) in California's aquatic ecosystems

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Abstract

A scientific advisory panel was convened by the State of California to recommend monitoring for chemicals of emerging concern (CECs) in aquatic systems that receive discharge of municipal wastewater treatment plant (WWTP) effluent and stormwater runoff. The panel developed a risk-based, screening framework that considered environmental sources and fate of CECs observed in receiving waters across the State. Using existing occurrence and risk threshold data in water, sediment and biological tissue, the panel applied the framework to identify a priority list of CECs for initial monitoring in three representative receiving water scenarios. The initial screening list of 16 CECs identified by the panel included consumer and commercial chemicals, flame retardants, pesticides, pharmaceuticals and personal care products, and natural hormones. The panel designed an iterative, phased strategy with interpretive guidelines that direct and update management actions commensurate with potential risk identified using the risk-based framework and monitoring data. Due to the ever changing nature of chemical use, technology, and management practices, the panel offered recommendations to improve CEC monitoring, including: development of bioanalytical screening methods whose responses integrate exposure to complex mixtures and that can be linked to higher order effects; development/refinement of models that predict the input, fate and effects of future chemicals; and filling of key data gaps on CEC occurrence and toxicity. Lastly, the panel stressed the need for adaptive management, allowing for future review of, and if warranted, modifications to the strategy to incorporate the latest science available to the water resources community.

Introduction

Chemicals of emerging concern (CECs) encompass a vast number of compounds that are largely unregulated in the US and abroad, and have no or limited monitoring data available for environmental

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media (e.g., air, water, sediment and biota). A wide variety of substances including pharmaceuticals, flame retardants, contemporary use pesticides and even food additives are considered CECs. Except for recently formulated compounds, many of these chemicals have likely been present in aquatic ecosystems for several years or even decades, but were not previously detectable using available analytical methodologies. However, recent advances in analytical chemistry have allowed detection of many CECs in environmental media, which in turn have led to efforts to estimate their potential hazard (Kolpin *et al.* 2002, Snyder *et al.* 2003, Oros *et al.* 2005). A multitude of chemicals that may be qualitatively identified cannot be quantified due to lack of analytical standards or robust methods of measurement. Thus, water quality managers in California have been trying to narrow the focus of chemical screening to CECs that have the greatest potential to pose an unacceptable risk to human and ecological health.

Regulations exist to protect the beneficial uses of California's water resources, ensuring that all fresh, brackish and ocean waters within the State are safe for human contact, harvested foodstuffs are safe to eat, and that aquatic life is not compromised. Analysis of chemical constituents as part of the National Pollutant Discharge Elimination System (NPDES) is performed at local and regional scales on known sources of CECs, including discharges from municipal wastewater treatment plants (WWTPs), and in waters that receive stormwater runoff (MS4) to ensure compliance with receiving water objectives and effluent limits, and to evaluate the effectiveness of human intervention. The trace measurement of CECs represents a challenge for water quality professionals and, thus, requires careful attention to quality assurance/quality control (QA/QC) measures, as well as appropriate designs and planning that adequately address the goals of the specific monitoring program.

Recognizing that assessing the effects of CECs is a rapidly evolving field and that investigative monitoring and, if warranted, regulatory requirements need to be based on the best available science, the State Water Resources Control Board (SWRCB) established a scientific advisory panel to provide guidance in developing monitoring programs that assess the potential ecological and human health impacts of CECs in freshwater, estuarine and oceanic ecosystems. Nominated and vetted through a stakeholder advisory group represented by the discharger, non-governmental organization (NGO), regulator, and natural resources communities, the panel was established in 2009 and included seven national experts in the fields of chemistry, biochemistry, toxicology, epidemiology, coastal and marine science, risk assessment, and engineering. The panel held six in-person meetings and numerous conference calls over a 15-month period. The face-to-face meetings included the opportunity for public input on the panel's charge, exchange of information and direct dialog with panel members. The product of this effort was a 220 page report, revised to address comments from the stakeholders and the public, detailing the recommendations, the process followed by the panel and supporting information in multiple appendices (Anderson *et al.* 2012). This paper represents a summary of the report, describing the key elements of the adaptive monitoring strategy developed by the panel, including an initial list of CECs for initial screening in different receiving water environments.

