ADVANCING THE NEXT GENERATION (NEXGEN) OF RISK ASSESSMENT: PUBLIC DIALOGUE CONFERENCE

SUMMARY REPORT

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ADVANCING THE NEXT GENERATION (NEXGEN) OF RISK ASSESSMENT: PUBLIC DIALOGUE CONFERENCE

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Office of Research and Development
U.S. Environmental Protection Agency
Washington, DC 20460

DISCLAIMER

This document summarizes the discussions presented at the NexGen Public Conference held February 15-16, 2011, in Washington, DC. This document is not all inclusive or binding. Conclusions and recommendations to the U.S. EPA may not represent full consensus. The views expressed in this document are those of the Conference Participants and do not necessarily reflect the views and policies of the U.S. Environmental Protection Agency. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

This document was prepared initially by ICF Inc., an EPA contractor (Contract No EP-C-09-009 Work Plan, Budget, Work Assignment 1-37). This report captures the main points and highlights of the meeting. It is not a complete record of all detailed discussion, nor does it embellish, interpret, or enlarge upon matters that were incomplete or unclear. Statements represent the individual views of each participant.

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1. Conference Background and Objectives

In collaboration with federal and state agencies, the U.S. Environmental Protection Agency (EPA) is beginning a process to better use molecular biology to understand risks posed by environmental exposures. This transformation is driven by several recent and important reports from the National Research Council (NRC) and volumes of new test data emerging from the Toxicity for the 21st Century (Tox21) project and the European Union's Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). This new collaborative effort—Advancing the Next Generation of Risk Assessment (NexGen)—will make this transformation a reality over the next decade. NexGen collaborating organizations include EPA and the National Institute of Environmental Health Sciences (NIEHS), National Toxicology Program (NTP), the National Insttutes of Health Chemical Genomics Center, Centers for Disease Control and Prevention (CDC) Agency for Toxic Substances and Disease Registry (ATSDR), and State of California's Environmental Protection Agency.

To engage stakeholders in the early stages of the NexGen project, EPA sponsored a public conference titled "Advancing the Next Generation of Risk Assessment" on February 15 and 16, 2011, in Washington DC. This conference presented stakeholders with an opportunity to learn about the NexGen project in its early phases and to provide their thoughts on the challenges it faces and its path forward.

The first day of the conference began with presentations describing the NexGen project and its drivers. Presenters also discussed early-stage prototype risk assessments that will be used to explore and refine various approaches to using molecular biology data in risk assessment. A question and answer session between the conference participants and a speaker panel followed the presentations. The first day of the conference concluded with parallel breakout sessions, which enabled conference participants to convene into smaller, multi-stakeholder breakout groups to discuss the advantages, challenges, and future direction for the NexGen project. The breakout groups reconvened the next day to finalize their discussions and develop a report for presentation to the entire conference during a parallel breakout presentation session.

Approximately 160 participants representing 11 stakeholder groups attended the conference. Figure 1 presents the breakdown of conference participants by stakeholder group.

2. Introduction

Ms. Becki Clark, Acting Director of EPA's National Center for Environmental Assessment (NCEA), welcomed the conference participants, presented a brief introduction to the NexGen project, and described the purpose of the conference. She noted that advances in systems and molecular biology can help the Agency better conduct assessments aimed at protecting human health and the environment. She noted that this conference is the beginning of a longer term effort, and encouraged participants to focus on the utility of these new types of data and how they can be incorporated into the NexGen approach, rather than discuss specific conclusions from these recent advances.

Ms. Clark concluded by introducing the two keynote speakers, Dr. Paul Anastas, who presented EPA's vision for chemical safety and sustainability and NexGen's supporting role, and Dr. Linda Birnbaum, who described ongoing Federal research efforts such as Tox21 and other efforts at NIEHS and NTP, as they relate to NexGen.

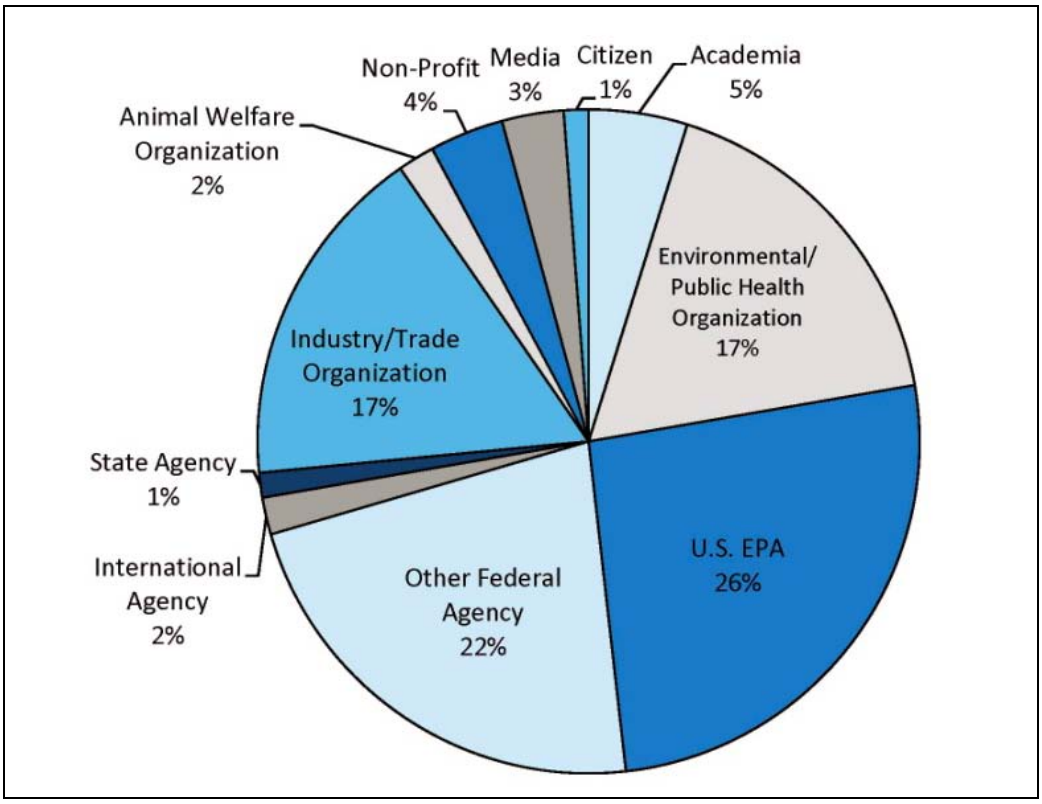


Figure 1. Conference attendance by stakeholder group.

2.1. Vision for Safer Products for a Sustainable World – Dr. Paul Anastas

Dr. Anastas, Assistant Administrator of EPA's Office of Research and Development (ORD), began his presentation by stating that the science EPA uses to address risk has evolved and been refined over the years. As the discussion moves to the next generation of risk assessment, there is an opportunity for to think differently about the health and environmental challenges we face today. For instance, there is a disconnect between those who create chemicals and those who are charged with understanding the consequences of chemicals on human health and the environment. Dr. Anastas emphasized that as we come to understand the consequences and problems associated with chemicals in the environment, we must consider this information when developing the next generation of chemicals so that we do not continue to see the same issues time and again.

Molecular systems biology tools will support both traditional risk assessment and green chemistry approaches. To further these latter efforts, EPA has initiated an extensive research program, focused on developing and implementing greener choices such as design and synthesis of less hazardous chemicals and processes, optimizing lifecycle risks and functions, use in real-time pollution prevention, and improving built environment choices. Dr. Anastas described how the definition of performance in the creation of synthetic chemicals has changed since the 19th century, and that today we need to measure performance by accomplishing the primary goal without causing adverse unintended consequences, whether we are talking about creating a product, process, or system. Thus, many potential environmental problems can be avoided by intelligent choices. He indicated, however, that we will not be able to meet this challenge until we define the appropriate performance metrics and incorporate consideration of environmental impacts intrinsically into chemical designs.

Dr. Anastas offered that our objective should be to pursue perfect sustainability, which will result in continuous improvements and an integrated, cohesive approach to solving the problems we understand and achieving the designs that need to happen. EPA's goals, as described by Administrator Lisa Jackson, are to inform improvements for a better future, and to pursue wellness instead of treating the problems as they arise. Molecular approaches will be used with increasing frequency to harness chemical innovation and to meet environmental and economic goals simultaneously.

2.2. Linking Research to Risk Assessment – Dr. Linda Birnbaum

Dr. Birnbaum, Director of NIEHS, NTP detailed NIEHS' commitment to translating "bench science" into environmental public health policy and its focus on preventing negative impacts from the environmental exposures on human health and disease. She stated that the challenges facing us today include how to come together to think broadly about an environmental health research strategy that provides the data we need and that incorporates new and better methodologies. As this risk assessment community moves forward in identifying priority areas in environmental health sciences, Dr. Birnbaum highlighted the need to incorporate the conceptual shift that has occurred in recognizing that susceptibility to disease persists long after exposure, and that chemicals at low doses can act like hormones in the body to disrupt development. NIEHS efforts through the Center for Risk and Integrated Science and a Superfund program done in conjunction with EPA and ATSDR are focusing on using new and developing science to provide key information for policy makers.

