



**U.S. Environmental Protection Agency's (EPA)  
National Center for Environmental Research (NCER)  
and  
International Council of Chemical Associations' (ICCA)  
Long-Range Research Initiative (LRI)**

# **Public Health Applications of Human Biomonitoring Workshop Summary Report**

**March 18, 2008  
FINAL**



**The Risk Assessment Paradigm.** This framework summarizes the factors necessary to characterize a chemical's risk. Sources, environment, exposure, dose, and associated response (i.e. biological effects) must be evaluated, as well as the relationships among them. Biomonitoring helps in understanding each of these elements. The goal of the workshop was to address challenges in the application of biomonitoring to public health scenarios.

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# **Public Health Applications of Human Biomonitoring Workshop Summary Report**

**September 24 & 25, 2007  
U.S. EPA  
Research Triangle Park, North Carolina  
FINAL**

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## List of Acronyms

ACC	American Chemistry Council
BE	Biological equivalents
BUSPH	Boston University School of Public Health
CDC	Centers for Disease Control and Prevention
Cefic	European Chemical Industry Council
CHAMACOS	Center for the Health Assessment of Mothers and Children of Salinas
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
EPA	Environmental Protection Agency
ESBIO	Expert Team to Support Biomonitoring Research in Europe
FAEE	Fatty acid ethyl esters
ICCA	International Council of Chemical Associations
IOM	Institute of Medicine
IRB	Institutional Review Board
NIEHS	National Institute of Environmental Health Sciences
NGO	Non-governmental organization
JCIA	Japan Chemical Industry Association
LRI	Long-Range Research Initiative
MICA	Mechanistic Indicators of Childhood Asthma
NCS	National Children's Study
NHANES	National Health and Nutrition Examination Survey
PBPK	Physiologically-based pharmacokinetic
POP	Persistent organic pollutant
RfD	Reference Dose
STAR	Science to Achieve Results

## 1.0 INTRODUCTION

On September 24 and 25, 2007, the U.S. Environmental Protection Agency's (EPA) National Center for Environmental Research (NCER) hosted a workshop on the public health applications of human biomonitoring in Research Triangle Park, North Carolina. The workshop centered on challenges in the application of biomonitoring research to public health. It focused discussion on the interpretation and communication of biomonitoring data and on the use of biomonitoring data to identify and prioritize vulnerable populations for public health tracking. Issues regarding the ethics of human biomonitoring practice and the responsible communication of biomonitoring information to the general public (including targeted subpopulations) were highlighted and discussed in the context of recent scientific advances in the biomonitoring field. The workshop was co-sponsored by the U.S. EPA's NCER and the International Council of Chemical Associations (ICCA)'s Long-Range Research Initiative (LRI), which is composed of the LRI's of the American Chemistry Council (ACC), Cefic (European Chemical Industry Council), and Japan Chemical Industry Association (JCIA). It was attended by 191 representatives from industry, academia, media, non-governmental organizations (NGOs), and various government agencies (see Exhibit 1).

Starting in 2002, LRI programs in both the U.S. and Europe have funded research to identify ways to understand predominant sources and pathways of exposure, characterize the relationship between exposure to environmental contaminants and biomonitoring data, and identify holistic ways to elucidate the relationship among biomonitoring data, dose, and health outcomes. The ICCA-LRI identified the interpretation of biomonitoring data as its highest priority research area in 2005. The U.S. EPA has also identified biomarker research as a priority, recognizing the usefulness of biomonitoring for assessing exposure, understanding vulnerability, and evaluating public health outcomes. Through its Science to Achieve Results (STAR) grants program, EPA has funded a large body of work focused on the development and validation of biomarkers, the use of biomarkers for assessing exposure and risk, and most recently, the sound interpretation of biomarkers. The most recent awards, which were announced this September, total nearly \$4 million and are intended to help develop advanced modeling techniques that will improve understanding of existing biomonitoring data.

In 2006, the ICCA-LRI convened a biomonitoring workshop that helped to coordinate and spur its research activities in this field (Bahadori et al. 2007). For this year's biomonitoring workshop, ICCA collaborated with U.S. EPA to bring together colleagues across a wide range of sectors. The workshop was designed to investigate the relationships among several key topics in biomonitoring research and application: recent advances in the scientific community; communication of biomonitoring data to the medical community, individual study participants, the broader public, and the media; and setting priorities for public health, such as the application of biomonitoring data for the protection of vulnerable populations and the appropriate communication of health and safety information. For both the ICCA-LRI and U.S. EPA's NCER, the international workshop provided a basis for continued collaboration among interested stakeholders, for maintenance and expansion of partnerships in biomonitoring research and application, for the improvement of networking across stakeholders to further maximize resources and for continued research into the public health applications of human biomonitoring.

