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Critical Review

Toward Sustainable Environmental Quality: Priority Research Questions for North America

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Global Horizon Scanning™

This article includes online-only Supplemental Data.

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Abstract: Anticipating, identifying, and prioritizing strategic needs represent essential activities by research organizations. Decided benefits emerge when these pursuits engage globally important environment and health goals, including the United Nations Sustainable Development Goals. To this end, horizon scanning efforts can facilitate identification of specific research needs to address grand challenges. We report and discuss 40 priority research questions following engagement of scientists and engineers in North America. These timely questions identify the importance of stimulating innovation and developing new methods, tools, and concepts in environmental chemistry and toxicology to improve assessment and management of chemical contaminants and other diverse environmental stressors. Grand challenges to achieving sustainable management of the environment are becoming increasingly complex and structured by global megatrends, which collectively challenge existing sustainable environmental quality efforts. Transdisciplinary, systems-based approaches will be required to define and avoid adverse biological effects across temporal and spatial gradients. Similarly, coordinated research activities among organizations within and among countries are necessary to address the priority research needs reported here. Acquiring answers to these 40 research questions will not be trivial, but doing so promises to advance sustainable environmental quality in the 21st century. *Environ Toxicol Chem* 2019;38:1607–1624. © 2019 The Authors. *Environmental Toxicology and Chemistry* published by Wiley Periodicals, Inc. on behalf of SETAC.

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INTRODUCTION

The face of the planet is changing. Increasingly shaped by global megatrends, including demographic patterns of human populations and the food–energy–water nexus, multiple challenges and opportunities exist for sustainable management of the environment and human health (National Intelligence Council 2012). Demographic transitions to cities, in which most humans now reside (United Nations 2018), are concentrating consumption of resources and production and use of chemical substances in an unprecedented fashion. Interdependencies among increased food production, energy generation, and source waters for human and ecological uses are self-evident. Further, implications of climate change for environmental sustainability in light of these megatrends are pronounced, yet consequences for environmental quality remain disparately understood and engaged by research organizations. The United Nations Sustainable Development Goals (SDGs; United Nations 2016) provide a global framework to assist in advancing a more sustainable future for all people. However, realizing the SDGs requires strategic partnerships and sustainable environmental quality. For example, the 2019 Global Assessment Report on Biodiversity and Ecosystem Services by the Intergovernmental Panel on Biodiversity and Ecosystem Services (IPBES 2019) recently reported unprecedented declines of species and acceleration of extinction rates at the global level. Identifying and prioritizing research efforts that are necessary to address these timely problems and meet the SDGs remain challenges, particularly when financial resources for research and development activities are stressed. This reality necessitates the question, what are the big research needs to achieve more sustainable environmental quality?

Strategic environment and public health research programs are developed routinely in response to existing challenges or in recognition of imminent research opportunities. For example, "grand challenge" is an increasingly common term aimed at structuring important needs (Hicks 2016; Kaldeway 2018). In 2003, the Gates Foundation announced its "Grand Challenges in Global Health" initiative (Varmus et al. 2003). In the United States, the National Academies subsequently initiated the "Grand Challenges of Engineering" and the "Grand Challenges of Health and Medicine." More recently, the Centers for Disease Control and Prevention launched the Understanding Needs, Challenges, Opportunities, Vision and Emerging Roles in Environmental Health (UNCOVER-EH) initiative (Gerding et al. 2017, 2019). Key question exercises have also emerged as an approach to identify and prioritize research needs. In fact, previous key questions projects have been used for conservation biology (Sutherland et al. 2009), agriculture (Pretty et al. 2010), and marine science (Kennicutt et al. 2014). Other efforts have focused on identifying and prioritizing key research questions needed to reduce environment and health risks from pharmaceuticals and personal care products in the environment (Boxall et al. 2012; Rudd et al. 2014). Building from these collective experiences, a unique opportunity was initiated to leverage the key question model to identify research needs toward achieving sustainable environmental quality (Brooks et al. 2013).

We report a novel effort to identify important environmental quality research questions in North America as part of a larger global initiative. The Global Horizon Scanning Project (GHSP) was launched to identify key research questions that could make significant advances toward more sustainable environmental quality over the next decade. Priority research questions for Europe (Van den Brink et al. 2018) and Latin America

(Furley et al. 2018) were published recently. In the North America exercise, from which we report findings and priorities in the present study, we specifically engaged North American members from Canada, the United States, and Mexico representing multiple sectors (business, academia, government) of the Society of Environmental Toxicology and Chemistry (SETAC) and the American Chemical Society's (ACS) Environmental Chemistry (ENVR) and Agrochemicals (AGRO) Divisions. We solicited research questions from these scientists and engineers, which was followed by a synthesis workshop in which the top research questions were identified. After the workshop, a ranking exercise of these questions was performed again by scientists and engineers from the North American academic, government, and business sectors who were members of SETAC and the ACS ENVR and AGRO Divisions. This effort was intentionally transparent, bottom-up, multidisciplinary, and inclusive of perspectives from multiple stakeholders.

METHODS

Research questions were solicited by e-mail from members of the North American Geographic Unit of SETAC and the North American members of the ACS ENVR and AGRO Divisions. These members represented diverse disciplines and sectors of environmental science and technology. Consistent with previous efforts in conservation biology (Sutherland et al. 2011) and the GHSP activities in other geographic regions (Van den Brink et al. 2018; Furley et al. 2018), we provided guidance on the scope of an ideal question: 1) questions should address important knowledge gaps; 2) questions should be answerable within a decade given sufficient research funding; 3) questions should be answerable through a realistic research design; 4) questions should provide a factual answer that does not depend on value judgments; 5) questions should cover a spatial and temporal scale that could realistically be addressed by a research team; 6) questions should not be answerable by "it all depends" or "yes" or "no"; and 7) questions should contain a subject, an intervention, and a measurable outcome. Submitted questions were then reviewed by the project team to remove duplicate questions and questions outside the scope of the exercise. The final list of questions was taken forward for discussion at a horizon-scanning workshop.

The North America workshop was held at the 2015 SETAC Annual Meeting in Salt Lake City, Utah, USA, and followed the format of workshops in Europe (Van den Brink et al. 2018) and Latin America (Furley et al. 2018). The ACS ENVR and AGRO Divisions sent delegates from the academic, government, and business sectors. The submitted questions were partitioned to 9 themes that were discussed in breakout sessions by multidisciplinary participants from the academic, government, and business sectors. Again, consistent with methods employed elsewhere (Boxall et al. 2012; Furley et al. 2018; Van den Brink et al. 2018), workshop participants identified 2 to 5 priority research questions in each breakout group, in which members could rephrase or combine candidate questions or could propose new questions to address issues not directly covered by candidate question submissions. A combined list of priority research questions was discussed and then agreed on through a consensus of members from all the breakout groups in a final plenary session to generate the top 40 list of priority questions. After the workshop, following methods employed during the European exercise (Van den Brink et al. 2018), an Internet-based survey of North American members of SETAC and the ACS ENVR and AGRO Divisions was performed to rank the priority questions using a best-to-worst scaling method (Rudd et al. 2014). This hierarchical Bayesian approach identified ranks for each question by respondent and subsequently calculated the overall rank of top research questions for all respondents.

RESULTS AND DISCUSSION

Three hundred and four individual questions were submitted by North American members of SETAC and the ACS ENVR and AGRO Divisions (Supplemental Data, Table S1). Following removal of duplicate and invalid questions, 223 of these research questions were discussed during the Salt Lake City workshop. Workshop participants identified a list of 40 research questions that were considered consensus priorities (Figure 1). The best-to-worst ranking analysis of these top 40 questions performed after the workshop was based on 575 individual responses (Table 1). In this section we discuss these top 40 questions, grouped within 7 interconnected themes (Table 2 and Figure 2), which collectively outline timely challenges and opportunities for environmental toxicology and chemistry research.