Dr. Birnbaum continued by indicating that NTP is charged not only with doing toxicity testing, but also with developing and coordinating toxicity testing across the U.S. Federal Government. To this end, Dr. Birnbaum described NTP's goals to increase its expertise in the development of physiologically based pharmacokinetic (PBPK) modeling, dosimetry, and new "data rich" toxicology techniques. She described Tox21, a partnership with EPA, the NIH Chemical Genomics Center, and the Food and Drug Administration (FDA) that aims to promote the understanding and incorporation of high-throughput screening methodologies and other high-content technologies (such as "-omics") into current science. Dr. Birnbaum also described an initiative at NIH that is examining the interactions of genetics and the environment with respect to influences on asthma, diabetes, cancer, and other common illnesses, through support such as the development of new procedures for analyzing genetic variation and new technologies for measuring environmental exposures. Dr. Birnbaum concluded that linking research and risk assessment is possible through partnerships between research and regulatory agencies, and strategies such as new technologies, individual and team approaches, and improved communication.

3. Setting the Stage

Following the introductory presentations, a plenary session provided the context for the conference participants by introducing the NexGen project and describing a proposed framework for risk assessments that use new data and technologies. The goal of this session was to provide information to the conference participants so that they could gain a better understanding of the NexGen project and how it will change risk assessment. Presentations in this session included an introduction to NexGen's drivers, goals, and objectives by Dr. Ila Cote and a summary of a proposed framework for conducting NexGen risk assessment by Dr. Daniel Krewski.

3.1. The Next Generation of Risk Assessment (NexGen) Program: Overview and Invitation to Engage – Dr. Ila Cote

Dr. Cote, Senior Science Advisor at EPA's NCEA, began by providing a brief overview of the NexGen project, including its collaborators. She highlighted how molecular systems biology has been advancing, but most of these advances are not incorporated currently into risk assessment. The goal of NexGen,

therefore, is to advance risk assessment science by incorporating recent progress in molecular systems biology. To accomplish this, the NexGen project has defined the following three objectives: (1) piloting a NexGen framework, (2) refining bioinformatics systems for knowledge mining, and (3) developing prototype health assessments that are refined through discussions with scientists, risk managers, and stakeholders, and are responsive to the context of risk. Dr. Cote also outlined the differences among Tier 1, 2, and 3 assessments and how the NexGen project could be used to generate data to address some of frequently asked questions associated with data uncertainty as one moves across the tiers (Figure 2).

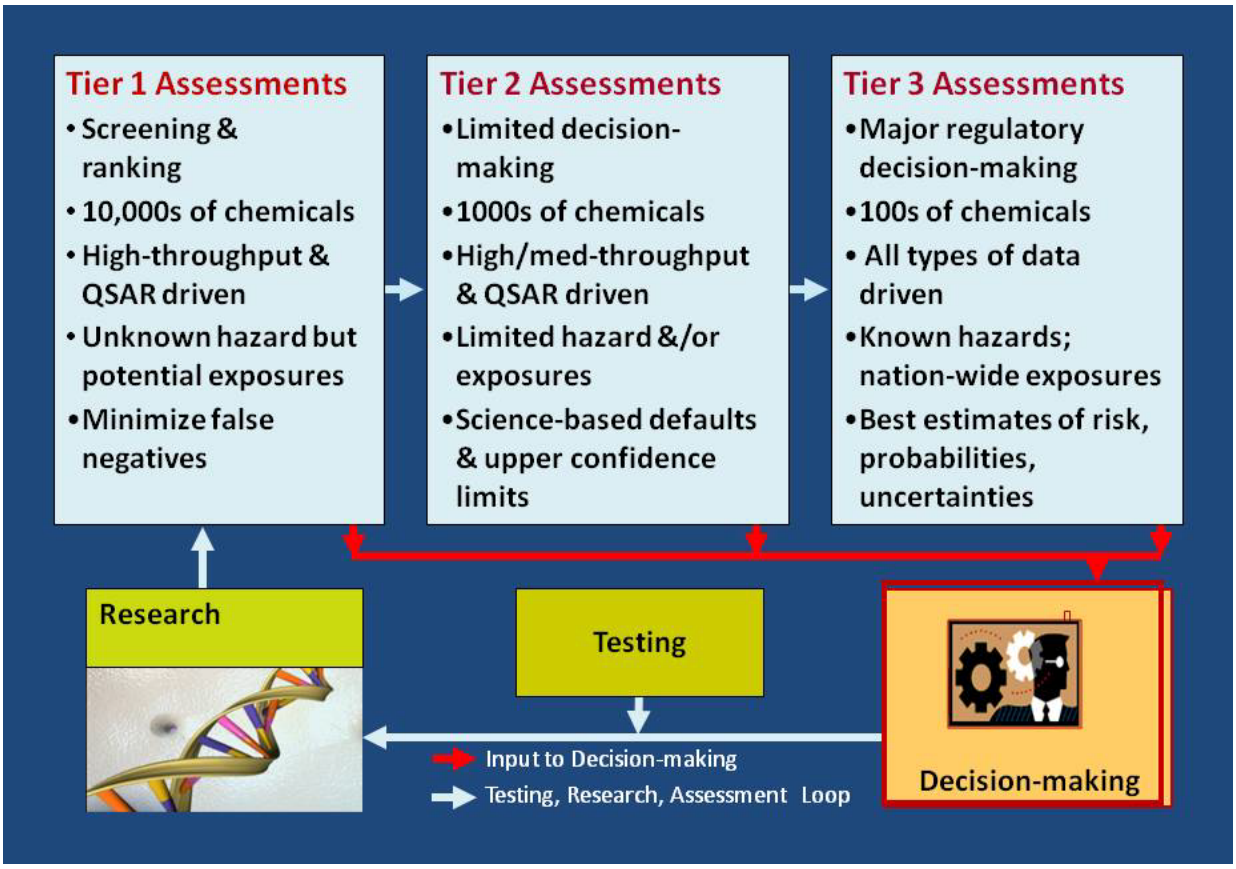


Figure 2. Tiered NexGen-informed Risk Assessments Targeted to Risk Context.

Dr. Cote described the first effort in this new initiative, the November 2010 workshop, *NexGen: The Prototypes Workshop*. Experts were invited to this workshop to discuss the draft prototypes; identify and discuss a wider variety of new data, methods, and knowledge; consider how information from new approaches might augment, extend, or replace traditional data in health assessment; and discuss options for expanded work and research needs. She reviewed the main themes heard during this workshop and stated that a summary of the workshop is publicly available on EPA's NexGen Web site (www.epa.gov/risk/nexgen).

Dr. Cote concluded by reviewing the expected timeline for the NexGen project's next steps through mid-2012 (see Figure 3) and invited the conference participants to engage in this effort by asking questions during these early stages. She emphasized that NexGen is interested in hearing the conference participants' thoughts about the benefits, challenges, and path forward.

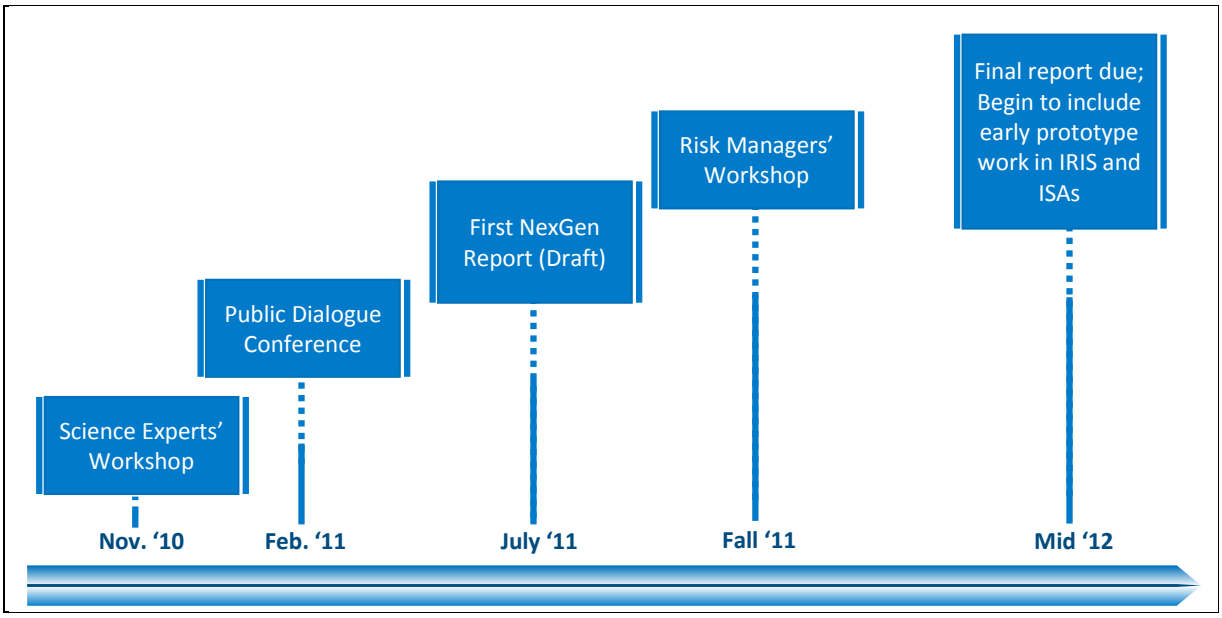


Figure 3. NexGen program health assessment timeline through mid-June.