**Exhibit 1**  
**Affiliations of Participants Who Attended the**  
**U.S. EPA – ICCA 2007 Biomonitoring Workshop**

3M	International Life Sciences Institute
American Chemical Society	International Union of Pure & Applied Chemistry
American Chemistry Council	Japan Chemical Industry Association
Arch Chemicals, Inc.	Lanxess Corp.
Bayer AG	LifeLine Group
Bayer CropScience	Lion Corporation
Bayer MaterialScience	Lockheed Martin
BASF	LR Risk Consulting
Battelle	McMaster University
BNA, Inc.	Minnesota Department of Health
Boston University	Mitsui Chemicals, Inc.
California Environmental Protection Agency	National Geographic
Canadian Chemical Producers' Association	National Institutes of Health
Case Western Reserve University	National Laboratory Training Network
Cefic (European chemical industry council)	North Carolina Central University
Centers for Disease Control and Prevention	North Carolina State University
Ciba Specialty Chemicals	Ohio State University
Clark University	RTI International
Colorado State University	Shell
CropLife America	Soap and Detergent Association
Cytec Industries, Inc.	State University of New York at Buffalo
Dow Chemical Company	Summit Toxicology
Dow Corning Corporation	Syngenta Crop Protection, Inc.
DuPont	United Nations Environment Programme
Eastman Chemical Company	VITO (Flemish Institute for Technological Research)
Environmental Defense	University of California at Berkeley
Environmental and Occupational Health Sciences Institute	University of California at Davis
Exponent, Inc.	University of Copenhagen
ExxonMobil	University of Leicester
Hamner Institutes for Health Sciences	University of North Carolina at Chapel Hill
Health Canada	University of Pittsburg
Health Protection Agency, UK	U.S. Environmental Protection Agency
ICF International	U.S. Government Accountability Office
Inside Washington Publishers	Verband der Chemischen Industrie e.V. (VCI)
	Weinberg Group, Inc.

The agenda for the two-day workshop, which includes the speakers, is provided in Appendix A. The first day of the workshop featured presentations by invited speakers, who set the stage for the focused discussions that followed later in the day during the parallel symposia. These symposia incorporated speakers on specialized topics and panel discussions. There were three parallel symposia, and each focused on one of the following topics: (1) scientific advances in interpretation of biomonitoring data, (2) challenges faced in communication of biomonitoring information, and (3) the application of biomonitoring data to usefully characterize and prioritize vulnerable populations for public health tracking. A poster session was held in the evening of the first day, showcasing biomonitoring research from 30 projects in both the U.S. and Europe; a list of the posters presented is included in Appendix B. The parallel symposia concluded on the second day, with rapporteurs from each session presenting a summary of their deliberations and conclusions to the reconvened main workshop body. International perspectives were shared by invited speakers from Europe, Canada, and Japan. Finally, the workshop closed with presentations looking ahead at future directions of the field.



These proceedings are a summary of the presentations, discussions, and overarching themes from both the plenary and parallel symposia. This report is intended to summarize the main themes of the discussions and is part of a process that is intended to enhance communication among all parties and to document the current state of the field of biomonitoring.

## 2.0 SESSION HIGHLIGHTS

Although several definitions of biomonitoring were presented by speakers during both days of the workshop, all definitions were quite similar in terms of the basic concept and the breadth to which they can be applied. See Exhibit 2 for a description and potential applications of biomonitoring. A summary of the plenary sessions and highlights of the presentations are presented in the sections that follow.

### 2.1 Setting the Stage for the Meeting

The overarching theme of the speaker presentations in this session was the interpretation and practical application of biomonitoring information to identify and characterize health risks from chemical exposures. The value of biomonitoring data will be greatly increased if they can be used to evaluate responses to the chemical exposures as well as the presence of an exposure.

Speakers from this session represented two very different scales of involvement in the biomonitoring research field: academic research, with an emphasis on uncovering the underlying mechanisms for biological response to chemicals, and large-scale government research, focusing on coordinating studies across large population segments. Significant points of commonality between the speakers included the focus on particularly vulnerable subpopulations and on uncovering adverse effects to low chemical exposures. In this session, and throughout the entire workshop, the development of partnerships between stakeholders emerged as a key element to building successful biomonitoring programs.

#### **Exhibit 2** **What is Biomonitoring?**

Human biomonitoring is the measurement of chemicals—or their biological breakdown products, known as metabolites or biological markers—in biological media such as blood and urine. A breathalyzer test is an example of biomonitoring. While biomonitoring can reveal whether exposure and absorption have occurred and whether levels are increasing or decreasing over time, it may not necessarily indicate whether there is any risk to health. Also, biomonitoring data do not always reveal when or how often an exposure has occurred, the concentration of the exposure, or the pathways of exposure (i.e., biomonitoring data integrate all sources/routes of exposure). Correctly measuring exposure depends on the chemical and the frequency of sample collection and analyses. And certain chemicals leave fingerprints, depending on the sources (e.g., dioxin-like compounds, volatile organic compounds).