Addressing environmental analytical chemistry challenges in the 21st century

Environmental analytical chemistry is a central foundation to the study of chemical fate and exposure assessment as well as for regulatory activities on chemicals. It has evolved over the past 50+ yr, drawing on expertise and methodology from disciplines such as organic and inorganic geochemistry, food chemistry, and analytical chemistry. There are many well-known success stories such as the discovery of the ubiquity of polychlorinated biphenyls (PCBs; Jensen et al. 1969), determination of chlorinated dioxins and furans at ng/kg concentrations (Buser et al. 1985), discovery of perfluorooctane sulfonate (PFOS) in terrestrial and marine wildlife (Giesy and Kannan 2001), trace analysis of lead (Patterson and Settle 1976), and multi-isotope analysis of mercury and other metals (Evans et al. 2001). Over the past 30 yr, confidence in the reliability and interlaboratory comparability of environmental measurements has increased because of 1) development of standardized and validated analytical methods by the US Environmental Protection Agency, the US Geological Survey (National Environmental Methods Index 2018), and the International Organization for Standardization (2002); 2) reference materials by the National Institute of Standards and Technology (2018) and the European Commission (2018); 3) increased availability of certified analytical standards (e.g., individual PCB and chlorinated dioxin/furan isomers); and 4) interlaboratory comparisons (Quality

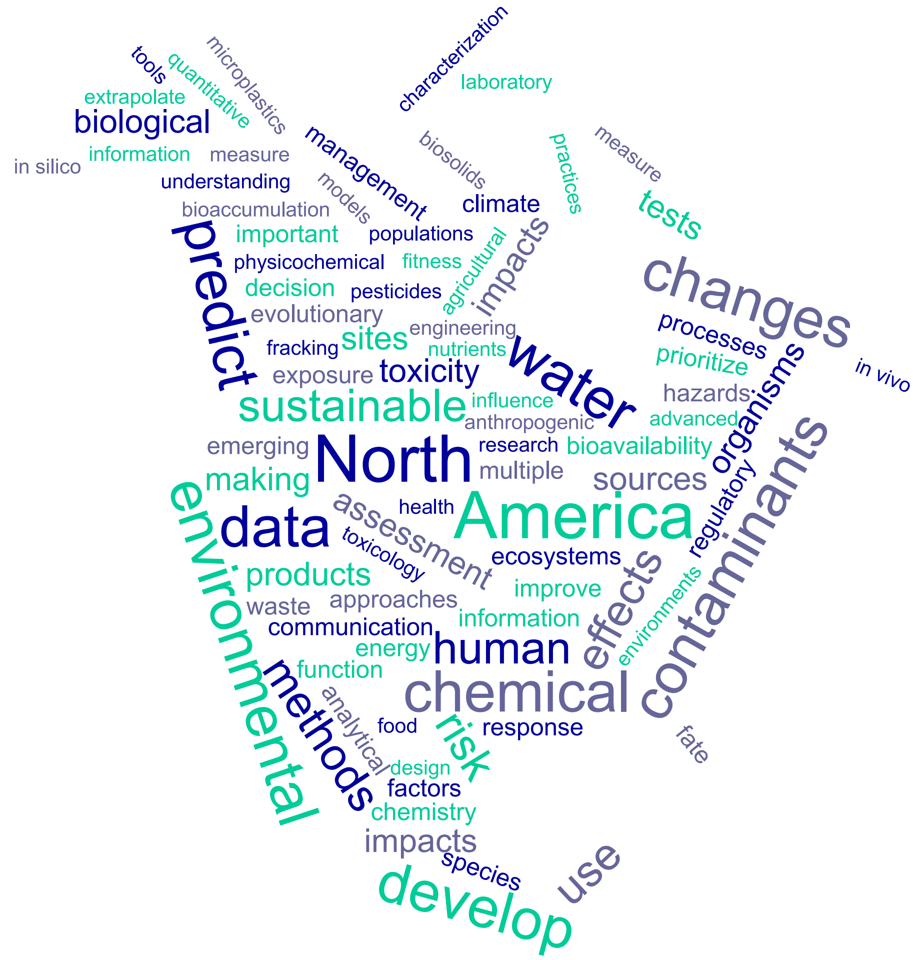

FIGURE 1: Word cloud of 40 priority research questions from North America.

Assurance of Information for Marine Environmental Monitoring in Europe 2018) and certification (International Organization for Standardization 2017).

A top-ranked question (Q2) under this topic was how to develop quantitative analytical methods for next-generation emerging contaminants (e.g., nanomaterials, microplastics, fracking fluids, organometallics, ionizables, engineered biomolecules—synthetic biology/biologically inspired design, degradation products, speciation and metabolites of parent compounds). The term "emerging contaminants" became widely used starting in the early 2000s (Daughton 2016). Diamond et al. (2011) found that there was no precise definition of chemicals of emerging concern (CECs), but they noted that CECs generally were substances that were currently unregulated and for which there were reliable concerns about potential risks to humans and aquatic and terrestrial ecosystems. Such chemicals face numerous analytical challenges as they can occur and elicit effects below historical detection limits, are found in complex mixtures, and are temporally and spatially variable. The early 2000s saw the widespread introduction of liquid chromatography-tandem mass spectrometry (MS/MS) instruments that greatly expanded the compounds that could be analyzed routinely to include polar, ionizable, and ionic organics such as pharmaceuticals and perfluoroalkyl acids. More recently, the increased availability of instruments, such as high-resolution MS, Orbitraps, and time of flight instruments, has permitted assignment of molecular formulas based on exact mass analysis. The availability of large MS databases has allowed identification of thousands of molecules via "suspect and nontarget" analysis (Schymanski et al. 2015; Hollender et al. 2017). Progress has also been made on the analysis of inorganic (Montaño et al. 2016) and carbon-based (Goodwin et al. 2018) nanoparticles, on antibiotic resistance genes in natural waters (Singer et al. 2016), and on detection of microplastics (Rochman et al. 2017) and minerals using diverse instrumentation (e.g., X-ray diffraction, scanning electron microscopy-energy dispersive X-ray spectroscopy, Brunauer-Emmett-Teller surface area analysis, synchrotron analysis).

Despite advances in instrumentation, there has been increased recognition that the number of substances for which analytical chemistry methods are available represents only a small subset of the hundreds of thousands of possible molecules based on the known chemicals in commerce and their possible transformation products (Hollender et al. 2017). Thus, a closely related question from the workshop (Q23) on how to develop advanced forensics (e.g., chemical fingerprinting) for tracing and modeling the sources of contaminants also

TABLE 1: Top 40 priority research questions from the North American portion of the Global Horizon Scanning project with associated ranking and scores