3.2. The Next Generation of Risk Assessment (NexGen): A Proposed Framework – Dr. Daniel Krewski

Dr. Krewski, Professor and Director of the R. Samuel McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, presented a draft framework for conducting NexGen risk assessments. This framework is comprised of three building blocks: (1) *Toxicity Testing in the 21st Century* (NRC, 2007); (2) *McLaughlin Centre Framework for Population Health Risk Assessment* (Krewski et al., 2007); and (3) *Science and Decisions: Advancing Risk Assessment* (NRC, 2009). The first building block, *Toxicity Testing in the 21st Century*, provides a vision that focuses on using computational methods in biology to predict chemical properties and characteristics. The vision also emphasizes the use of high throughput approaches for *in vitro* screening.

The second building block, the *McLaughlin Centre Framework for Population Health Risk Assessment*, addresses risk assessment on a population level. This framework is derived from the concept of integrating traditional human health risk assessment with population risk assessment, a comprehensive risk assessment of health risks in the general population based on multiple determinants of health. This comprehensive framework offers a more multidisciplinary approach to the assessment of human health risks within populations.

The final building block is NRC's *Science and Decisions: Advancing Risk Assessment* report, also known as "The Silver Book." This report provides a good foundation on risk assessment methodologies such as how to tailor the risk assessment effort for the risk management decisions in question. Dr. Krewski concluded that, independently, each of these building blocks serves to advance the field of risk assessment; together, however, these three building blocks produce a NexGen framework that could help shape the future of health risk science.

4. The Prototypes

The second plenary session focused on discussion of example approaches to assessing human health risks associated with environmental exposures to chemicals (i.e., prototypes). The NexGen approach is

focusing on developing prototypes that are informative for the three tiers of risk assessment (Figure 2). The data-rich prototypes (Tier 3) have robust human data and the best traditional estimates of public health risks (see Figure 4). These data rich prototypes are being used for: establishing proof of concepts, eliucidating value of information and determining decision rules by which molecular systems biology data could be used to inform risk assessment. Over time, expanding the diseases and the numbers of chemicals assessed will be possible. Additional examples of chemicals with more limited (Tiers 1 and 2) were also discussed.

The plenary session began with a presentation by Dr. Robert Devlin on the draft Ozone Prototype. This presentation detailed studies conducted to validate a systems biology approach to toxicity testing. Dr. Martyn Smith then presented the Benzene Prototype and discussed the challenges of using benzene in high-throughput studies and new technologies that are needed to evaluate the compound effectively. Finally, this session concluded with a presentation by Dr. David Dix, who discussed various additional approaches for chemicals with limited data.

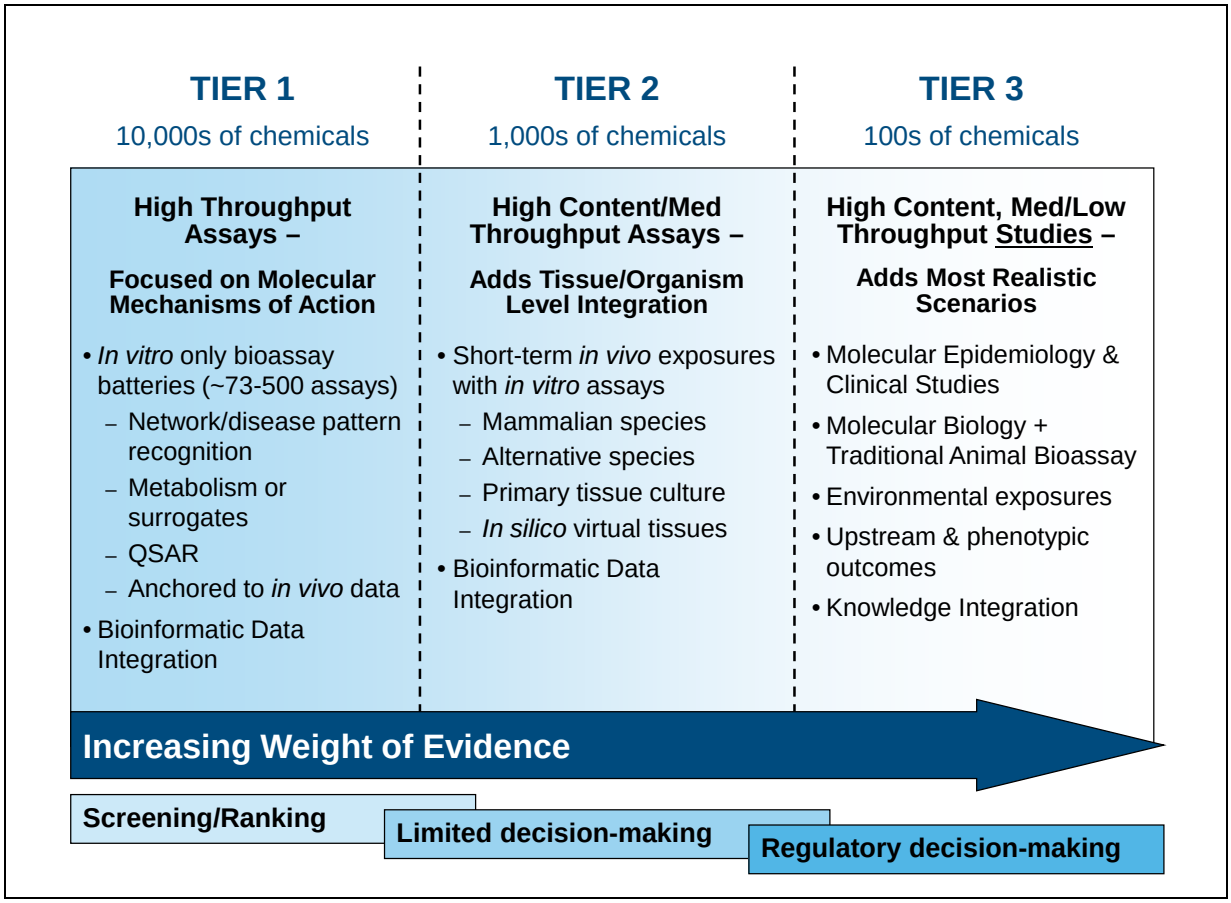


Figure 4. Descriptions of Tier 1, 2, and 3 methodologies. As the methodologies become more useful for regulatory decision-making, they are lower throughput and higher content methodologies. High throughput methodologies are used for screening and ranking chemicals of interest.

Lung Injury – Ozone – Dr. Robert Devlin

Dr. Devlin, Senior Scientist at the EPA's National Health and Environmental Effects Research Laboratory, noted that the goals of the Ozone Prototype include: (1) characterizing toxicity pathways in human lung cells exposed *in vitro* to ozone; (2) characterizing toxicity pathways (and downstream pathophysiological responses) in human volunteers exposed to ozone; and (3) developing models that can assess how accurately the *in vitro* pathways predict human responses. Dr. Devlin also described the reasoning behind selecting ozone for prototype development. A wealth of human exposure and animal toxicology studies is available for ozone as is a number of *in vitro* toxicology studies that have characterized some of the mechanisms by which ozone causes effects in humans.

He continued by describing studies conducted to validate a systems biology approach to toxicity testing. One ozone study involved an *in vivo* exposure study using human volunteers exposed to predetermined air ozone concentrations. Researchers then removed some airway epithelial cells and used microarray technology to identify toxicity pathways. They looked at the expression pattern of 20,000 genes and looked at proteins via quantitative two-dimensional electrophoresis. The experiments were then repeated for an *in vitro* study, which used airway epithelial cells from the same human volunteers that were exposed *in vivo*. The *in vivo* study results were subsequently compared to the *in vitro* study results by computational modeling. Based on the results, Dr. Devlin found that, although *in vitro* experiments have limitations, some cellular pathways are activated in the absence of surrounding environment if the right exposure is used. He also emphasized that picking the right cell lines and the right dose is crucial for *in vitro* studies.

He noted that another challenge for risk assessors is accounting for genetic susceptibility. For example, if looked at independently, particulate matter (PM) does not look like it would cause harm; in susceptible populations, however, PM could cause effects. Dr. Devlin noted that a number of polymorphisms have been shown to be associated with susceptibility to air pollutants (e.g., GSTM1 polymorphism). To address this issue of genetic susceptibility, Dr. Devlin described another study where researchers exposed humans to three types of PM (i.e., ultrafine, fine, and coarse). Preliminary findings were that each fraction of particles induced a different set of genes, and coarse particles (between 2.5 and 10 microns) caused the most overt inflammation compared to ultrafine and fine PM. The same results were obtained in an *in vitro* test.

Dr. Devlin concluded by summarizing that based on the studies evaluated, there is good reason to believe that in some systems *in vitro* assays might be used in lieu of animal or human exposure studies. Based on the preliminary results from the PM study, he hopes to determine quantitatively just how accurate the *in vitro* assays really are using ozone as a model toxicant. If successful, this approach could then be expanded beyond ozone to include other toxicants.

4.1. Cancer – Benzene – Dr. Martyn Smith

Dr. Smith, University of California, Berkeley, introduced the Benzene Prototype, stating that benzene is an environmental leukemogen. He discussed the toxicity of benzene, primarily its relationship to leukemia, lymphoma, and multiple myeloma, and noted that evidence of benzene toxicity has been observed for more than 100 years. Biological plausibility for a causal role of benzene (or its metabolites) in these diseases comes from its genotoxic effects and toxicity to hematopoietic stem cells or progenitor cells, from which leukemias arise. The impact of this toxicity is manifested as lowered blood counts (hematotoxicity). The mechanism of action for benzene-induced leukemia is still unknown, however, making assessment of risk in the low-dose region uncertain.