Conceptual Approach

As of December of 2011, several reports were published by state and non-governmental agencies to address the potential risks of CECs to ecological and human health (e.g., Snyder *et al.* 2010, Diamond *et al.* 2011). Many of these reports utilized a risk-based framework, i.e., considering key CEC sources and their fate in receiving environments, and then comparing environmental concentrations with a biological threshold of adverse effect to screen for chemicals of interest. The panel adopted a similar approach as the basis for identifying CECs that are relevant in California's aquatic ecosystems (Figure 1). Accurate determination of chemical concentrations in the appropriate exposure matrix as well as extensive biological characterization under the same conditions is required to reduce uncertainty in traditional risk-based assessments. When evaluating a large number of CECs, the availability of high quality occurrence and effects data is typically limited; thus, substantial uncertainty is often associated with most screening evaluations. While this approach has obvious limitations, it is currently the default method for identifying CECs that have the greatest potential to pose a risk and require further study until the necessary information for reducing uncertainty can be obtained.

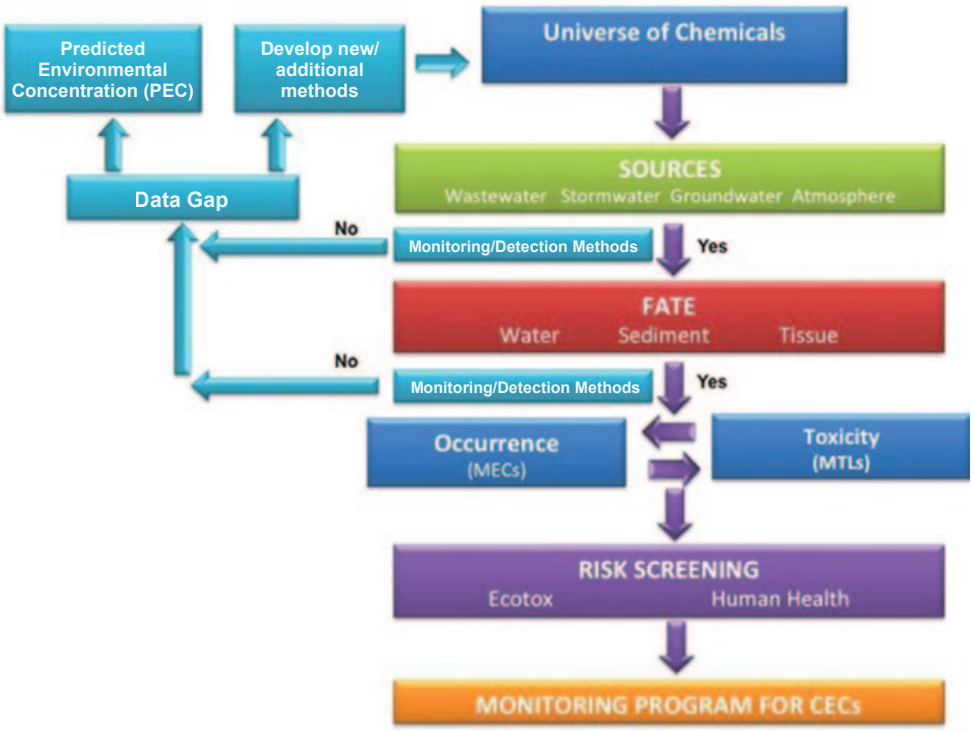

Figure 1. Conceptual approach for identifying chemicals of emerging concern (CECs) for monitoring considers risk to both aquatic life and human health. MTL = Monitoring Trigger Level. MEC = Measured Environmental Concentration.

Focusing the Universe of Unregulated Chemicals

The universe of known chemicals considered by the panel was derived from several databases, reports and studies. Compounds that were previously screened through a panel of scientific experts convened to recommend monitoring of CECs in recycled water applications in California (Drewes *et al.* 2013) were given first priority for inclusion. These CECs were derived from the USEPA's Candidate Contaminant List 3 (CCL3; http://water.epa.gov/scitech/drinkingwater/dws/ccl/ccl3.cfm) and from occurrence data compiled for California wastewater effluent samples. Given that the aforementioned recycled water panel focused specifically on potable reuse and landscape irrigation scenarios, these data were representative of effluent from WWTPs that utilized secondary or tertiary treatment in California. A second tier of chemicals associated with WWTP discharge across the US provided by an effort which evaluated freshwater impacts (Diamond *et al.* 2011) were also screened as were high production volume chemicals with persistent and bioaccumulative properties (Drewes *et al.* 2009; Howard and Muir 2010, 2011; Kumar and Xagoraraki 2010). Peer-reviewed and review articles that evaluated the risk of CECs in various media (i.e., water, sediment and tissues) served as a third tier source to identify potential chemicals for assessment (Shaw and Kannan 2009, Vidal-Dorsch *et al.* 2012, Maruya *et al.* 2012, Sedlak and Greig 2012). Lastly, some chemicals without occurrence data available to the panel at the time of assessment (e.g., levonorgestrel) were included for review if toxicological studies revealed a no observed effect concentration (NOEC) of less than 0.1 mg/L.