Rank	Question	Mean	95% Upper	95% Lower
1	How can research in environmental toxicology and chemistry inform agricultural (water and energy use) practices and the use of chemical pesticides/nutrients for the sustainable production of food?	332.54	333.29	346.42
2	How can we develop quantitative analytical methods for next-generation emerging contaminants (e.g., nanomaterials, microplastics, fracking fluids, organometallics, ionizables, engineered biomolecules—synthetic biology/biologically inspired design)?	326.81	323.83	338.25
3	How well do laboratory toxicity and bioaccumulation tests predict what happens at real-world sites?	326.29	322.58	336.12
4	How can we improve the characterization of the exposure–response relationship of multiple chemical stressors?	325.38	321.26	334.57
5	How can we better describe and predict the fate of chemical species in waste treatment, recycling, and disposal (e.g., water, solid waste, biosolids, e-waste), especially emerging chemicals, to support decision-making?	321.99	318.53	332.62
6	How can we design and predict the biological and physicochemical properties of chemicals during development to minimize environmental hazards?	318.89	316.29	330.73
7	What are the most effective methods to communicate science-based risk, and science in general, to impact public perception and regulatory policy development?	318.29	312.78	328.85
8	What characteristics of environmental stressors (chemical and nonchemical) are most important for prioritizing effects on ecosystem structure, function, and services?	314.74	311.43	325.84
9	How can we revise the environmental risk assessment process to integrate and make full use of both human health and ecotoxicity data?	305.95	297.96	314.08
10	How well do exposure models work, what are their sources of uncertainty, and what data should be collected to reduce uncertainty?	302.26	294.15	312.16
11	What are the factors that affect the bioaccumulation of contaminants in organisms/wildlife, and how can we predict when and where specific factors are most important?	301.03	294.61	310.65
12	What changes in human behavior would have the greatest benefits on sustainability of terrestrial and aquatic ecosystems?	295.42	294.39	310.17
13	What are the best methods to measure bioavailable/freely dissolved/chemical activity of organic chemicals and metals in environmental media?	289.74	286.83	305.31
14	How can we ensure that the drinking water that is derived from marginal sources (e.g., brackish groundwater in certain aquifers, eutrophic lakes/rivers) is acceptable for human consumption?	289.47	284.40	301.74
15	What environmental and human health risks should be managed and monitored in water reuse?	286.63	284.43	300.86
16	How accurate are the predictions of and the results from site-specific risk assessments based on ecological monitoring data?	284.87	275.06	294.00
17	What are the impacts of contaminants over multiple generations: incorporating evolutionary concepts of adaptation, plasticity, epigenetics, fitness costs?	278.09	275.26	291.81
18	What tools do we need to develop chemical products to quantify environmental sustainability for science-based decision-making?	277.68	271.95	289.18
19	How can the efficacy of prospective risk assessment and management approaches be assessed for environmental chemicals of concern?	277.65	269.35	287.43
20	What are the high-throughput tests that are most predictive of in vivo hazards, and how can these be standardized among labs?	276.23	266.87	285.53
21	What is the influence of abiotic and biotic stressors (independent of climate change) on bioavailability and effects of contaminants?	273.15	266.70	284.57
22	How can diverse information representing multiple levels of biological organization from in vitro and in vivo data, read-across, in silico, etc. be coalesced into coherent hazard frameworks?	272.53	265.85	283.89
23	How can we develop advanced forensics (e.g., chemical fingerprinting) for tracing and modeling the sources of contaminants?	270.68	262.66	282.15
24	What networks or mechanisms are required to enable sustainable communication across a wide range of disciplines that support environmental science and regulatory decision-making?	269.04	261.56	280.94
25	How can we develop and improve screening levels (e.g., sediment, soils) and prioritization approaches?	265.70	259.22	278.62
26	How can computational chemistry approaches (in silico) be improved to advance understanding of physicochemical properties to understand fate/toxicity and prioritize for testing and analytical method development?	264.49	257.67	276.09
27	How can we coordinate, curate, and ensure access to quality data for environmental chemical management?	259.99	254.00	273.32
28	How can we measure fitness changes (e.g., behavior, immune function), translating to the population and community levels to incorporate these changes into regulatory processes?	259.68	252.76	271.48
29	How is urbanization impacting ecological and human exposure to and release of contaminants?	259.14	250.75	270.66
30	How can we extrapolate dose from in vitro to in vivo data?	257.38	246.95	266.09
31	How does alteration of food web structure affect contaminant accumulation and long-term consequences?	250.89	246.38	265.81
32	How do organisms in dynamic (e.g., tidal, ephemeral streams, high mountain habitats, polar regions) environments deal with anthropogenic stresses (climate change, xenobiotics, etc.)?	249.40	244.03	264.40
33	What environmental factors, natural or anthropogenic, lead to microbial resistance?	248.36	243.37	262.64

(*Continued*)

TABLE 1: (*Continued*)

Rank	Question	Mean	95% Upper	95% Lower
34	What is the influence of climate change on bioavailability and effects of contaminants?	247.62	240.25	260.77
35	What role does the microbiome play in the response of organisms to contaminants?	237.92	234.03	254.34
36	How can we extrapolate effects data across species using evolutionary conservation of biological pathways?	235.55	227.84	248.09
37	How do fate and toxicity differ in marine and estuarine environments versus freshwater?	225.41	215.42	235.47
38	What are the potential environmental and economic impacts of using energy-bearing secondary materials (by-products) as alternative fuel sources in sustainable manufacturing processes?	211.90	204.11	225.27
39	How can we develop and employ -omics methods as diagnostic tools in field settings?	206.97	196.71	217.63
40	How can we determine the variability of reference populations and sites?	202.46	194.85	215.17

addressed an important challenge for environmental analytical chemists. In addition, this advanced forensic research would address challenges such as identifying sources of contaminants from activities like fracking, accidents such as oil spills, or long-range transport of atmospheric emissions. From an instrumental technology point of view, there have been tremendous advances in environmental forensics. For example, high-resolution separations, using comprehensive 2-dimensional gas chromatography, have successfully been applied for fingerprinting oil samples (Aeppli et al. 2012). High-resolution MS has been used to identify organic substances in mixtures such as fracking fluids (Ferrer and Thurman 2015a, 2015b) and per- and polyfluoroalkyl substances in groundwater (Barzen-Hanson et al. 2017). Advances in the interpretation of multicollector ICP-MS data have led to identification of sources of mercury based on very high-precision analysis of isotope ratios (Demers et al. 2015; Blum and Johnson 2017). However, understanding and predicting transformation products and rates of biodegradation or photooxidation remain major challenges that need to be addressed by interdisciplinary approaches. Indeed, another top-5 question from the workshop (Q5) asked how to better describe and predict the fate of chemical species during waste treatment, recycling, and disposal (e.g., water, solid waste, biosolids, e-waste), especially emerging chemicals, to support decision-making. A recent review of pharmaceuticals and other emerging contaminants also identified the need for more research on the variables and conditions influencing the environmental fate and attenuation of these chemicals in aquatic environments (Wilkinson et al. 2017). To support decision-making in the absence of data, chemical "read-across" approaches from structurally related substances have been proposed for assessment of persistence and biodegradation of chemicals as part of hazard assessments (Rauert et al. 2014).

Enhancing prediction of chemical exposure in environmental assessments

Defining exposure to chemical contaminants is foundational to characterizing risk to human or ecological receptors and retrospectively assessing the probability that harm was caused by environmental contaminants. Exposure models characterize the magnitude, frequency, and duration of exposure and can include sources, environmental pathways, routes of exposure, and associated sources of uncertainties (National Research Council 2007). Several environmental exposure modeling approaches are available from global (water- or airshed) to field-scale simulations to simple fugacity-based, single-compartment screening applications. On the scale of individual organisms, bioavailability has been addressed with biotic ligand models for metals, equilibrium partitioning for neutral organics, and physiologically based toxicokinetic models for other organic substances. In some cases, models encompassing abiotic transport/fate processes have been combined with bioaccumulation and food web modeling to assess exposure in remote environments or along the indoor-urban, rural continuum (Czub et al. 2008; Li et al. 2018). Predictive modeling of chemical concentrations present in various media (e.g., water, air, soil, sediment, biota) is thus a critical practice during chemical management efforts to protect public health and the environment. Additional research is required to accurately predict chemical movement through the biosphere and throughout the life cycle of chemical products (Powers et al. 2012).

A highly ranked question (Q10) in this category focused on chemical exposure models, their sources of uncertainty, and what data should be collected to reduce uncertainty. Di Guardo and colleagues (2018) examined this question in a review of mass balance models that generate exposure information for organic contaminants. They noted that there has been much progress in the development and use of fate and exposure models since the mid-1990s, including better comparability between model results and site monitoring and greater transparency and reliability of models. In addition, guidelines for good modeling practice have been published (Buser et al. 2012). Sensitivity and uncertainty analyses are now an integral part of many models that generate exposure data. The sources of uncertainty are widely recognized to be related to chemical properties and process rates (e.g., biotransformation), emissions data, and spatial and temporal variability within the environment. A major source of uncertainty is the application of exposure models beyond their domain of applicability. This is particularly an issue for the application of models developed for neutral organics to ionizable organics. In fact, the importance of ionization influencing bioavailability, bioaccumulation, and toxicity was previously identified as a key research need (Boxall et al. 2012) and recently has received increased attention (Nichols et al. 2015; Armitage et al. 2017).