Dr. Smith cautioned that benzene is not an ideal compound for high-throughput screening due to its volatility, lack of cytotoxicity, and other factors, thus creating a challenge for *in vitro* benzene studies.

Dr. Smith emphasized that, to move toward an *in vitro* method for screening leukemogens, better methodologies need to be developed, such as three-dimensional (3D) modeling. The draft prototype proposes a systems biology approach, encompassing toxicogenomic, epigenomic, and phenomic endpoints relevant to leukemia. The prototype proposes using a biomarker of early effect that is predictive of leukemia to examine dose-response relationships in low-dose regions (e.g., hematotoxicity, chromosome changes, and altered gene expression). The systems biology approach focuses on reverse engineering to predict risk. This is helpful in that it can support epidemiological data conclusions, explore dose-response, identify susceptible populations, and provide information about effects from co-exposures.

Dr. Smith concluded that in addition to the need to develop better methodologies for *in vitro studies*, a more comprehensive study of benzene is needed, along with better training and development of guidance for use of 'omics data in risk assessment and exploration of quantitative approaches for continuous health outcomes. Finally, Dr. Smith summarized the following next steps for development of the Benzene Prototype:

- Explore use of hematological parameter data to predict leukemia risk in a biomarker-based approach.
- Explore a systems biology-based risk model of benzene, integrating single and multiple datasets, including:
    - Phenomic data;
    - Newly available data from multiple "omic" studies in humans at low exposures; and
    - Disease-specific pathway data.
- Examine predictability by comparison of "omic" and biomarker-based approaches with a dose-response model based on leukemia epidemiology data.
- Identify data gaps and opportunities for model refinement.

4.2. Human Health Risk Assessment Approaches for Chemicals with Limited Data – Dr. David Dix

Dr. Dix, the Deputy Director of the EPA ORD National Center for Computational Toxicology, described how the various methodologies for screening chemicals can be divided into three tiers of increasing throughput (from Tier 3 to Tier 1). He noted, however, that as the methodologies increase in efficiency, there is a tradeoff and a subsequent decrease in relevance to humans and ease of use in regulatory decision making (Figure 4). Methodologies in Tiers 1 and 2 examine tens of thousands to thousands of chemicals, while methodologies in Tier 3 are appropriate for addressing hundreds of chemicals in a similar time-span. Examples of high-throughput screening methodologies involve assays conducted by robotic systems that examine *in vitro* chemical exposures to rank compounds of concern. Tox21 and ToxCast™, two programs for collecting and aggregating data, examine a concentration-response curve to deduce a potency value for a chemical. Dr. Dix explained how conducting hundreds of assays with the same chemicals enable scientists to examine the effect of the chemicals on an entire pathway instead of merely individual components of a pathway.

Dr. Dix noted, however, that the large abundance of data needs to be translated into manageable and informative "chunks" of information. He described the Tox Prioritization Index (ToxPI) as a method for aggregating and visualizing the data effectively. He showed how the collected data are used in ToxPI to rank the chemicals from most to least potent for each gene or target in a pathway to find the chemicals of concern for the most pathways or targets. High-throughput risk assessment methodologies are promising for examining the thousands of chemicals that have little or no animal data to determine a starting point for setting health-protective exposure levels. The process involves identifying pathways

linked to adverse outcomes, measuring the effect of a chemical on those pathways at certain doses, and then translating the data to be relevant for identifying the *in vivo* hazard (using methods such as reverse toxicokinetics). Dr. Dix concluded that the high-throughput risk assessment approach he described should be used as a starting point for discussing how best to analyze and prioritize data-poor chemicals.

5. Question and Answer Session with Speaker Panel

A speaker panel fielded questions from conference participants. Participants posed several types of questions to the panelists, ranging from clarification questions regarding their presentations to general concerns about NexGen's role in risk assessment. Speaker responses are summarized in the following paragraphs.

One participant asked Dr. Devlin to elaborate on his finding that coarse particles caused more overt inflammation, which seemed to differ from what other studies have observed. Dr. Devlin acknowledged that earlier studies suggested that fine and ultrafine particles were the most problematic. He was using this study, however, to demonstrate that *in vitro* studies could be used in lieu of *in vivo* studies if the study uses the right *in vitro* cell lines. He cautioned, however, that researchers cannot use this approach on some chemicals, particularly if those chemicals target susceptible populations.

Participants inquired about the implications of developing a novel set of pathways. Dr. Krewski expressed optimism regarding the number of pathways that could be identified in the future. Currently, a speculative range of new pathway discoveries is from hundreds to thousands. Dr. Krewski further emphasized that the identification of pathways is a large-scale science project on the order of the human genome project, which would require significant resources. In contrast, Dr. Birnbaum stated that the use of toxicity pathways alone might not be the ideal, and noted that information on disease pathways is available which could supplement toxicity pathway information in the future. Furthermore, she indicated that diseases are multifactorial and most biochemical actions have multiple modes of action, thus we run a great risk in assuming that understanding a single mode of action will be protective of the population.

The need to consistently and appropriately define adversity was a common theme throughout the conference. Dr. Birnbaum expressed concern about defining adversity for an entire population. Adversity depends on the question being proposed and the ideal degree of protection for the population of concern. Overall, she is not convinced that there is a way to declare biological change as non-adverse. Although Dr. Krewski agreed with Dr. Birnbaum's statement generally, he questioned whether there are biological events that are non-adverse for the general population (e.g., radio frequency fields). Dr. Dix stated that defining adversity is contingent on the percent of the population you aim to protect.

Another participant asked about the methods for disseminating information regarding the NexGen project to interested parties outside of the toxicology field. Dr. Cote assured the audience that the plan is to provide tools for public consideration and refinement. Follow-up questions related to NexGen's role in advancing the understanding of chemical mixtures and exposure science. Dr. Birnbaum noted that Toxcast™ and Tox21 cannot screen mixtures at the moment, but there is potential for that in the future. Exposure science is currently lagging behind toxicology, but the chemical-based approach is a good starting point. If aggregated properly, U.S. Census data and CDC blood data could be useful in advancing exposure science. Extracting periodicity quantitatively in dose-time studies was acknowledged to be one of the most critical issues in risk assessment.

At the end of the session, Dr. Krewski summarized the presentations and next steps for the NexGen project. He linked the studies of Dr. Devlin and Dr. Dix to the NRC vision, particularly with regard to how their studies transition from an *in vivo* to an *in vitro* approach. He further commented that the linkage

between population health and risk assessment is developing parallel to the linkage between toxicity and disease pathways. The term "toxicity pathway," should be redefined, however, so that it is made consistent across stakeholders, and perhaps biological pathway is a better term. Finally, Dr. Krewski shared his definition of "omics", which includes the human genome, exposome, and toxome.

6. Breakout Group Discussion and Cross-Cutting Themes

To promote a public dialogue on EPA's NexGen approach, the conference included parallel breakout group discussions and a reporting session. This time served as a forum for participants to discuss their concerns and questions and provide recommendations for the NexGen project's going forward. The goal was to gather individual input, rather than obtain consensus. The breakout groups met during the latter part of the first day and the beginning of the second day. To facilitate the discussion, conference participants were pre-assigned to breakout groups, each consisting of multiple stakeholders, and each breakout group was assigned a discussion theme on which to focus. Independent facilitators roamed to ensure participation and engagement.

At the conclusion of the breakout group discussions, conference participants reconvened for a breakout group report-back plenary session. In several instances, two breakout groups sharing a common, assigned theme combined their discussions and developed a joint presentation. Conference participants also were encouraged to submit their individual responses by the end of the conference via the questionnaire to ensure that all points of view were captured. The individual responses to the discussion questions are incorporated in the discussion in this section, while the responses to the short-answer questions included on the questionnaire are discussed in Section 7. The discussion questions posed to conference participants were organized by theme and are presented in the following text box.

6.1. Themes A and B – Applying Advances in Molecular Biology and New Approaches/Tools to Better Understand and Address Risk Assessment Issues

Although Themes A and B addressed distinct questions, the group discussions and presentations overlapped. The groups recognized that advances in molecular biology and new approaches/tools (e.g., high-throughput screening assays and new computational tools) provide a better understanding of risk assessment issues, including identification of disease pathways, information on the role metabolites play in health outcomes, and production of other data that could feed back into additional research. The breakout groups for both themes also noted, however, a number of questions and concerns still need to be addressed before these advances and new approaches/tools can be incorporated into risk assessment. For example, common questions heard during the breakout group presentations regarding creating a framework or toolbox to implement this approach included:

- What tools and approaches should be included in the toolbox and how will they be weighed to select the most applicable tool?
- How will these approaches and tools be implemented into risk assessment?
- How will the data generated from these approaches and tools be interpreted and communicated?
- How does a chemical move from tier to tier as more data are generated?

Additionally, the breakout groups voiced concerns regarding validation of these new approaches/tools. For example, they asked: How much confidence exists in the ability of assays to detect or negate effects? How likely are the assays to produce false positives and/or negatives? How relevant are the assays to human physiology and disease? Breakout participants noted is the importance of addressing sensitivity and specificity and having an established validation process. They also indicated a need to

better define the meaning of biological perturbations and to characterize exposure and dose to ensure that exposures and doses being tested are biologically relevant.

Based on their discussions, the breakout groups identified several potential advantages and challenges for applying the NexGen approach to risk assessment. They also identified some potential solutions for EPA to consider when addressing the challenges and concerns identified regarding the NexGen approach. Highlighted advantages, challenges, and potential solutions are presented in Table 1.