The panel also concluded that for a chemical to be selected for monitoring, an analytical method capable of detecting the chemical in at least one of three environmental matrices -- water, sediment or biological tissue -- must be available. Surface water measurements from freshwater, estuarine, and/or oceanic samples were considered. Given that hydrophobic CECs preferentially partition onto sediment and particulate matter and can subsequently be transferred via food web exposure, sediment and biological tissue measurements were also sought out. Inclusion of sediment and tissue was deemed important as monitoring of WWTP discharges typically includes filtration of effluent samples prior to analysis likely resulting in an underestimate of the total loading for non-filtered final effluents. For tissues, recent studies that reported the occurrence

of CECs in aquatic biota, potentially leading to exposure of birds or mammals, including humans were reviewed. Given the almost certain existence of unknown CECs, the panel concluded that providing an adaptive framework, i.e., one that can be modified through periodic re-evaluation as additional data or methodologies come forward, was the most prudent approach to develop guidance for assessing the environmental risk of CECs.

Screening of CECs Using a Risk-Based Assessment Framework

To focus the universe of CECs on those with the greatest potential to pose a risk to ecological receptors or human health, a risk-based screening framework was adapted from a previous scientific advisory panel (Drewes *et al.* 2013). For each CEC with available occurrence and toxicity information, the framework compared the measured or predicted environmental concentration (MEC or PEC) to an effects-based threshold to derive a monitoring trigger quotient (MTQ):

$$MTQ = [(MEC \text{ or } PEC)/MTL)] \quad \textbf{Eq. 1}$$

where the monitoring trigger level (MTL) was derived from the no observed effect concentration (NOEC) and/or predicted no effect concentration (PNECs). If the resulting MTQ was less than unity (i.e., MEC or PEC <MTL), the potential risk was assumed to be negligible and the CEC was not considered further for monitoring. If the MTQ was greater than unity (i.e., MEC or PEC > MTL), the CEC was assumed to have the potential to pose a risk that warranted further consideration for monitoring.

The maximum MEC in water, sediment or tissue was used as a conservative representation of potential exposure. Predicted concentrations were estimated from MECs using representative dilution factors for embayment and offshore marine scenarios (see also Model Scenarios for CEC Sources, Fate and Exposure). No observable or predicted no effects concentrations (NOECs or PNECs) were employed to impart conservatism in executing the framework. The purpose of developing MTQs using these conservative assumptions adopted by the panel was solely to determine whether a CEC should be included in a monitoring program. Thus, an MTQ of greater than unity does not necessarily indicate that an actual risk exists, only that additional evaluation of that CEC may be needed. To determine whether a potential risk may actually be present, the information and assumptions used in the risk-based assessment would require further refinement.

Model Scenarios for CEC Sources, Fate, and Exposure

A simple mass balance model was used to guide the development of three representative exposure scenarios to test the conceptual approach and to provide examples of transport and potential exposure of CECs to receptors of interest in coastal aquatic ecosystems. Although several sources may contribute CECs to the environment, the panel was specifically charged to address the impact of WWTP effluent and stormwater discharges. The fate of CECs in these scenarios was divided into particulate (bound) or aqueous (dissolved) phases. Subsequently, direct (aqueous) or indirect (dietary) routes of exposure were identified for each scenario. The following scenarios were selected to represent freshwater, brackish (estuarine) and marine systems across California, based upon the most common and relevant discharges permitted under the NPDES. Scenarios that focused on leachate from solid waste management facilities, atmospheric deposition or runoff from agricultural operations were not addressed.

Scenario 1 - WWTP Effluent Dominated Inland Waterway

A highly modified and/or channelized freshwater system or "waterway" was selected to represent this scenario given the availability of data associated with WWTP effluent compared with stormwater discharge. Exposure to receptors in this scenario was conservatively assumed to be equal to the concentration of CECs in secondary/tertiary effluents from WWTPs or measured values from the literature, i.e., no dilution of discharged effluent was considered. This scenario focuses exclusively on dissolved aqueous exposure, operationally defined as the mass of chemical not retained by a 0.7 µm (effective pore diameter) filter, given that Scenario 2 (below) addresses indirect exposure from particulate-bound CECs. However, particulate-bound CECs could be addressed in future assessments of Scenario 1.