It is also important to note that most models and model scenarios were designed to understand chemical exposure based on freshwater aquatic environments; however, seawater has been shown to modify chemical properties (e.g., solubility,

TABLE 2: Top 40 priority research questions from the North American portion of the Global Horizon Scanning project by theme

Rank	Themes and priority research questions
Addressing environmental analytical chemistry challenges in the twenty-first century	
2	How can we develop quantitative analytical methods for next-generation emerging contaminants (e.g., nanomaterials, microplastics, fracking fluids, organometallics, ionizables, engineered biomolecules—synthetic biology/biologically inspired design)?
5	How can we better describe and predict the fate of chemical species in waste treatment, recycling, and disposal (e.g., water, solid waste, biosolids, e-waste), especially emerging chemicals, to support decision-making?
23	How can we develop advanced forensics (e.g., chemical fingerprinting) for tracing and modeling the sources of contaminants?
Enhancing prediction of chemical exposure in environmental assessments	
10	How well do exposure models work, what are their sources of uncertainty, and what data should be collected to reduce uncertainty?
11	What are the factors that affect the bioaccumulation of contaminants in organisms/wildlife, and how can we predict when and where specific factors are most important?
13	What are the best methods to measure bioavailable/freely dissolved/chemical activity of organic chemicals and metals in environmental media?
31	How does alteration of food web structure affect contaminant accumulation and long-term consequences?
35	What role does the microbiome play in the response of organisms to contaminants?
Extrapolating chemical effects across diverse assessment scenarios	
3	How well do laboratory toxicity and bioaccumulation tests predict what happens at real-world sites?
9	How can we revise the environmental risk assessment process to integrate and make full use of both human health and ecotoxicity data?
16	How accurate are the predictions of and the results from site-specific risk assessments based on ecological monitoring data?
17	What are the impacts of contaminants over multiple generations: incorporating evolutionary concepts of adaptation, plasticity, epigenetics, fitness costs?
32	How do organisms in dynamic (e.g., tidal, ephemeral streams, high mountain habitats, polar regions) environments deal with anthropogenic stresses (climate change, xenobiotics, etc.)?
40	How can we determine the variability of reference populations and sites?
Challenges and approaches to addressing multiple stressor interactions	
4	How can we improve the characterization of the exposure–response relationship of multiple chemical stressors?
8	What characteristics of environmental stressors (chemical and nonchemical) are most important for prioritizing effects onecosystem structure, function, and services?
21	What is the influence of abiotic and biotic stressors (independent of climate change) on bioavailability and effects of contaminants?
34	What is the influence of climate change on bioavailability and effects of contaminants?
37	How do fate and toxicity differ in marine and estuarine environments versus freshwater?
Employing new approach methods and concepts in chemical risk assessment	
20	What are the high-throughput tests that are most predictive of in vivo hazards, and how can these be standardized among labs?
22	How can diverse information representing multiple levels of biological organization from in vitro and in vivo data, read-across, in silico, etc. be coalesced into coherent hazard frameworks?
28	How can we measure fitness changes (e.g., behavior, immune function), translating to the population and community levels to incorporate these changes into regulatory processes?
30	How can we extrapolate dose from in vitro to in vivo data?
36	How can we extrapolate effects data across species using evolutionary conservation of biological pathways?
39	How can we develop and employ -omics methods as diagnostic tools in field settings?
Anticipating and predicting human health and ecological impacts of chemicals	
6	How can we design and predict the biological and physicochemical properties of chemicals during development to minimize environmental hazards?
14	How can we ensure that the drinking water that is derived from marginal sources (e.g., brackish groundwater in certain aquifers, eutrophic lakes/rivers) is acceptable for human consumption?
15	What environmental and human health risks should be managed and monitored in water reuse?
19	How can the efficacy of prospective risk assessment and management approaches be assessed for environmental chemicals of concern?
25	How can we develop and improve screening levels (e.g., sediment, soils) and prioritization approaches?
26	How can computational chemistry approaches (in silico) be improved to advance understanding of physicochemical properties to understand fate/toxicity and prioritize for testing and analytical method development?
27	How can we coordinate, curate, and ensure access to quality data for environmental chemical management?
33	What environmental factors, natural or anthropogenic, lead to microbial resistance?
Risk assessment and communication at the science–societal interface	
1	How can research in environmental toxicology and chemistry inform agricultural (water and energy use) practices and the use of chemical pesticides/nutrients for the sustainable production of food?
7	What are the most effective methods to communicate science-based risk, and science in general, to impact public perception and regulatory policy development?
12	What changes in human behavior would have the greatest benefits on sustainability of terrestrial and aquatic ecosystems?
18	What tools do we need to develop chemical products to quantify environmental sustainability for science-based decision-making?
24	What networks or mechanisms are required to enable sustainable communication across a wide range of disciplines that support environmental science and regulatory decision-making?
29	How is urbanization impacting ecological and human exposure to and release of contaminants?
38	What are the potential environmental and economic impacts of using energy-bearing secondary materials (by-products) as alternative fuel sources in sustainable manufacturing processes?

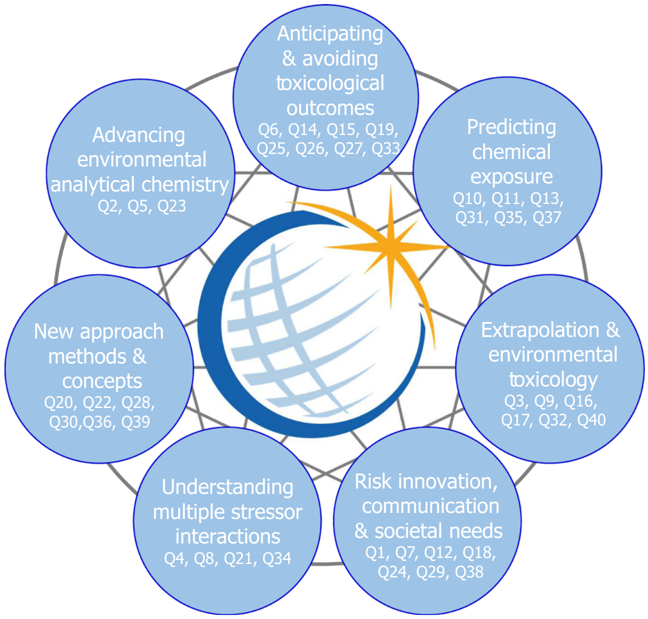

FIGURE 2: Forty priority research questions, ranked (denoted by number) among 7 themes, from North America. Q = question.

octanol–water partition coefficient [K_{OW}]) and process rates (e.g., hydrolysis and photodegradation) of organics entering marine and estuarine ecosystems (Saranjampour et al. 2017; Vebrosky et al. 2018). These changes can dramatically influence bioavailability and ultimately toxicity (Brander et al. 2017). One of the priority questions (Q37) identifies the importance of addressing this research need by asking how chemical fate and effects differ in marine and estuarine systems versus freshwater environments. This timely question is highly relevant given that most human populations are concentrated within coastal counties and coastal watersheds. In the United States, 39 and 52% of the population resided in coastal shoreline and coastal watershed counties, respectively, even though these areas comprise less than 10 and 20% of US land area (National Oceanic and Atmospheric Association 2013).