Discussion Questions by Theme

Theme A – Applying Advances in Molecular Biology to Understand Risk

- What do you think are the most important possible advantages of using recent advances in molecular biology to better understand the potential risks that may result from environmental exposures?
- What do you think are the most important challenges or concerns associated with using recent advances in molecular biology to understand the potential risks that may result from environmental exposures? How might these challenges/concerns be addressed?

Theme B – Applying New Approaches/Tools to Address Risk Assessment Issues

- Are there specific risk assessment issues for which these new approaches and tools might be particularly informative?
- What might be the challenges/concerns associated with the use of these new methods to address the specific issues you have identified? How might these challenges/concerns be addressed?

Theme C – Applying New Methods/Data to Address Environmental Challenges

- For what kinds of environmental challenges might these new methods and data be suitable?
- What are some of the concerns associated with utilizing these new methods and data to help resolve environmental challenges? How might these concerns be addressed?

Theme D – Communicating Advances in Risk Assessment

- What are good ways to communicate the advances in risk assessment to the public and hear responses and suggestions from the public?
- Should there be different methods for communicating to different segments of the public?
- What kinds of educational opportunities/outreach are needed to help the public understand the potential for this new science to be used for a variety of applications? What is the best way to tailor these efforts for various types of stakeholder groups?

Table 1. Advantages, Challenges, and Potential Solutions for Applying the NexGen Approach to Risk Assessment

Advantages	Challenges
➢ Obtaining a greater understanding of the mode of action (MOA) and ability to test MOA hypotheses ➢ Better characterizing interspecies and intraspecies variability ➢ Enabling use of a toxicity reference value range instead of a point estimate to better account for susceptible populations ➢ Reducing uncertainty and further refining chemical safety adjustment factors, uncertainty factors, and health effect levels ➢ Better evaluating the human relevance of observed effect ➢ Observing effects at a molecular level to help inform pathways to disease, including identifying chemicals that behave in a similar way and create similar adverse effects ➢ Increased testing of mixtures across a range of doses, including low doses, and potentially understanding the cascade of adverse and non-adverse effects caused by closeness of chemicals ➢ Enabling predictive toxicology and priority setting ➢ Potentially reducing animal testing and costs ➢ Improving efficiency of testing	➢ Effectively incorporating results in risk assessment due to lack of established processes and experience o Understanding the limitations of the assays and biology o Addressing the volatility, solubility, and interactions of chemicals o Determining the relevant *in vivo* dose using *in vitro* systems o Overcoming the limited ability to model ADME [adsorption, dilution, metabolism, and excretion] *in vitro* ➢ Distinguishing between what is adverse versus adaptive versus reversible ➢ Accounting for false positives or negatives and over- or under-interpretation of the data ➢ Identifying what mixtures to use and the synergistic and antagonistic effects of mixtures ➢ Adequately capturing the wide human variability, complicated disease states, windows of susceptibility, and gene-environment interactions ➢ Reproducing and interpreting the data, including correlating data generated from new methods with data from old methods ➢ Managing and ensuring that the data are transparent and publicly available ➢ Communicating to various stakeholders and promoting public acceptance and organizational change ➢ Obtaining sufficient funding
Solutions	
➢ Developing and utilizing more complex *in vitro* systems to better model *in vivo* cell relationships (e.g., the virtual liver) ➢ Coordinating with additional well-studied compounds and evaluating relationships among chemicals in relation to potential common pathways ➢ Involving risk managers throughout the implementation process and ensuring knowledge translation and exchange between science and policy ➢ Improving the science through an iterative process ➢ Developing validation approaches and performing more validation with targeted toxicity testing ➢ Aligning this approach with competitive initiatives to promote innovation ➢ Continuing stakeholder engagement	

6.2. Theme C – Applying New Methods/Data to Address Environmental Challenges

Theme C breakout groups were charged with identifying environmental challenges where use of these new methods and data might be suitable. Breakout group participants noted that this discussion should involve consideration of timescale issues. For example, one group noted that the new technologies are in their infancy and methods are still evolving. Although these new technologies and methods have current utility, they should not be used independently, but rather as a collection of tools in a toolbox. These methods and data might be used for improving:

- Hazard assessment for environmental risk assessment, including screening and prioritization of chemicals for additional consideration and research
- Early design of chemicals by streamlining research and development to create safer chemicals
- Mode-of action characterization
- Mixtures assessment (i.e., better understanding the effects of the mixtures to which we are exposed)
- Mitigation/preventive measure development in time-sensitive situations for which rapid methods are needed (e.g., measuring Gulf oil dispersants)
- Soil sample composition characterization
- Occupational risk assessments (e.g., updating permissive exposure levels by better characterization and grouping of chemicals)
- Herbal supplement evaluations

Theme C breakout groups also were charged with identifying concerns associated with using these new methods and data to help resolve environmental challenges and to recommending potential solutions for addressing these concerns. The Theme C breakout group participants shared similar concerns as those previously described for Themes A and B, but they also recognized that, to obtain regulatory acceptance, further validation, confidence, and communication that the new methods are adequately addressing human risk will be required. For example, one Theme C breakout group indicated that these new methods and data should not yet be used for supporting costly regulatory decisions or addressing metabolism, certain classes of chemicals, or matrix effects. Another participant suggested that due to limited funding, using available resources for gathering data on known issues to reduce uncertainty might be more effective than exploring a new approach. Additionally, one conference participant noted that when human health risk assessment transitions to non-animal testing, ecological risk assessors could lose a source of toxicological data. They indicated a potential danger in failing to identify critical toxicological stressors for non-human taxa if human responses to stressors are being measured by *in vitro* methods only. Furthermore, linking *in vitro* responses to *in vivo* responses in non-human taxa would be a considerable undertaking requiring additional resources.

Finally, the Theme C breakout groups discussed potential solutions for addressing these concerns. Their solutions were similar to those presented for Themes A and B. They also suggested, however, that EPA support development of guidance for interpreting and applying results via appropriate experts, provide training on the new methods for scientists and regulators, and engage with industry (e.g., the pharmaceutical industry) and share data to achieve a more coordinated effort.

6.3. Theme D – Communicating Advances in Risk Assessment

The breakout groups focusing on Theme D discussed what approaches should be used to communicate advances in risk assessment to the public and to enable the public to provide feedback. They also addressed whether different methods for communicating to different segments of the public should be

developed, and if so, what kinds of educational opportunities and outreach are needed to help the various stakeholder groups in understanding the potential for this new science to be used for a variety of applications.

The breakout groups noted that identifying the message NexGen wishes to communicate is important, and once the message is identified, it should remain consistent when it is conveyed. For example, is it the "vision" or "actual advances" in risk assessment? One breakout group agreed that "vision" is better because consensus has not yet been reached on whether the advances are real and ready for practical application. The group also cautioned, however, that clearly differentiating between hazard and risk when describing the vision is essential. They suggested developing five or six key phrases that explain why this new approach will be better than the traditional approach without being too technical. Some suggested key phrases to explain why EPA thinks the new vision will be "better" include that this approach will:

- Be more cost effective
- Result in better decisions by focusing on "right" stressors
- Require fewer animal tests
- Consider more chemicals and provide faster results
- Assist in identifying sensitive populations
- Help manage risks better

The breakout groups further suggested that when developing key messages, being specific in defining the target audience is critical because the best method of communication will depend on the audience to be reached (see adjacent textbox). Also essential is to identify lessons learned from previous communication attempts. The messages should be active and show that there is scientific agreement, but should not promise too much too soon. Additionally, when conveying these messages, communicating the uncertainties and limitations is as important as communicating the benefits. The communicator also should recognize that the public might be fearful of uncertainty, so such communications must be carefully crafted.

Advice to EPA for NexGen: Define and Effectively Communicate to Your Target Audience

When communicating, identifying the target audience is critical. This step influences the entire communication effort. Each target audience could require a different language, level of complexity and detail, organization and duration of message, and method of communication. For example, reporters need to find the information quickly (e.g., within three "clicks" on the Internet) to meet deadlines. By organizing the message effectively, risk communicators can help reporters to publish the "right" message. Potential target audiences for the NexGen approach include:

- Interested public
- Media
- Bloggers
- Non-governmental organizations
- Federal agencies
- Industry
- Management and supply chain organizations
- Science/risk assessment/contract lab communities

Communication is two-way. To be effective, therefore, communication also should include a component to allow the public to provide feedback. Suggested approaches for effectively communicating and for hearing responses and suggestions from the public include:

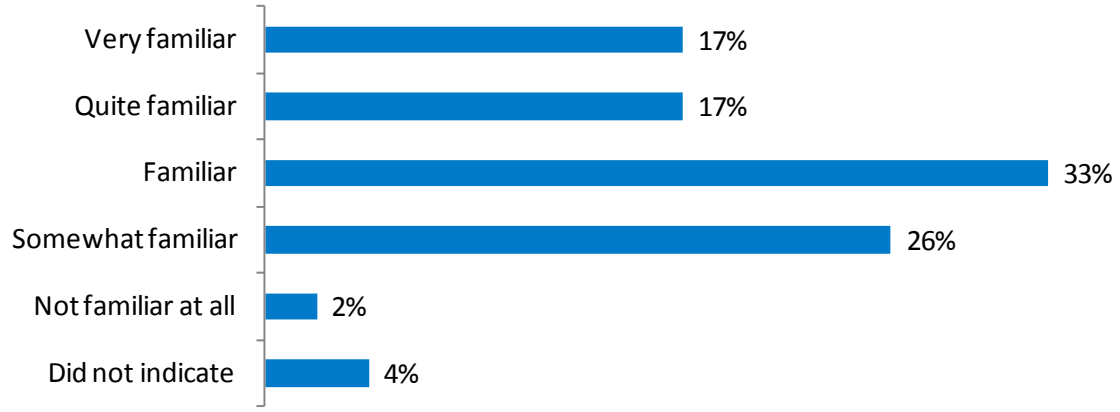
- Using accepted and novel risk communication methods and tools such as workshops, town hall meetings, professional societies, publications, newspapers, radio, television talk shows, Web- and video-based tools, social media (e.g., Facebook), and blogs.