Scenario 2 - Coastal Embayment

San Francisco Bay (SFB) was used to represent this scenario as concentration data and a loading and fate model using PCBs as a model chemical have

been previously published and were available to the panel (Davis 2003, Davis *et al.* 2007). Aqueous exposures were based on MECs determined in this water body, or by applying a 10-fold dilution factor to measured concentrations in WWTP effluent. Indirect exposure (i.e., bioaccumulation) for SFB wildlife was modeled for 2,2',4,4'-tetrabromodiphenyl ether (PBDE 47), a representative hydrophobic CEC. Sediment concentrations derived from discharged WWTP effluent and stormwater were estimated using a 1-dimensional box model and the model output was compared to MECs (Anderson *et al.* 2012). Tissue concentrations were calculated from bioaccumulation factors derived from SFB actual monitoring data.

Scenario 3 - Ocean Discharge of WWTP Effluent

Concentrations of CECs in off-shore discharges from WWTPs in southern California were used to represent conditions for this scenario. A summary of MECs for dozens of CECs was recently published for four off-shore WWTP outfalls, together representing 1 billion gallons per day of design discharge capacity (Vidal-Dorsch *et al.* 2012). Measured concentrations of CECs were available or were predicted from discharged WWTP effluent using a dilution factor of 100 for direct exposure assessment. A recent study on dissolved CECs at these same marine outfalls indicated instantaneous dilution factors to be ~1000 (Vidal-Dorsch *et al.* 2012) relative to discharged final effluent, affording a ten-fold safety factor to the assumed dilution factor of 100. Sediment and biological tissue concentrations for a regionally abundant flatfish (*Pleuronichthys verticalis*; Maruya *et al.* 2012) were used for indirect exposure assessment.

Initial Risk-Based Screening of CECs

Toxicity benchmarks (e.g., NOECs or PNECs) for survival, growth and reproduction in sensitive aquatic (fish and non-fish) species from previously published studies were compiled and summarized in Supplemental Information (SI) Tables SI-1 and SI-2 (ftp://ftp.sccwrp.org/pub/download/DOCUMENTS/AnnualReports/2013AnnualReport/ar13_001_012SI.pdf). Assuming that most CECs occur in the environment in the ng-µg/L range, the panel focused on compounds with NOECs <0.1 mg/L (<100,000 ng/L) for aqueous exposure (Table 1). The corresponding MTLs were then derived by dividing NOECs or PNECs by appropriate uncertainty factors. Specifically, an uncertainty factor of 10 was applied for each of the factors listed below:

- CECs with an unknown mode of action (MOA)
- CECs where a potential endocrine disrupting mode of action was not incorporated into either the PNEC or NOEC
- To convert a freshwater NOEC/PNEC to a saltwater NOEC/PNEC
- To convert an acute NOEC/PNEC to a chronic NOEC/PNEC

If NOECs were not available, published acute LC_{50}s were utilized. If no acute information was available, the EPA's ECOSAR (Diamond *et al.* 2011) was used to estimate effects thresholds, utilizing the lowest NOEC. The potential for antibiotic resistance (ABR) was evaluated for indicator bacteria or pathogens as a basis for determining adverse effects within microbial communities (Uyaguari *et al.* 2009) or increased public health risk associated with recreational water use (Spellberg *et al.* 2011). The lowest observed concentration causing inhibition of bacterial growth (minimum inhibitory concentration, or MIC) was used as the basis for establishing MTLs for antibiotic CECs, incorporating uncertainty factors to account for the range of published MICs and the relative abundance of published information. Similar to non-ABR endpoints, uncertainty factors of 100 to 1000 were used to derive MTLs for antibiotic resistance-related endpoints and anti-microbial toxicity, using the corresponding NOECs.

For some CECs and exposure scenarios where data for appropriate endpoints and test species were available, MTLs were derived without the use of uncertainty factors; in other cases, multiple uncertainty factors were used as appropriate. The maximum cumulative uncertainty factor applied was 1000; thus, compounds with (NOEC/1000) in the ng/L range were considered to have the highest probability of posing a potential risk. Sediment NOECs were developed only for those CECs with known occurrence data.

Multimedia occurrence data for CECs were compiled using a tiered relevance framework with preference given to data generated for California. Maximum concentrations of CECs in WWTP effluent, in waterbodies receiving stormwater runoff and other CEC sources, and in sediment and biological tissues were adopted as MECs for use in

Table 1. Chemicals with published no observable effects concentrations (NOECs) less than 0.1 mg/L in aquatic species that were considered for initial monitoring using a risk-based assessment.