Several other priority questions were related to determining and predicting bioavailability and bioaccumulation, including a question (Q13) about the best methods to measure bioavailable/freely dissolved concentrations or the chemical activity of organic chemicals and metals in environmental media. The issue of bioavailability of contaminants is an important one for ecological and human health risk assessments to ensure the accuracy of adsorption and internal exposure estimates (Ortega-Calvo et al. 2015; Gobas et al. 2018). It is widely recognized that total concentration is a poor predictor of bioavailability, especially for environmental compartments dominated by solid phases, such as sediments and soils (Di Toro et al. 1992; Parkerton and Maruya 2013; Ortega-Calvo et al. 2015). Two approaches have been recommended in an International Organization for Standardization (2008) guideline on bioavailability; for example, passive sampling and desorption methods are applicable for both organics and metals in soils. The development of passive sampling techniques clearly has had a huge impact on this field because they are relatively simple to apply and are economically attractive. Key issues for organic contaminants include selection of an appropriate polymer, that is, for nonpolar versus polar compounds, polymer–water partition coefficients, determination of equilibrium status, and confirmation of nondepletive measurement conditions as well as deployment issues such as biofouling (Ghosh et al. 2013). Similar issues apply for metals/metalloids; however, sediment geochemistry, including the composition of the solid and the aqueous (porewater) phase and the oxidation/reduction potential of the system, strongly affects the fraction of metal that is actually available for interaction with biological sorption sites for binding of metals (Peijnenburg et al. 2013). This may be further complicated with metal-based nanomaterials that may undergo chemical transformations based on the chemistry of the aquatic system in which they are released (Lowry et al. 2012). Diffusive gradients in thin films (DGT) represent the most widely used passive samplers for metals but have their own challenges for accurate prediction of the bioavailable fraction. Expanding the applicability of DGT to data-poor metals and metalloids and linking DGT predictions to modeled speciation data were recommended by Peijnenburg et al. (2013).

Building from the need to further an understanding of bioavailability, 2 priority research questions were focused on advancing bioaccumulation science. One of these highly ranked questions (Q11) was specifically aimed at more concretely defining factors influencing bioaccumulation in wildlife, which could then support the development of improved tools for prediction of bioaccumulation across environmental gradients. Prospective bioaccummulation studies for regulatory compliance largely focus on derivation, or prediction, of a bioconcentration factor (BCF) for a specific chemical (Meylan et al. 1999), in which log K_{OW} of organic chemicals is the key parameter to predict BCFs in fish and aquatic invertebrates. However, BCFs are laboratory-derived using aqueous exposures, do not consider dietary chemical uptake, and may not be equally predictable in terrestrial environments (Van den Brink et al. 2016). As the science of bioaccumulation has advanced, so has an understanding of metabolism and elimination in wildlife. Standard aquatic bioassay protocols for bioaccumulation have been expanded to include dietary uptake (e.g., OECD 305; Organisation for Economic Co-operation and Development 2016) and biotransformation (Arnot et al. 2009). Unfortunately, a limited comparative understanding of bioconcentration exists for diverse biological species; there are limited comparative BCF models among these species and for groups of high-profile ionizable contaminants (e.g., per- and polyfluoroaklyl substances); and the extent to which differential metabolic pathways and transporters among species influence metabolism, elimination, and subsequently bioaccumulation is largely unknown. Further, the role of the microbiome on bioaccumulation and subsequent adverse outcomes is unknown for aquatic and terrestrial wildlife but represents another timely research question (Q35) that was also identified. The impact of the gut microbiome has been investigated in relation to the excretion of methyl mercury (MeHg) in humans (Rothenberg et al. 2016). The gut microbiome may play a role in the demethylation of MeHg in the fish intestinal tract (Wang et al. 2017). Further, the microbiome may play a key role in the adaptability of individuals to environmental stressors; however, these studies have yet to be conducted, especially in the cases of other bioaccumulative contaminants.

Translating laboratory observations in model species to the field remains a timely challenge for bioaccumulation science. Though food web bioaccumulation models are providing useful bridges from the lab to the field (Arnot and Gobas 2006), recent efforts employing trophic magnification factors (TMFs) in aquatic ecosystems have been advancing the science (Borgå et al. 2012; Burkhard et al. 2013; Walters et al. 2016). Estimates of TMFs rely on stable isotopes of nitrogen ($\delta^{15}N$) to discriminate trophic positions and analytical determination of a chemical of concern to determine the extent to which chemicals may biomagnify in an aquatic system (Borgå et al. 2012; Lavoie et al. 2013). Historically, most of the focus on biomagnification has been on nonionizable organic contaminants such as PCBs, although ionizables such as MeHg and PFOS are also known to biomagnify (Cabana and Rasmussen 1994; Martin et al. 2004). In contrast, ionizable base pharmaceuticals and more readily metabolizable chemicals, such as many essential elements and phthalates, display trophic dilution (Du et al. 2014; Lazarus et al. 2015; Kim et al. 2016; Haddad et al. 2018), and some nanomaterials such as carbon nanotubes do not appreciably bioaccumulate (Bjorkland et al. 2017). Furthermore, whether whole-body or tissue-specific analyses are chosen for organisms within a food web can affect biomagnification models (Campbell et al. 2005; Schäfer et al. 2015), with important examples such as lead and cadmium which tend to accumulate in calcium-bearing structures, mercury biomagnifying in muscle tissue, and PCBs concentrating in lipid tissues (Schäfer et al. 2015). Whether, how, when, and where changes in the aquatic food web structure alter bioaccumulation and biomagnification dynamics was further identified as a priority research question (Q31) with a focus on how alteration of food web structure may affect contaminant accumulation and long-term consequences. Trophic structure inherently varies among systems, can change with seasons (Zhang et al. 2012), and responds to natural and anthropogenic stress (Hogsden and Harding 2012; O'Gorman et al. 2012), yet research in this domain is scarce. Clearly, research and establishing standard sampling and modeling protocols are needed in the future because higher-level trophic positions are experiencing elevated exposure to some contaminants, which consquently present risks for human health when these organisms are consumed for food.

Extrapolating chemical effects across diverse assessment scenarios

Ecosystems are extremely complex, with multiple species interacting over space and time in highly unpredictable ways. Yet ecotoxicologists are charged with predicting how systems, species, and individuals will respond to anthropogenic introductions of xenobiotic chemicals or enrichment or diminishment of naturally occurring substances with a high level of certainty. For example, there are nearly 3000 species of vertebrate animals and over 18 000 plant species in North America alone (Osborn 2018), and it is clearly impossible to determine how each will react to the 67 000 chemicals currently listed in the Toxic Substances Control Act (TSCA) chemical substance inventory (US Environmental Protection Agency 2018a). Therefore, research must continue to develop reliable methods for extrapolating responses of test species exposed to chemicals to the thousands of others that are present in the environment but untested. Methods such as interspecies correlation estimation models (Raimondo et al. 2007; Awkerman et al. 2014) and interspecific differences in enzyme induction (Head et al. 2015) or receptor binding (Schmieder et al. 2003) are examples of such approaches, though additional research in cross-species extrapolation within and among aquatic and terrestrial species is warranted (Ortiz-Santaliestra et al. 2018). However, research and funding of chemical effects on people at the cellular and molecular levels are much more robust, raising the obvious questions of how to make full use of research on human health to develop methods that are best for integrating such information with ecotoxicity data when conducting ecological risk assessments (Q9). Further, there remain many timely questions about how well laboratory toxicity and bioaccumulation test results predict what happens in the field (Q3; Vignati et al. 2007; Burkhard et al. 2011).

Given the previously mentioned complexity of ecosystems and their responses to introduced chemicals, it is reasonable to suggest that research is needed to determine the accuracy of site-specific ecological risk assessments that are based on field monitoring data and extrapolations of laboratory-based toxicity values (Q16). A particularly difficult question to address when attempting to extrapolate laboratory-based results to field conditions is how organisms in dynamic and/or transitional environments (e.g., estuaries, ephemeral streams, high mountain habitats, polar regions, other ecotones) that are constantly dealing with a multitude of natural stressors respond to anthropogenic pressures (e.g., climate change, xenobiotics; Q32). It may be that such organisms are better equipped to handle additional stressors, or it may be that they are already living close to their tolerance limits and simply cannot withstand additional stress (Holling 1986). Moreover, migratory and nonmigratory species may have differential exposure at various times of the year. In addition, long- and short-lived species are likely to be differentially impacted as their reproductive strategies vary with their life history, long-lived species often having fewer offspring/breeding seasons. Similarly, biological systems are inherently variable, resulting in the need to determine and predict the natural variability of reference populations against which contaminated sites are compared (Q40).