- Incorporating new methods and approaches into curricula at all levels of education.
- Developing partnerships with various stakeholders (e.g., non-profit organizations).
- Involving primary care physicians to help spread key messages.
- Training members of the community to help communicate the message (e.g., Promotores).

7. Summary of Conference Questionnaire Short-Answer Responses

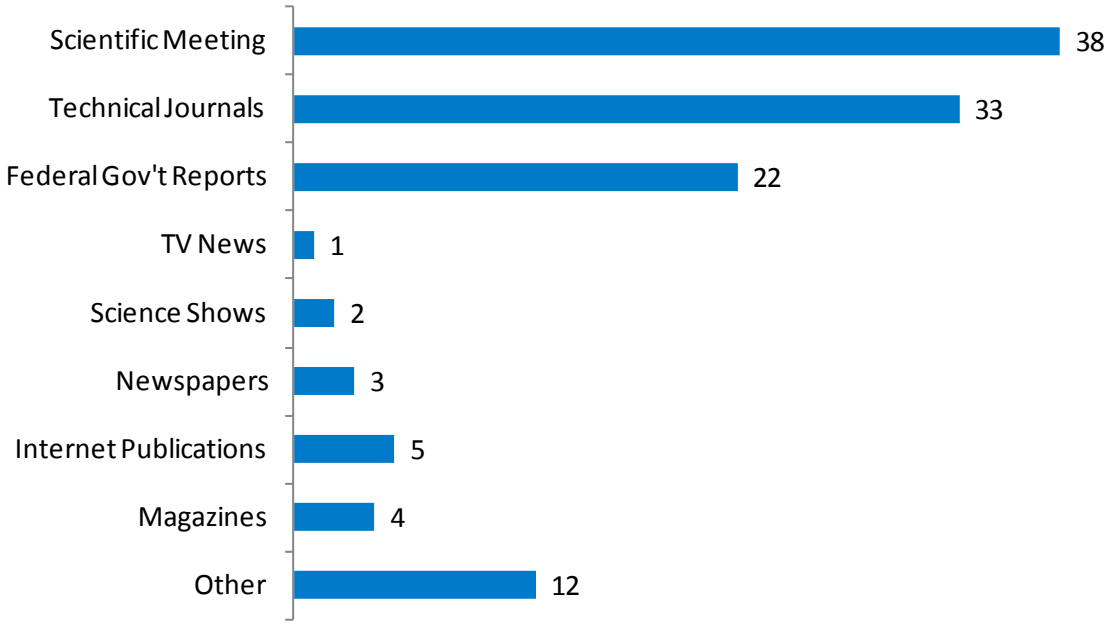
As previously mentioned, the purpose of the conference questionnaires was to obtain feedback from all participants and to ensure that they had a chance to voice their opinion on the NexGen approach. The questionnaire asked specifically about familiarity with the advances in systems biology and stakeholder engagement with projects such as NexGen. Questionnaires were provided to conference participants via their meeting folders and collected at the conclusion of the conference. The number of responses was 46, giving a response rate of approximately 28 percent. This section includes a summary of the responses to the short answer questions included in the questionnaire.

1. Are you familiar with recent advances in molecular and systems biology, and its potential uses in understanding disease?



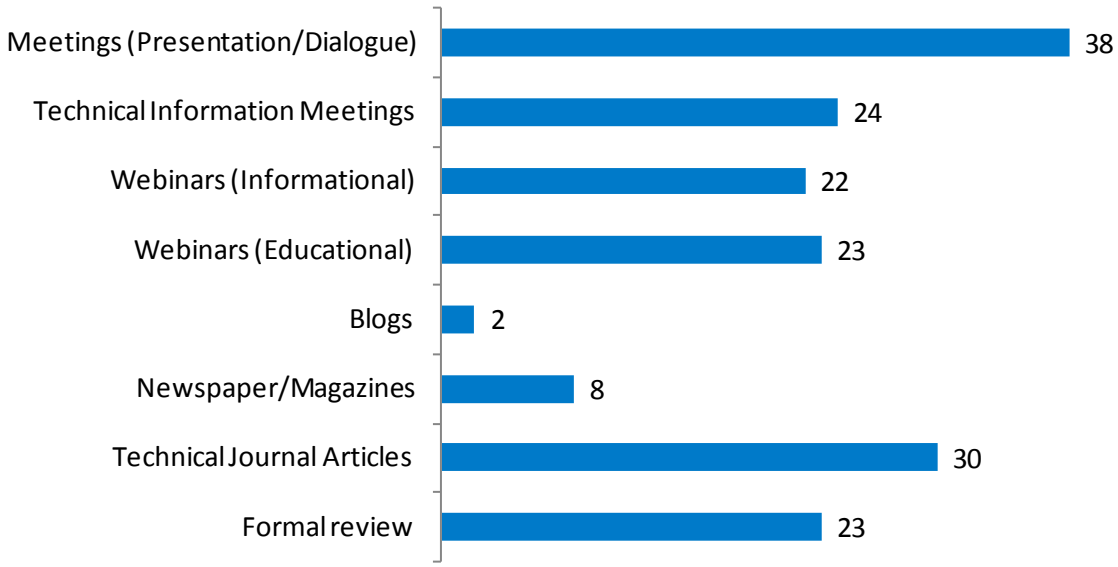
2a. What sources of information have been the most informative to you on this subject? Please provide examples.

* Note: Respondents indicated more than one option.



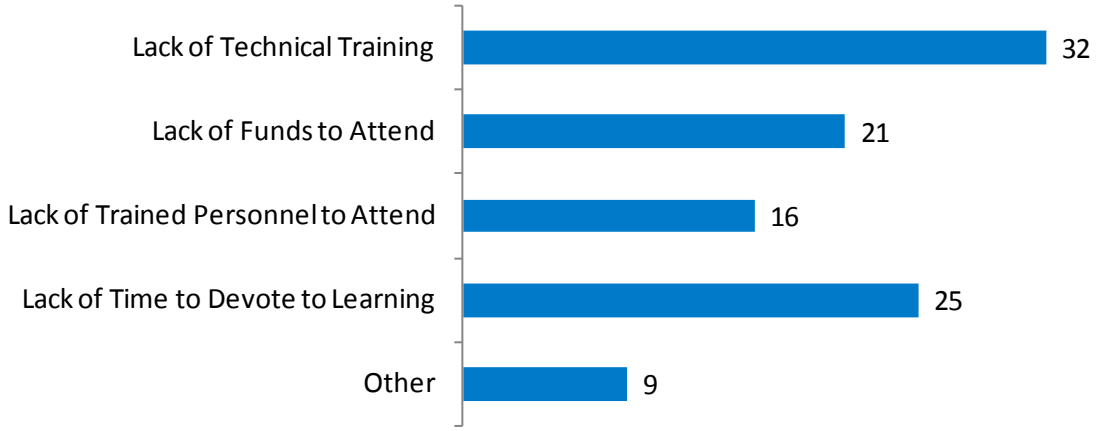
2b. Sources of Information Examples

Source of Information	Examples Identified by Respondents	
Scientific Meetings	• American Association for Cancer Research • American Association for the Advancement of Science • EnviroTox • U.S. Environmental Protection Agency (U.S. EPA) • Food and Drug Administration (FDA) • ILSI Health and Environmental Sciences Institute	• National Academy of Sciences (NAS) • NexGen November Workshop • NexGen Public Conference • Society for Risk Analysis • Society of Epidemiological Research • Society of Toxicology • Toxicology seminars
Newspapers/Newsletters	• *Risk Policy Report*	• *The Washington Post*
Internet Publications	• International Life Science Institute (ILSI) • National Institute of Environmental Health Sciences (NIEHS)	• PubMed • U.S. EPA – Office of Pesticide Programs
Magazines	• *Economist* • General pamphlets • *Science*	• *Science News* • Technical journals • *TIME*
Technical/Scientific Journals	• *Bioinformatics* • *Cancer Epidemiology, Biomarkers & Prevention* • *Critical Review of Toxicology* • *Environmental Health erspectives*	• *Environmental Science & Technology* • *Genome Biology* • *Nucleic Acids Research* • *Risk Analysis* • *ToxSci*
Federal Government Reports	• FDA • NAS • NIEHS • Occupational Safety and Health Administration (“Genomics in the Workplace”)	• U.S. EPA – Office of Research and Development, Office of Pesticide Programs
Science Shows	• 60 Minutes	• NOVA
Other	• Academic training • Co-worker attendance at meetings • E-mails from Agency and Agency Workshop • Interagency discussions	• NexGen Public Dialogue Conference National Research Council • Professional meetings (e.g., Environmental Health) • Web sites of manufactures who are developing arrays



4. Please indicate what obstacles stakeholders may face when engaging with the NexGen or SPSW projects:

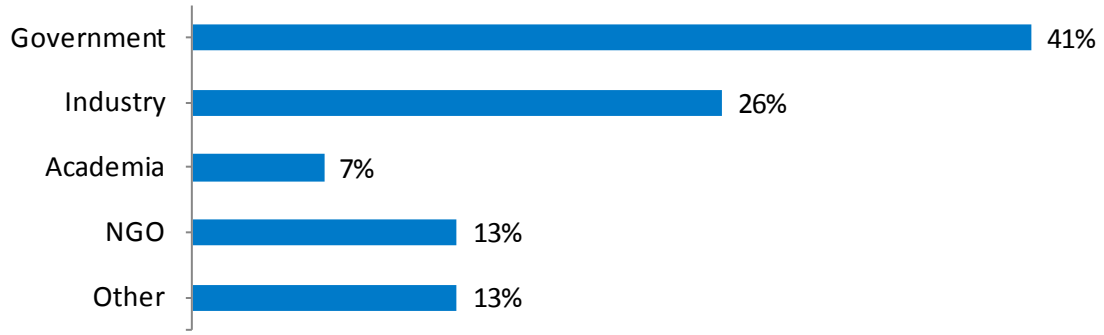
*Note: Respondents indicated more than one option.