Fish	Non-Fish	Non-Fish (cont.)
p-nonylphenol[b]	AHTN	Ibuprofen[b]
Octylphenol	p-nonylphenol[c]	Miconazole
AHTN (tonalide)	Octylphenol	Nonylphenol monoethoxylate (NP1EO)
Atrazine	Atenolol	Octocrylene
Bisphenol A (BPA)	Atorvastatin	PBDE-47, PBDE-99[c]
Chlorpyrifos	Atrazine	Permethrin[b,c]
Cis-androstenedione	Azithromycin[a]	PFDA
Diclofenac[b]	Bifenthrin[b,c]	PFOS[c]
Droperinone	Bis (2-ethylhexyl) phthalate[c]	Progesterone
17-beta estradiol (E2)[b]	Butylbenzyl phthalate[c]	Sulfamethoxizole[a]
Estrone[b]	Carbamazepine	Testosterone
Galaxolide	Chlorpyrifos[b]	Triclosan[a,b]
Ibuprofen[b]	Ciprofloxacin[a]	Trimethoprim[a]
Levonorgestrel	Desulfinyl fipronil	Ziprasidone
Miconazole	di-n-butylphthalate[c]	
Nonylphenol monoethoxylate (NP1EO)	Erythromycin[a]	
PBDE-47	Fenofibrate	
PBDE-99	Fipronil	
Permethrin	Fluorouracil	
Propranolol	Fluoxetine	
Setraline	Galaxolide[b]	
Triclosan	Gemfibrozil	

[a] antibiotic

[b] monitoring trigger quotient (MTQ) >1 for aqueous phase exposure

[c] monitoring trigger quotient (MTQ) >1 for sediment exposure

the risk-based assessment. Peer-reviewed literature values for other geographical regions were considered when no occurrence data from California were identified for a specific CEC.

Monitoring trigger quotients (MTQs) were computed using Equation 1 for each of the three exposure scenarios. Chemicals with MTQs that exceeded unity were considered for monitoring (Tables SI-3 through SI-8). Aqueous concentrations and NOECs from aqueous routes of exposure were used in every aqueous phase scenario. Where MECs were not available, PECs were estimated by applying dilution factors of 10 and 1000 to secondary WWTP effluent data for embayment and off-shore marine waters (Scenarios 2 and 3), respectively. No aqueous phase CECs exceeded an MTQ of unity for the off-shore ocean scenario. Indirect exposure using sediment and tissue values were determined for Scenarios 2 and 3. Antibiotic resistance was considered for aqueous phase antibiotics (listed in Table 1) in all scenarios due to the lack of ABR sediment exposure and effects data.

Adaptive Monitoring Strategy

The panel recommended an adaptive monitoring approach with four sequential phases that balanced the potential risks identified for CECs, including uncertainty, against escalating actions (Figure 2). The phased approach first develops a list of CECs from the risk-based framework, performs initial monitoring at appropriate spatial and temporal scales using robust analytical methods and evaluates emerging monitoring and assessment technologies, analyzes and interprets initial monitoring data using the most current information and modeling tools, and implements control actions commensurate with potential risk. The panel further recommended revisiting the conceptual approach periodically (e.g., every 5 years) to respond in a timely fashion to recently developed monitoring data as well as changes in the state of