Evolutionary processes and multigenerational effects add complexity to environmental assessments (Q17). For example, differences in plasticity and evolved adaptations introduce variability in the tolerance to contaminants between populations and can do so quite rapidly (Reid et al. 2016). However, natural selection of tolerant individuals may influence standing genetic variation to reduce genetic diversity (Reid et al. 2016) and induce fitness costs, which can have lasting effects (Bickham et al. 2000). Likewise, epigenetic alterations caused by chemical exposure may also result in impacts over multiple generations (Brander et al. 2017). Effort and resources directed toward understanding these multigenerational processes will greatly improve our ability to predict variability across populations. For example, population-level studies of evolved pollution tolerance in fish have demonstrated that some common pathways (e.g., the aryl hydrocarbon receptor pathway) provide significant fitness effects and seem to be prominent targets for natural selection (Wirgin et al. 2011; Reid et al. 2016). As tools required to study genome variation in populations become more accessible, data may exist to provide insight into population- and site-specific differences. For example, there have been over 1000 Superfund sites that have been remediated in the nearly 40 yr since the passage of Comprehensive Environmental Response, Compensation and Liability Act in 1980 in the United States (US Environmental Protection Agency 2018b). These sites provide a rich history of required 5- and 10-yr monitoring data that could be used during studies of questions on this theme and to determine whether cleanup goals were adequate and how well the affected ecosystems are recovering.

Challenges and approaches to addressing multiple stressor interactions

One of the highly ranked questions was related to characteristics of environmental stressors (chemical and nonchemical) which are the most important for determining their effects on ecosystem structure, function, and services (Q8). This is clearly an important issue for regulatory action, but it appears that little work has been done in this area. Ecosystem structure will be affected by chemicals present at toxicologically relevant concentrations, but long-term effects on structure often depend on persistence of the chemical(s), area polluted, resiliency, and rate of recovery, including evolutionary considerations, of the affected organisms or populations. The challenge is using these characteristics in a ranking scheme to identify those chemicals that require the highest amount of regulatory attention. A related priority question asked how the characterization of exposure–response relationships for multiple chemical stressors could be improved (Q4). A framework has been proposed (Moretto et al. 2016) in the context of human health (Boobis et al. 2011) including a suggested process for problem formulation (Solomon et al. 2016). One of the important issues for ecotoxicology is that of temporal differences in exposure and response, which can confound the characterization of additive, antagonistic, and synergistic effects. This is of particular importance when determining ecological effects because groups of organisms have different life spans and reproductive strategies that result in differences in resiliency and redundancy of function (Ottinger 2010).

Two questions focused on the influence of nonchemical stressors on the bioavailability and effects of contaminants (Q21 and Q34). The latter was related to global climate change, whereas the former was asked in the context of other abiotic and biotic stressors. Several authors have addressed the impact of climate only (e.g., Doney et al. 2012), whereas others (e.g., Schiedek et al. 2007; Sokolova and Lannig 2008; Noyes et al. 2009; Hasenbein et al. 2018; Cambronero et al. 2018) have focused on climate-induced changes in exposure to and effects of contaminants resulting from changes in bioavailability and movement of inorganic and organic toxicants, pesticides, and persistent organic pollutants (POPs). In the case of POPs, it is anticipated that these chemicals, currently sequestered in the cryosphere, will be released as ice melts and permafrost thaws (Foster et al. 2019). Increased release to surface waters of chromophoric dissolved organic matter normally considered innocuous is also predicted to affect photolytic degradation of potentially toxic substances, such as pesticides and other anthropogenic pollutants (Sulzberger et al. 2019). Although there have been some studies on the interaction of contaminants with other abiotic and biotic stressors on organisms in the environment (e.g., Coors and De Meester 2008; Scherer et al. 2013; Sulmon et al. 2015; Cambronero et al. 2018), there seems to be a lack of information on the effects of these on biological availability and potentially adverse effects (Q21). As noted for Q31, one can postulate that changes in food webs will result in changes in the movement of bioaccumulative substances. Indeed, several modeling studies have examined effects of warming on exposure to chemicals in food webs in the Great Lakes (Ng and Gray 2011) and in the Arctic marine environment (Borgå et al. 2010). However, there is a paucity of information in this area to test such hypotheses. Experimental research into effects such as these presents logistical challenges, but modeling might suggest hypotheses that could be tested in simplified experimental setups. Gouin et al. (2013) urged a complementary approach that utilized information obtained from both multimedia models and long-term time-series data.

Employing new approach methods and concepts in chemical risk assessment

Over the past decade, there have been significant changes in the scope of expectations relative to assessment of chemical safety. Legislative mandates such as the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) program in Europe and recent revisions to the TSCA in the United States dictate consideration of the possible human health and ecological effects of a far greater number of chemicals than in the past (European Commission 2006; US Congress 2016). This has forced regulatory toxicologists and risk assessors/managers to increasingly rely on predictive approaches to assess risks from chemicals. These methods employ data that can be rapidly generated in a cost-effective manner using techniques such as computational models (e.g., quantitative structure–activity relationships [QSARs]), in vitro assays (including high-throughput [HTP] systems), and short-term in vivo tests with pathway-specific molecular and biochemical endpoints, including -omics data. Although certainly promising in theory, these new approach methodologies present many pragmatic and conceptual challenges relative to their routine use in risk assessments. Several of these challenges were highlighted in the 40 priority questions from the North American horizon scanning exercise.

Two of the questions involve HTP assays and their interpretation (Q20 and Q30). There are literally hundreds of different HTP assays available (e.g., Dix et al. 2007), so there is a need to identify and standardize those most applicable for the prediction of apical biological responses, in terms of both hazard and exposure to a wide variety of aquatic and terrestrial species. The adverse outcome pathway (AOP) framework has been proposed as one means to help translate in vitro HTP data into relevant in vivo hazard information (Ankley et al. 2010; Schroeder et al 2016). However, AOPs are not designed to address in vitro to in vivo dose extrapolation, which already is a high priority research topic in HTP testing. One particularly challenging aspect of this exposure extrapolation involves accounting for the fact that most HTP assays lack an ability to metabolize xenobiotics. A third question in the new approach methodologies area (Q39) focused on the use of -omics for diagnosing causative stressors in a field setting. Promising avenues to address this question include evaluating -omic data in the context of discrete biological pathways, as well as enhancing approaches to better link biological responses to state-of-the-art analytical chemistry techniques (see also Q2 and Q23). In addition, it will be important to characterize natural variability captured in -omics data (see also Q40) to discern adverse effects in specific populations.

Two other questions focused on how we can best employ the exponentially increasing amount of publicly available genomic data to address challenges in ecotoxicology. One involves using knowledge of evolutionary conservation of biological pathways to enhance cross-species extrapolation of the effects of chemicals (Q36), arguably one of the greatest uncertainties facing ecotoxicologists. Some excellent progress already has been made in this area through the development of approaches to compare the degree of evolutionary structural conservation of protein targets of chemicals, such as receptors or enzymes, across species (e.g., Gunnarsson et al. 2008; LaLone et al. 2016). However, other large-scale comparative genomic investigations across multiple species have revealed that signaling and metabolic pathways are typically imperfectly conserved across species (Huynen et al. 1999; Snel et al. 2002), meaning that it is important to consider functional relationships across organisms at the pathway or cellular level rather than individual genes (Nehrt et al. 2011). For example, several studies have demonstrated that pathways or biological processes (when discovered) are more likely than genes to be functionally conserved throughout the metazoan lineage (e.g., DNA repair; Taylor and Lehmann 1998), chromatin state, and epigenetic information (Gerstein et al. 2014). Collectively, these examples demonstrate that as functional genomic tools become more accessible across phyla, further work is needed to understand functional conservation of these targets, as well as the degree to which other pathway components are conserved (Perkins et al. 2013). This challenge was expanded on in Q17 (see section, *Extrapolating chemical effects across diverse assessment scenarios*). Collectively, these priority questions highlight the potential to use evolutionary concepts in genetics to better understand and predict the cross-generational effects of chemicals, from both epigenetic and adaptive perspectives.