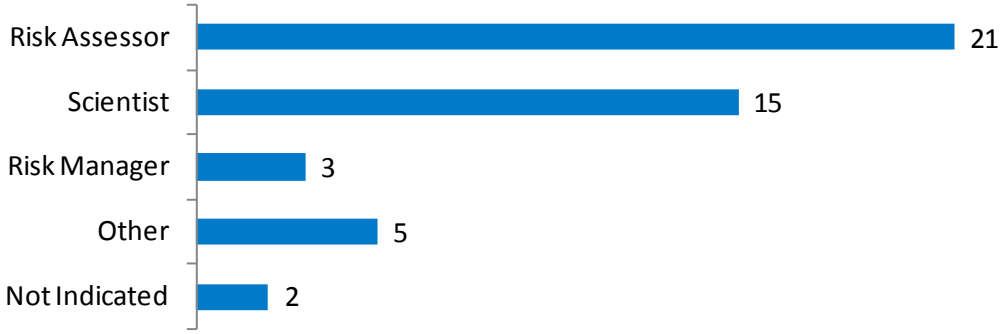
5. **Did this meeting help you better understand what EPA is doing to explore the use of these data in understanding the potential for risks that may occur from environmental exposures to chemicals and non-chemical stressors?**

- **43** participants indicated that the NexGen conference was somewhat helpful to helpful
- **4** participants did not find the conference particularly helpful and **4** participants would have preferred more information on non-chemical stressors
- **2** participants complimented the structure of the conference, while **1** participant praised the high quality of the speakers at the plenary session
- **3** participants stated that the conference provided insight into EPA's goals for NexGen and status update on EPA's progress to date in meeting these goals

6. **If you are representing an organization, how would you characterize the organization you represent?**



7. **How would you characterize your role within your organization or yourself if you are not representing an organization?**



8. Do you have any additional comments?

Conference Structure

- **5** respondents stated that they enjoyed the conference
- **1** respondent said they liked the use of case studies to illustrate advances in risk assessment
- **2** respondents stated that a few of the discussion questions overlapped too greatly and would have liked to see more focused questions
- **1** respondent stated that a question and answer session would have been more effective after each speaker, while **1** respondent felt that more background was needed prior to attending the conference

Stakeholder Involvement

- **6** respondents indicated that they appreciated both the government's engagement with stakeholder and the diversity of stakeholders at the conference
- **1** respondent would have liked the EPA participants to mix with other stakeholders for the breakout groups
- **1** respondent stated that NexGen should expedite public communication on the topic for all audiences
- **1** respondent would like to partner with EPA on the NexGen effort

8. References

Krewski, D., Hogan, V., Turner, M.C., Zeman, P.L., McDowell, I., Edwards, N., and Losos, J. (2007). An integrated framework for risk management and population health. *Human and Ecologicial Risk Assessment* 13: 1288-1312.

National Research Council (NRC). 2009. Science and Decisions: Advancing Risk Assessment. The National Academies Press, Washington, DC.

National Research Council (NRC). 2007. Toxicity Testing in the 21st Century: A Vision and a Strategy. The National Academies Press, Washington, DC.

Appendix A. Final Agenda: Advancing the Next Generation (NexGen) of Risk Assessment: Public Dialogue Conference

Day 1, February 15, 2011 – Capital Ballrooms B, C, and D	
8:00 – 9:00 am	**Registration**
9:00 – 9:50 am	**Welcome and Introduction – Ms. Becki Clark**, Acting Director, U.S. Environmental Protection Agency (U.S. EPA), Office of Research and Development, National Center for Environmental Assessment **Vision for Safer Products for a Sustainable World – Dr. Paul Anastas**, Assistant Administrator, U.S. EPA, Office of Research and Development *This presentation will introduce EPA's vision for chemical safety and sustainability and* NexGen's *supporting role.* **Linking Research to Risk Assessment – Dr. Linda Birnbaum**, Director, National Institutes of Health, National Institute of Environmental Health Sciences (NIEHS) *This presentation will summarize ongoing federal research efforts such as Tox21, and NIEHS/National Toxicology Program as related to Advancing the Next Generation of Risk Assessment.*
9:50 – 10:00 am	**Meeting Objectives, Desired Outcomes, and Meeting Process/Guidelines – Mr. Scott Graves**, Facilitator, ICF International (ICF)
Plenary Session I: Setting the Stage	
10:00 – 11:00 am	**The Next Generation of Risk Assessment (NexGen) Program: Overview and Invitation to Engage – Dr. Ila Cote**, Senior Science Advisor, U.S. EPA, Office of Research and Development, National Center for Environmental Assessment *This presentation will introduce the NexGen project, its drivers, goals and objectives, and potential uses to stakeholders. The presentation will invite engagement and discuss the value of stakeholder engagement in the project for both the implementers and the stakeholders.* **The Next Generation of Risk Assessment (NexGen): A Proposed Framework – Dr. Daniel Krewski**, Professor and Director, R. Samuel McLaughlin Centre for Population Health Risk Assessment, University of Ottawa *This presentation will present a proposed framework for NexGen, discuss the value of a new framework, and acknowledge methodological and communication challenges.*
11:00 – 12:30 pm	**Lunch** (On your own; cart in Foyer or see list of restaurants in folder)

Plenary Session II: Prototypes and Tier 2 Assessments	
12:30 – 1:30 pm	**Example Approaches to Understanding Human Health Risks Associated with Environmental Exposures to Chemicals** **Ozone – Dr. Robert Devlin**, Senior Scientist, U.S. EPA, Office of Research and Development, National Health and Environmental Effects Research Laboratory **Benzene – Dr. Martyn Smith**, Professor, University of California – Berkeley, School of Public Health, Environmental Health Sciences
1:30 – 2:00 pm	**Human Health Risk Assessment Approaches for Chemicals with Limited Data – Dr. David Dix**, Deputy Director, U.S. EPA, Office of Research and Development, National Center for Computational Toxicology
2:00 – 3:00 pm	**Question and Answer Session with Speaker Panel**
3:00 – 3:15 pm	**Charge to Breakout Groups – Mr. Scott Graves**, ICF
3:15 – 3:30 pm	**Afternoon Break**
Parallel Breakout Sessions	
3:30 pm – 5:00 pm	**Breakout Group Discussions** *Pre-assigned breakout groups will brainstorm as guided by the assigned discussion questions. Comments will be captured on flip charts. ICF Facilitators will be roaming to ensure focus and engagement by all.* 3:30 – 3:40 Group selects Leader and Note-taker. 3:40 – 5:00 Group discusses assigned questions. 5:00 – 5:30 Leaders and Note-takers from groups who considered the same questions collaborate to develop a joint summary.
Day 2, February 16, 2011 – Capital Ballrooms C and D	
8:45 – 8:50 am	**Welcome and Clarification of Path Forward for Day 2 – Mr. Scott Graves**, ICF
Parallel Breakout Sessions Continued	
8:50 – 9:35 am	**Breakout Group Discussions Continued** *Breakout groups will meet to review joint summary and complete their discussions.*
Parallel Breakout Presentations	
9:35 am – 12:45 pm (including 20-minute break)	**Breakout Group Presentations** *Breakout Group Leaders will present joint reports. These presentations will include a question and answer session with NexGen Project staff to clarify understanding of comments.*
12:45 – 12:55 pm	**Common Themes Heard – Mr. Scott Graves**, ICF
12:55 – 1:00 pm	**Closing Message to Participants – Dr. Ila Cote**, U.S. EPA
1:00 pm	**Meeting Adjourns**

Appendix B. Participants in the Advancing the Next Generation (NexGen) of Risk Assessment: Public Dialogue Conference

Name	Affiliation
Dr. Linda Abbott	U.S. Department of Agriculture
Dr. Paul Anastas	U.S. Environmental Protection Agency
Dr. David Andrews	Environmental Working Group
Dr. Jay Ansell	Personal Care Products Council
Dr. Kay Austin	U.S. Environmental Protection Agency
Dr. Ambuja Bale	U.S. Environmental Protection Agency
Ms. Barbara Bankoff	Private Citizen
Dr. Brenda Barry	American Chemistry Council
Dr. Nancy Beck	Office of Management and Budget
Dr. Souad Benromdhane	U.S. Environmental Protection Agency
Dr. Lynn Berndt-Weis	Health Canada
Dr. Linda Birnbaum	NIH, National Institute of Environmental Health Sciences
Ms. Patricia Bittner	U.S. Consumer Product Safety Commission
Ms. Susan Blaine	ICF International
Dr. Franziska Boerner	University of Alberta
Dr. Samuel Brock	Air Force Center for Engineering and the Environment
Ms. Liz Buckley	Pesticide & Chemical Policy
Dr. Michele Burgess	U.S. Environmental Protection Agency
Dr. Deborah Burgin	CDC, Agency for Toxic Substances and Disease Registry
Dr. Lyle Burgoon	U.S. Environmental Protection Agency
Dr. Stuart Cagen	Shell Health
Mr. Michael Callahan	MDB, Inc.
Dr. Cheng Cao	U.S. Army Public Health Command
Ms. Patricia Casano	GE - Corporate Environmental Programs
Dr. Christine Chaisson	The LifeLine Group
Ms. Cynthia Cheatwood	EA Engineering, Science and Technology
Dr. Weihsueh Chiu	U.S. Environmental Protection Agency
Dr. Amechi Chukwudebe	BASF Corporation
Ms. Becki Clark	U.S. Environmental Protection Agency
Dr. Patricia Cline	Strategic Environmental Analysis, Inc.