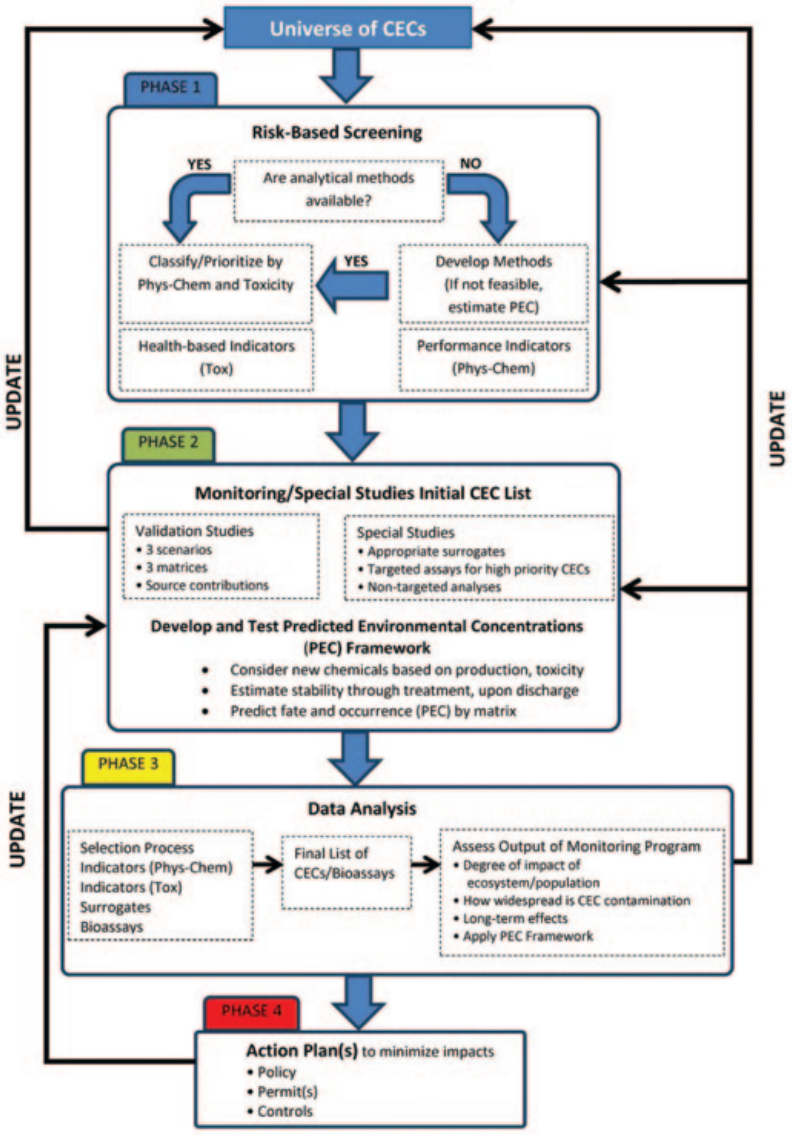

Figure 2. A four-phase monitoring sequence focuses on chemicals of emerging concern (CECs) with the highest risk, development of new monitoring and assessment tools and periodic assimilation and interpretation of new information to refine the monitoring enterprise, as needed.

knowledge concerning CECs. In addition, the panel recognized the advantages of incorporating elements of this phased monitoring approach with existing monitoring programs to maximize leveraging of resources committed to water quality monitoring across the State.

Initial Monitoring and Special Studies

Phase 1 of the proposed monitoring program develops an initial list of CECs by applying the risk-based screening framework to the focused universe of CECs. A total of 16 CECs were identified in the initial screen: 10 chemicals were identified for aqueous monitoring in effluent dominated waterways (Scenario 1); 8 chemicals, for aqueous monitoring in embayments (Scenario 2); 4 and 3 CECs identified for monitoring in embayment and offshore marine sediments, respectively; and 2 CECs for wildlife tissue (Table 2). The composite list represents several classes of CECs, including pharmaceuticals (diclofenac, ibuprofen), personal care products (galaxolide), pesticides (bifenthrin, chlorpyrifos) and commercial chemicals [p-nonylphenol, polybrominated diphenyl ethers (PBDEs), and perfluorooctanesulfonate (PFOS)]. In addition to providing lists of chemicals matched to the scenario and environmental matrix of interest, the panel recommended monitoring of WWTP effluent prior to discharge and in waterways receiving stormwater discharge (Table 2) to address their relative contribution as CEC sources.

Table 2. Chemicals recommended for initial monitoring by exposure scenario and environmental matrix (i.e., aqueous, sediment, tissue). M = include in monitoring program (E = embayments, F = freshwater, O = ocean waters); WWTP = municipal wastewater treatment plant; NA = not applicable. Monitoring trigger quotient (MTQ) is given in parentheses.

Compound	Inland Waterbody Aqueous Scenario 1	Embayment Aqueous Scenario 2	WWTP Effluent	Waterbody Receiving Stormwater Aqueous, Sediment[a]	Embayment Sediment Scenario 2	Marine Sediment Scenario 3	Tissue
Bis(2-ethylhexyl) phthalate	NA	NA	M-O	NA	NA	M(3.8)	NA
Bisphenol A	M(8.7)	M(2400)	M–E/F	M	NA	NA	NA
Bifenthrin	M(210)	M(750)	M-E/F	M	M(1500)	NA	NA
Butylbenzyl phthalate	NA	NA	M-O	NA	NA	M(16)	NA
Permethrin	M(46)	M(46)	M-E/F	M	M(260)	NA	NA
Chlorpyrifos	M(38)	M(220)	M-E/F	M	NA	NA	NA
Estrone	M(12)	M(12)	M-E/F	M	NA	NA	NA
Ibuprofen	M(10)	NA	M-F	M	NA	NA	NA
17-beta estradiol	M(4.2)	M(4.2)	M-E/F	M	NA	NA	NA
Galaxolide (HHCB)	M(4.0)	M(4.0)	M-E/F	M	NA	NA	NA
Diclofenac	M(2.3)	NA	M-F	M	NA	NA	NA
p-Nonylphenol	NA	NA	M-O	NA	NA	M(30)	NA
PBDE -47 and 99	NA	NA	M-E/F/O	M	M(5700)	M(15)	M(850)
PFOS	NA	NA	M-E/F/O	M	M[b]	M[b]	M(1.8)
Triclosan	M(2.0)	NA	M-F	M	NA	NA	NA