The final 2 questions associated with this category involve integrating and using new/alternative data streams to assess chemical risks (Q22 and Q28). For example, although chemicals can impact endpoints related to immune function and behavior, the ability to translate this information into assessments of ecological risk based on population-relevant (apical) endpoints has proven challenging. One approach to achieve this is to identify/develop pathway-based linkages between measures of immune and behavioral endpoints and the endpoints commonly used to link assessments to the population level: survival, growth, development, and reproduction. This makes sense from the standpoint that overall fitness incorporates all these aspects, including endocrine and behavioral components of reproduction. In addition, these sublethal endpoints can be linked within a dynamic energy budget modeling framework (Murphy et al. 2018). Question 22 is an even broader variant of this challenge in the context of integrating responses across varying assay systems and biological levels of organization to produce predictions of ecological risk. Here again, AOPs provide a translational framework to capture key linkages to enable better utilization of different types of new approach methodologies data in a coherent manner.

Anticipating and predicting human health and ecological impacts of chemicals

By 2025, two-thirds of the global human population will live in water-stressed regions. Given the dramatic rainfall gradients across North America and projections of climate change, beneficial uses of marginal drinking water sources, including brackish groundwaters, reclaimed waters, and eutrophic rivers and lakes, which are increasingly impaired by harmful algal blooms (Brooks et al. 2016, 2017), are becoming critically important within the "one water" management framework. A priority question (Q14) specifically identified the need for future research to define and reduce human health risks associated with drinking water derived from these sources. Such nontraditional waters are being employed during de facto or planned reclamation including for agriculture (terrestrial and aquaculture), provisioning instream flows for ecosystem services and biodiversity, injection for aquifer recharge as barriers to saltwater intrusion, and diverse direct and indirect potable reuse projects (National Research Council 2012; Brooks and Conkle 2019). Another question in this category identified the need to understand ecological and health risks associated with water reuse (Q15). Development and consistent implementation of defensible risk-based strategies, tailored for diverse reuse scenarios, is necessary, particularly in regions experiencing rapid population growth, droughts, and natural disasters. Though efforts have progressed in this area of study (Mehinto et al. 2015; Maruya et al. 2016), particularly for direct potable applications, additional research is warranted to advance nontarget analytical chemistry methods (Hollender et al. 2017), next-generation computational toxicology, and HTP in vitro bioassays for integrated diagnostic applications. Advancing research toward integration of these emerging approaches further promises to support development and improvement of screening values for diverse matrices and chemical prioritization schemes (Q25).

Related to the water reuse questions, another priority question identified the importance of understanding natural and anthropogenic factors influencing the development of antimicrobial resistance (AMR) in the environment (Q33). Following identification of this area as a priority research need by Boxall et al. (2012), antibiotics and antibiotic-resistant genes in raw sewage, effluents, groundwaters, and surface waters have received heightened attention because AMR represents one of the leading threats to global health. In fact, predicted-no-effect concentrations (PNECs) for development of antibiotic resistance have been proposed for several antibiotics (Bengtsson-Palme and Larsson 2016), yet these PNEC values are globally exceeded in effluents 58 and 24% of the time for ciprofloxacin (Kelly and Brooks 2018) and erythromycin (Schafhauser et al. 2018), respectively. In addition to several key environment and health research questions for AMR that were recently identified (Larsson et al. 2018), research is required to identify mechanisms by which such proposed PNECs may diverge across geographic regions, treatment technologies, and environmental gradients.

In addition to AMR, environmental chemical pollution is now recognized as a direct major global threat to human health, resulting in 9 million premature deaths in 2015 alone, which is 15 times more deaths than all wars or other forms of violence during 2015 (Landrigan et al. 2018). With most humans now living in cities, an unprecedented concentration of resource consumption, including use of chemical products, is occurring in urban areas; in many regions of the world this global megatrend is happening faster than environmental management systems, technologies, and other interventions can be implemented (Brooks 2018). For example, 80% of global sewage remains untreated, and 2 billion people still lack reliable access to drinking water of acceptable quality. A highly ranked question (Q6) identified the need to design chemicals and predict chemical properties and biological activities in an effort to minimize environmental and human health hazards. Herein, advances are occurring for sustainable molecular design of less hazardous chemicals (Schug et al. 2013; Coish et al. 2016), which, coupled with next-generational computational chemistry modeling typically employed during pharmaceutical development and mechanistic toxicology, results in de novo design of new, safer organic chemicals. These efforts promise to fuel innovation, increase confidence in more sustainable chemical substitutions, and support several of the United Nations SDGs (Anastas and Zimmerman 2018; Brooks 2018, 2019). It is therefore perhaps not surprising that similar priority research questions related to sustainable and green chemistry were identified during GHSP efforts in Europe (Van den Brink et al. 2018) and Latin America (Furley et al. 2018). But to facilitate this work, research is needed to advance computational chemistry intersections with environmental toxicology and ecotoxicology beyond historical QSARs (Q26) and to optimize coordination, curation, and access to high-quality physical and life science data sets (Q27). Recent environmental applications of molecular docking (McRobb et al. 2014), quantum mechanics (Kostal et al. 2015; Kostal 2016; Clymer et al. 2019) and machine learning (Dreier et al. 2019) are promising but need to be extended to encompass other molecular initiation events, adverse outcomes, and species.

Coordination across disciplines and sectors also is necessary to increase our understanding of environmental exposures and adverse ecological or health outcomes in the field and in local communities. Specimen banks, such as the Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey program in the United States, present tremendous opportunities to define environmental exposures in humans, to assess the reliability of prospective environmental fate modeling predictions, and to support determinations of whether health protection goals are achieved following prospective or retrospective management activities. Similar programs focused on organisms in the environment would support initiatives to manage chemicals via retrospective and temporal analyses in fish and wildlife, by taking advantage of monitoring programs that have been ongoing for many years. Advancing the science to more robustly determine the efficacy of chemical management programs was specifically identified as a priority research question (Q19). Herein, developing more integrated environment and health banking programs across North America could support product stewardship goals of businesses, retrospective health and environment protection tracking efforts by government agencies, and risk communication, education, and outreach by citizens and policymakers. Taken together, priority research questions in this and other sections of this review will inherently benefit from incorporating life-cycle considerations within risk assessment and management.

Risk assessment and communication at the science–society interface

With the proliferation of blogs, e-journals, and commentaries on social media sites, the public is exposed to a constant stream of alarming stories about cancer-causing chemicals; risks of pesticides to mothers, babies, and bees; environmental degradation due to microplastics, climate change, urbanization, and deforestation; and other real or perceived risks to human health or the environment. Although it is known that people's willingness to accept risks is proportional to the degree to which they believe that they are in control and how much they might benefit from the risky action (Slovic and Peters 2006), the public frequently does not have the necessary tools to sort through the numerous claims to find those activities that may be hazardous but easily avoided, those that truly pose a risk, and those risks that have been shown to be de minimis. A large amount of resources can be consumed by government agencies that need to investigate low-level environmental risks or by litigation against industry or the government because of poorly understood concepts underlying science-based risk assessments (Kabat 2017). A high priority, therefore, is teaching scientists effective methods for communicating science-based risk, and science in general, to appropriately impact public perception and regulatory policy development (Q7; Hassan 2016; House et al. 2017). Such methods should be taught at all levels of education so that scientists can report their significant findings in a manner that is easily understood by the general public and that clearly explains the difference between hazard and risk (Singley 2004).