Name	Affiliation
Dr. Ila Cote	U.S. Environmental Protection Agency
Dr. Doug Crawford-Brown	University of Cambridge
Dr. George Cruzan	ToxWorks
Dr. Louis D'Amico	U.S. Environmental Protection Agency
Dr. Genya Dana	Dana and Sharpe Risk Associates
Dr. Kerry Dearfield	U.S. Department of Agriculture
Ms. Kacee Deener	U.S. Environmental Protection Agency
Dr. Vicki Dellarco	U.S. Environmental Protection Agency
Dr. Dennis Devlin	ExxonMobil Corporation
Dr. Robert Devlin	U.S. Environmental Protection Agency
Dr. Rob DeWoskin	U.S. Environmental Protection Agency
Ms. Bridget DiCosmo	InsideEPA
Dr. David Dix	U.S. Environmental Protection Agency
Dr. Ronald Dobbin	Society for Occupational and Environmental Health
Ms. Nancy Doerrer	ILSI Health and Environmental Sciences Institute
Mr. Alexander Domesle	U.S. Department of Agriculture
Dr. David Dunlap	Koch Companies Public Sector, LLC
Ms. Britt Erickson	Chemical & Engineering News
Ms. Elizabeth Erwin	U.S. Environmental Protection Agency
Dr. Susan Euling	U.S. Environmental Protection Agency
Mr. Robert Fensterheim	RegNet Environmental Services
Ms. Julie Fitzpatrick	U.S. Environmental Protection Agency
Dr. Colleen Flaherty	U.S. Environmental Protection Agency
Dr. Claire Franklin	The LifeLine Group
Ms. Carol Freeman	ICF International
Dr. Leslie Friedlander	Center for Environmental Health
Ms. Bonnie Gaborek	DuPont Haskell Global Centers for Health and Environmental Science
Dr. Michael Gargas	Naval Medical Research Unit-Dayton
Dr. Ann Marie Gebhart	ToxServices
Ms. Robinan Gentry	ENVIRON International Corporation
Dr. Amber Goetz	Syngenta Crop Protection, LLC
Dr. Ping Gong	U.S. Army Engineer Research and Development Center
Ms. Ami Gordon	ICF International

Name	Affiliation
Dr. Robert Grace	U.S. Government Accountability Office
Dr. Scott Graves	ICF International
Dr. Annette Guiseppi-Elie	DuPont Engineering
Dr. Kate Guyton	U.S. Environmental Protection Agency
Dr. Pertti Hakkinen	NIH, National Library of Medicine
Ms. Kerry Hamilton	U.S. Environmental Protection Agency
Ms. Irene Hantman	University of Maryland- School of Law
Dr. Masih Hashim	U.S. Environmental Protection Agency
Dr. Kenneth Haymes	U.S. Environmental Protection Agency
Dr. Maria Hegstad	InsideEPA
Ms. Janet Hess-Wilson	Air Force Center for Engineering and the Environment
Dr. Ross Highsmith	U.S. Environmental Protection Agency
Dr. Chris Hofelt	North Carolina State University
Ms. Audrey Hoffer	U.S. Environmental Protection Agency
Dr. Stewart Holm	Georgia-Pacific
Dr. Barry Hooberman	U.S. Food and Drug Administration
Ms. Jane Houlihan	Environmental Working Group
Ms. Annette Iannucci	Occupational Safety and Health Administration
Dr. Audrey Ichida	ICF International
Dr. Maia Jack	Grocery Manufacturers Association
Dr. Michael Jayjock	The LifeLine Group
Dr. Jennifer Jinot	U.S. Environmental Protection Agency
Ms. Maureen Johnson	U.S. Environmental Protection Agency
Dr. Wendelyn Jones	CropLife America
Dr. Channa Keshava	U.S. Environmental Protection Agency
Dr. Michael Kniss	U.S. Government Accountability Office
Dr. Dan Krewski	University of Ottawa
Dr. Francis Kruszewski	American Cleaning Institute
Dr. Megan Latshaw	Association of Public Health Laboratories
Ms. Sheri Lausin	ICF International
Dr. Dan Levy	U.S. Food and Drug Administration
Dr. Ronald Lorentzen	U.S. Food and Drug Administration
Dr. Nai-chia Luke	CDM

Name	Affiliation
Dr. Margaret MacDonnell	Argonne National Laboratories
Dr. Andrew Maier	Toxicology Excellence for Risk Assessment
Mr. Joseph Manuppello	People for the Ethical Treatment of Animals
Dr. Elizabeth Margosches	U.S. Environmental Protection Agency
Dr. Pete May	Greenbiz.com
Dr. Ed McComas	West Virginia Department of Environmental Protection
Dr. Jennifer McLain	U.S. Environmental Protection Agency
Dr. Jennifer McPartland	Environmental Defense Fund
Dr. Paul Middendorf	CDC, National Institute for Occupational Safety and Health
Mr. Greg Miller	U.S. Environmental Protection Agency
Dr. Mark Mitchell	Connecticut Coalition for Environmental Justice
Dr. Robert Mitkus	U.S. Food and Drug Administration
Mr. Asish Mohapatra	Health Canada
Dr. Katie Moore	The Endocrine Society
Dr. Megan Morgan	Georgia-Pacific
Dr. Kristi Muldoon Jacobs	Food and Drug Administration
Mr. George Murnyak	U.S. Army Institute of Public Health
Dr. Hirohisa Nagahori	The Hamner Institutes/Sumitomo Chemical
Dr. Olga Naidenko	Environmental Working Group
Dr. Stephen Nesnow	U.S. Environmental Protection Agency
Dr. Edward Ohanian	U.S. Environmental Protection Agency
Dr. Raegan O'Lone	ILSI Health and Environmental Sciences Institute
Ms. Kim Osborn	ICF International
Dr. Chrissy Palermo	ExxonMobil
Dr. Greg Paoli	Risk Sciences International
Dr. Ralph Parod	BASF Corporation
Dr. Leslie Patton	U.S. Consumer Product Safety Commission
Dr. Bob Peoples	ACS Green Chemistry Institute
Dr. Richard Phillips	ExxonMobil Biomedical Sciences, Inc.
Dr. Kathy Plotzke	Dow Corning
Dr. Gerald Poje	Grant Group
Dr. Margaret Pratt	U.S. Environmental Protection Agency
Dr. Peter Preuss	U.S. Environmental Protection Agency

Name	Affiliation
Dr. Resha Putzrath	U.S. Navy, Navy and Marine Corps Public Health Center
Dr. Santhini Ramasamy	U.S. Environmental Protection Agency
Ms. Rebecca Reindel	Occupational Safety and Health Administration
Dr. Steve Risotto	American Chemistry Council
Ms. Pat Rizzuto	The Bureau of National Affairs, Inc.
Mr. Alan Roberson	American Water Works Association
Ms. Ruthann Rudel	Silent Spring Institute
Dr. Jennifer Sass	Natural Resources Defense Council
Dr. Val Schaeffer	Occupational Safety and Health Administration
Ms. Ruth Schelhaus	FAA, Federal Agency Center
Dr. Rita Schoeny	U.S. Environmental Protection Agency
Dr. Deborah Segal	U.S. Environmental Protection Agency
Dr. Jordi Serratosa	European Food Safety Authority
Dr. Mary Shackelford	Food and Drug Administration
Dr. Patricia Sheehan	RegNet Environmental Services
Dr. James Sherman	Monsanto
Dr. Christopher Sheth	U.S. Environmental Protection Agency
Dr. Cheryl Siegel Scott	U.S. Environmental Protection Agency
Dr. Arianna Simonetti	U.S. Food and Drug Administration
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Dr. Martyn Smith	University of California, Berkeley
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Dr. Thomas Weppelmann	U.S. Environmental Protection Agency
Mr. Philip Wexler	NIH, National Library of Medicine
Dr. Ronald White	Johns Hopkins Bloomberg School of Public Health
Dr. Andrew White	Unilever PLC
Ms. Jessica Wignall	ICF International
Dr. Catherine Willett	People for the Ethical Treatment of Animals
Dr. Timothy Williams	Department of Army
Dr. Kimberly Wise	American Petroleum Institute
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Dr. Melanie Young	U.S. Environmental Protection Agency
Dr. Jennifer Young	ACS Green Chemistry Institute