[a] Addresses data gap on relative contributions of storm water discharge and WWTP effluent

[b] Addresses route of exposure and data gap for estimation of biota sediment accumulation factors (BSAFs)

Phase 2 implements monitoring of CECs identified in the Phase 1 screening process. The occurrence information obtained will be used to "validate" the list of target CECs according to discharge scenario (i.e., inland freshwater, coastal embayment or open ocean), and also by matrix (e.g., aqueous, sediment and tissue). To assist with assessment and interpretation of monitoring data, and to provide managers with longer-term decision-making tools, mathematical models are also viewed as an integral component of Phase 2 activities. Lastly, several special ("pilot") studies recommended to complement and provide context to the CEC occurrence monitoring data, as well as to evaluate methods to improve the relevance and efficiency of monitoring, are recommended (Table SI-9).

Among these special studies are the development of bioanalytical methods to screen for CECs (and other chemicals) by mode of biological action and toxicity assays that focus on longer term, chronic endpoints such as those associated with adverse reproductive outcomes in fish and invertebrates (Chandler *et al.* 2004a,b; Miller *et al.* 2007; Ankley *et al.* 2008). Direct measurement of ABR in indicator bacteria was recommended as an initial monitoring tool for WWTP discharging into effluent dominated waterways and coastal embayments. The performance of these biological assays in tandem with chemical monitoring of CECs provides the opportunity to link *in vitro* responses with *in vivo* effects, a key step in evaluating the relevance and thus utility of cell-based screening level bioassays.

Interpretive Guidelines for Monitoring and Special Studies Data

To assess the validity of applying the risk-based screening framework as well as to respond to changing environmental conditions, the Panel recommended, as Phase 3, a reassessment of the initial CEC list and monitoring design based on the information developed by the initial monitoring effort. At the heart of this reassessment is comparison of refined MECs to MTLs, updated as necessary as more toxicological information becomes available. In essence, the intent is to evaluate the Phase 2 results within the context of a tiered risk-based monitoring and response framework as presented in Figure 3. An escalating level of management action was proposed, including continuing or increased monitoring, for CECs that consistently exhibit MTQs in excess of

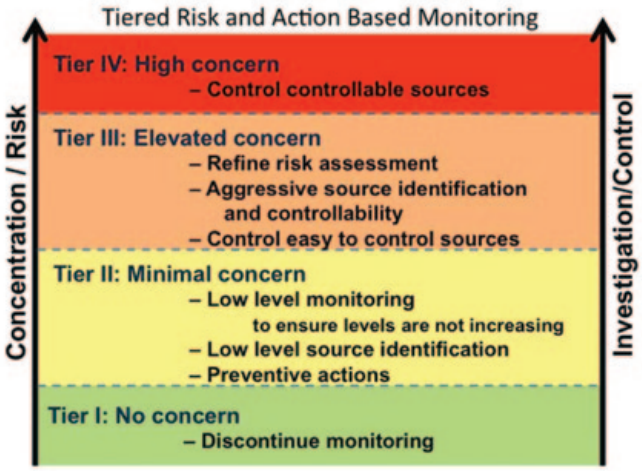

Figure 3. Interpretation of monitoring data for chemicals of emerging concern (CECs) considers a tiered management response commensurate with the magnitude of estimated risk, e.g. as measured by the monitoring trigger quotient (MTQ; y-axis).

unity. In contrast, CECs that consistently exhibit MTQs less than unity likely present a relatively low risk and, thus, may be subject to decreased monitoring (frequency and/or location) or removed from monitoring completely.

Another goal of Phase 3 is to update the list of CECs based on results of monitoring using conventional and non-targeted methods, and pilot studies using bioassays listed in Supporting Information (Table SI-9). In addition, the results of the environmental fate models will be evaluated to assess and prioritize future monitoring needs as well as to conduct a preliminary review of the effects of potential control actions aimed at protecting and/or improving water quality, and ultimately, human and wildlife exposure to CECs that result in an MTQ >1. The panel also recommended that an independent scientific advisory panel conduct Phase 3 re-assessment activities with opportunity for input by the stakeholder community. In the fourth and final phase, control actions are identified and implemented for CECs that present an urgent or on-going challenge to receiving water quality.