Although some fears about the health or environmental risks of some technologies have not been realized (e.g., vaccines do not cause autism), use of chemicals can result in significant global change (Gerber and Offit 2009; e.g., CO_2 from combustion of fossil fuels resulting in climate change). In a world where the human population is projected to reach 8 billion by 2025 (US Census Bureau 2018), there is a need for developing the means by which people can live sustainably in a resource-limited environment by relying on wise use of technology and chemistry. This was recognized at the turn of the century at the United Nations Conference on Environment and Development (the "Earth Summit"; United Nations 1992), with the subsequent Millennium Assessments (United Nations 2005) providing the scientific underpinnings of an appraisal of the state of the world's ecosystems and the beginnings of the development of a scientifically based approach to sustainability. The success of the Montreal Protocol on Substances that Deplete the Ozone Layer in avoiding severe damage to humans and the environment from UV radiation and the collateral benefit of reductions in global warming is a signpost for success (Bais et al. 2015). The sustainability goals published by the UN Development Programme, which came into effect in January 2016, are a "call to action" to end world poverty and to encourage sustainable consumption, among other ambitions, but require additional research for achieving these goals. Hossain et al. (2018) recently completed a horizon scanning project to identify research needs for understanding how to preserve biodiversity and necessary ecosystem services, thereby achieving environmental sustainability. In addition to recent contributions from Europe (Van den Brink et al. 2018) and Latin America (Furley et al. 2018), the North American part of the GHSP echoes many of the same themes although with a more chemical-directed focus. For example, a high priority for North America was placed on expanding and continuing ongoing research into green chemistry to develop environmentally sustainable chemical products and methods with the least health or environmental risks for science-based decision-making (Q18; Dorman et al. 2014). Such efforts should be expanded to assess the use of energy-bearing secondary materials (by-products) as alternative fuel sources to develop sustainable manufacturing processes (Q38). This necessarily requires a comprehensive understanding of emissions (types, rates) and potential emission control mechanisms to avoid unanticipated adverse secondary consequences.

Research continues to be needed to inform pesticide development for large-scale, sustainable agriculture to find chemistries that specifically target pests without affecting nontarget species such as beneficial insects and arthropods, fish, wildlife, or humans (Q1). Such important work should be embedded in a broad research program in agricultural practices, examining how patterns of chemical input in space and time change as a result of genetically modifying crops for pesticide resistance, drought tolerance, and nutrient requirements. A holistic program in agroecology research that includes methods for efficient water use, reduced energy inputs (e.g., fertilizers) and use (e.g., tractors), and proper waste disposal (e.g., manure from feedlots), in addition to understanding the social systems within which farmers work, will enable sustainable agriculture on a scale sufficient to feed a growing world population in the face of a rapidly changing climate (Altieri 2018).

Much like other regions around the world, populations of the United States and Canada are becoming increasingly urban, with >80% of all people living in cities and surrounding suburban areas (Statistics Canada 2016; US Environmental Protection Agency 2018c). Urban planners and environmental managers would benefit from additional research into how urbanization impacts ecological and human exposure to and release of contaminants (Q29). For example, urbanization resulted in a 10% increase in surface runoff in the United States between 2001 and 2011 (Chen et al. 2017), potentially causing increased nonpoint source pollution in urban waterways; freeways that are built near existing schools expose children to greater concentrations of contaminants from vehicle exhaust, which may result in decreased academic performance (Kweon et al. 2018). Sewage discharged into streams and rivers is exposing aquatic life to pharmaceuticals and personal care products at concentrations high enough to adversely affect some species (Ebele et al. 2017). Reduction in exposure to potentially hazardous chemicals can be achieved through technological advances in emission controls, but changes in human behavior can also have a significant impact on urban contamination. For example, reduced reliance on individually owned automobiles, moving instead to a greater reliance on public transportation, ride-sharing services, or (eventually) shared fleets of autonomous vehicles, can significantly reduce air emissions (Greenblatt and Shaheen 2015). Research is needed to determine which changes in human behavior would have the greatest benefits on sustainability of terrestrial and aquatic ecosystems (Q12) and how to gain public acceptance for implementation (deVries et al. 2018).

It is obvious that the development and adoption of the technologies, chemistries, social systems, and regulatory oversight that are needed for 8+ billion people to live sustainably on this planet requires a multigovernment and multidisciplinary approach. The traditional method of scientific communication through journal publication is slow, cumbersome, and rarely transdisciplinary, while adoption of new practices can be difficult to achieve (Anderson 2015). Directed research is needed to better leverage today's vast network of electronic communication mechanisms to enable timely and sustainable communication across the wide range of disciplines that support environmental science and regulatory decision-making (Q24; Hurd 2000; He and Jeng 2016). The challenge will be how to retain scientific objectivity, maintain rigorous peer review, and prioritize studies of real risks and workable solutions within an expanding blogosphere and increasing public demand for immediate answers.

OUTLOOK

Addressing grand challenges for environment and health is not trivial within and among countries but is decidedly necessary to achieve the UN SDGs (United Nations, 2016). A common theme among the inherently connected 40 priority research questions (Figure 2) reported in the present review is the degree to which they address increasingly complex environmental problems. These include technical challenges such as the need for new analytical approaches and methods and developing next-generation tools and models for predicting the effects of new chemicals, mixtures of chemicals, and contaminated media across temporal and spatial scales of biological organization and environmental complexity. Other challenges will require understanding or collaborating among private–public organizations and with other fields. Successful basic and applied approaches that are dependent on the principles and techniques from other disciplines can be facilitated across these increasingly interconnected disciplines by sustained cross-disciplinary collaboration. In fact, incorporating new technologies within exposure and effects assessment research is essential to address these complex problems (National Academies of Science, Engineering, and Medicine 2017). Herein, advancing systems-based approaches, including life cycle and one health efforts (Aguirre et al. 2016), are necessary.

In general, cross-disciplinary research can be encouraged through the competitive proposal and funding process. However, additional coordination of federal and other resources (e.g., from states, provinces, private, and nongovernmental organizations) should be encouraged to support multidisciplinary research in a greater proportion of their grants. For example, research on the environmental effects of nanotechnologies has been coordinated at the federal level in the United States through the National Nanotechnology Initiative (NNI). The NNI effectively coordinated academic and government research activities, and in several cases multiple federal agencies coordinated funding to address high-priority research needs. Unfortunately, as recently noted elsewhere (Bernhardt et al. 2017; Brooks et al. 2017; Burton et al. 2017), strategic funding has not been consistently allocated within and among disciplines necessary to engage sustainable environmental quality and ecosystem integrity research. Such observations are particularly relevant for ecotoxicology, which is critical for advancing predictive, integrative and evolutionary studies of basic and translational importance (Brooks 2018; Hahn 2018). Like the NNI, coordination of research priorities among federal agencies is needed to ensure that the benefits and synergies of the cross-disciplinary research questions identified in this horizon scanning project are realized. Strategic cross-regional (e.g., pan-American, North American–European, Asian, African, and Oceanian schemes) funding programs, which routinely derive reciprocally beneficial returns on investment, are warranted, particularly given the international relevance of these priority research questions to human well-being and ecological resilience. Addressing these research questions will yield additional benefits, including technological innovations while meeting workforce development needs of relevance to the government, business, academic, and nongovernmental organization sectors.

In this process, a unique collaboration was forged among ACS and SETAC members to identify and prioritize environmental quality research questions. Professional societies such as SETAC and ACS should strive to promote cross-disciplinary research to address these complex problems and should seek cross-disciplinary arrangements with other professional societies that emphasize complementary topics. Such efforts promise to advance theoretical, experimental, and practice-based approaches to these problems. Examples of coordination might include symposia, workshops, and focused topic meetings, perhaps focused on scientific communication with social scientists or coordination with public health organizations to leverage environmental science and engineering activities with other disciplines required to solve these grand challenges. It will remain critical for scientists and engineers to engage in appropriate and timely communication with stakeholders, including policymakers, funding agencies, business consortia, and the public. Answers to the questions generated by the North America portion of the GHSP will not be developed quickly, but doing so will shape sustainable management of environmental quality in the 21st century.

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Disclaimer—Certain commercial products or equipment are described to specify adequately the experimental procedure. In no case does such identification imply recommendation or endorsement by the National Institute of Standards and Technology, nor does it imply that it is necessarily the best available for the purpose.

Data Accessibility—See Supplemental Data or contact the corresponding author (Bryan_Brooks@Baylor.edu).

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