Recommended Future Activities

The Panel acknowledged that the current state of knowledge concerning the potential impact of chemicals discharged into the environment is far from complete, and moreover, remains a work in progress. The risk-based framework utilized by the Panel to identify the initial list of CECs for monitoring was necessarily limited in scope, e.g., to chemicals with both occurrence and toxicity data available at the time of their deliberations. Thus, thousands of chemical unknowns are not directly and/or adequately addressed using the traditional "chemical-by-chemical" monitoring strategy. Research is thus needed to develop and evaluate bioanalytical tools that will result in more comprehensive and efficient monitoring programs for CECs in California's receiving waters. A recent report on toxicological evaluation of chemicals for human health indicated that high through-put *in vitro* biological methods are a viable alternative to discrete chemical testing (USEPA 2009). Once optimized, such methods will allow regulators to focus on chemicals that elicit specific biological responses associated with adverse outcomes. However, this approach has not yet been applied to the assessment of ecological risk or chemical mixtures present in the environment.

As a complement to existing chemical-specific analytical methods, the panel recommended the development of bioanalytical techniques that integrate the exposure of CECs acting with a common mode of biological action. *In vitro* high-throughput bioassays that target, endocrine disrupting chemicals have been validated for chemical screening programs and show promise for use in water quality monitoring. Moreover, these cell-based tests produce a response that can be linked to higher order impacts (e.g., survival, growth and reproduction; Table 3).

The panel also saw value in filling data gaps on source contributions, occurrence and toxicity of CECs for which there is currently little or no data for California's aquatic systems. Examples of CECs in this category are newly developed pharmaceuticals, replacement flame retardants and recently registered pesticides. Measured environmental concentrations in receiving waters, sediments and biological tissue of sentinel species and in discharged WWTP effluent and stormwater runoff, as well as NOECs/LOECs for such "known unknown" chemicals are needed. This information could be gathered through focused special investigations and existing regional and statewide monitoring efforts, e.g., the recurring southern California Bight regional monitoring survey, the San Francisco Bay Regional Monitoring Program, and the State's Surface Water Ambient Monitoring Program (SWAMP).

A third recommendation was the development and/or refinement of models to predict environmental concentrations and toxicity as a means for prioritizing

Table 3. Cell-based *in vitro* bioassays that target endpoints of concern for aquatic life and humans exposed to a variety of chemicals of emerging concern (CECs).

Assay	Mechanism	Potential Health Implications
Estrogen receptor (ER) activity	Estrogen signaling	Reproduction, cancer
Androgen receptor (AR) activity	Maintenance of male sexual phenotype	Androgen insensitivity syndrome
Progesterone receptor (PR) activity	Embryonic development, cell differentiation, homeostasis	Cancer, diabetes, hormone resistance syndromes
Peroxisome proliferator-activated receptor gamma (PPAR-g)	Fatty acid storage and glucose metabolism	Obesity, diabetes, atherosclerosis, and cancer
Glucocorticoid receptor (GR) activity	cortisol, glucocorticoids	Development, metabolism, immune response, neuroendocrine integration
Genotoxicity	DNA mutations	Cancer
Cytotoxicity	General toxicity	Tissue integrity

chemicals on which to focus future monitoring and assessment resources. Validated model constructs that consider chemical production volume and use, population density and land use can be used to generate PECs more cost effectively than can be measured, particularly for chemicals for which no analytical methods are available. Hannah *et al.* (2009) describe such a process to develop PECs for ethinylestradiol, a pharmaceutical that is detectable in US surface waters. The Panel endorsed development of this capability for determining the potential of CECs to occur at concentrations that may be above thresholds of concern.

Lastly, the Panel stressed the need to evaluate the risk posed by CECs relative to other stressors, including priority pollutants, currently monitored chemicals, and general water quality parameters (e.g., ammonia). Annually, several million dollars are dedicated to obtaining monitoring data in the State's receiving waters for many water quality parameters, including dozens of individual chemical constituents. The panel submitted that such a ranking would aid water quality managers in allocating available resources most efficiently, i.e., focusing monitoring on the greatest potential of risk to receiving waters and diverting resources, if need be, from lesser to greater sources of potential risk.

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Supplemental Information

Supplemental Information is available at ftp://ftp.sccwrp.org/pub/download/DOCUMENTS/AnnualReports/2013AnnualReport/ar13_001_012SI.pdf.