#### **Potential Applications of Biomonitoring**

- Estimation of exposures
- Identification of fate of substances in the body
- Determination of exposure trends
- Provision of early warning signals about exposures
- Establishment of linkages between environmental exposures and (adverse) health effects
- Development of reference ranges (e.g., for public health tracking)
- Guidance for the design of animal toxicology studies and exposure and health effects research by providing information on more environmentally-relevant doses

Biomonitoring research performed across international borders, or even from one institution to another, can reflect different priorities and can lead to different policies and interventions. Such differential approaches can make it difficult to pool resources or compare results. Therefore, international collaboration represents a worthwhile effort that can foster universal (rather than national) strategies, as does the Expert Team to Support Biomonitoring Research in Europe (ESBIO), which is a collaboration of European Union member states, with input from industry and NGOs. ESBIO is intended to meet objectives that reflect the goals of the international biomonitoring community, including the following priorities:

- Integration of environmental and health monitoring data;
- Implementation of a coordinated framework for human biomonitoring;
- Development of approaches for interpretation of human biomonitoring data for public health applications;
- Communication, management, and reduction of risks identified with environmental and human biomonitoring data; and
- Creation of scenarios for input into policymaking (ESBIO 2007).

Coordinated or international approaches, such as that used in ESBIO, are an attempt to bridge the differences among current national approaches, thus resulting in more global, comparable data, providing wider access to biomonitoring data (Reis et al. 2007), and enabling the pooling of resources.

Research results that can be readily applied to policy development are of paramount concern to the public. Scientists in research programs must be able to translate the data into practical applications to be usable by policymakers. A key step to reducing risks posed by chemical exposures is to fill in the knowledge gaps in the risk assessment process (Albertini et al. 2006). Frequently, the least understood element in the risk assessment paradigm is the mechanism by which a chemical exposure produces an adverse health effect. Therefore, improving our understanding of these mechanisms can help identify, prioritize, and ultimately reduce risks from chemical exposures. For example, researchers have used biomarkers to shed light on the mechanism through which benzene exposure results in toxic metabolites (Kim et al. 2006, 2007; Lin et al. 2007). Characterizing differences in subpopulations is also important, as some groups may be more vulnerable than others to chemical exposures. Ethical concerns (e.g., intervention, reporting of exposure and health risks to participants) must be considered when conducting biomarker research, even in places where intervention is politically unwelcome or socially stigmatized.

## **2.2 Applications of Biomonitoring in Public Health**

The presentations in this session focused on important considerations in the application of biomonitoring in public health. Biomonitoring can be used to inform environmental policy and provide information for personal decision-making. Current research must overcome ethical,

technological, and political hurdles to adequately address public health concerns (Paustenbach et al. 2006).

Policies and regulations that dictate environmental concentration and source emission limits should be based on robust data, which links exposures to health outcomes. Biomonitoring is one tool in an integrated system of data gathering tools that includes self-reporting (through interviews or questionnaires), environmental and personal measurement, exposure modeling, and physiologically-based pharmacokinetic (PBPK) modeling. These tools, when used to provide complementary information, can assist in the construction of strategies for reducing risk from chemical exposures (Needham et al. 2007). Agencies that regulate environmental concentrations and source emissions must obtain information from these tools to determine what actions, if any, should be taken to mitigate risks, and to measure and assess the effectiveness of actions taken. Past successes in the use of biomonitoring data in risk assessment have involved lipophilic, bioaccumulative substances, such as dioxin, but the next phase of research will involve chemicals that are not so easily detected by biomonitoring. To adequately meet these challenges, scientists must develop reliable sampling techniques to determine chemical concentrations. Implementation of such techniques may help agencies use biomonitoring to fill data gaps and to set environmental concentrations and limit source emissions that are more data-driven.

Even in the absence of environmental monitoring information, biomonitoring data can be analyzed to identify environmental risks and set environmental priorities. Subpopulations, defined by geographic location or other population factors, can be compared to reveal differential health effects corresponding to differential chemical exposures. For example, comparisons of biomonitoring data from urban and rural areas in the Flanders Region revealed that use of the pesticide DDT had not ceased in rural areas, despite a ban on its use (Staessen et al. 2001). Analytical and statistical techniques, such as multivariate regression modeling, can be used to detect trends in subpopulations; however, caution must be taken in the interpretation of these analyses when attempting to identify causal relationships.

Vulnerable populations pose unique challenges for the application of biomonitoring studies. With regard to children, a vulnerable subpopulation, these challenges derive from their differential exposures and doses, the importance of the timing of exposure with regard to developmental stage and incidence of disease, and their vulnerability to environmental risks. Exposure assessment, dose calculations, and mechanisms of toxic effects must be performed separately for both children and adults, because developmental and behavioral patterns of children result in different intakes of environmental contaminants. New, large-scale biomonitoring studies are underway in the U.S., Canada, Europe, and elsewhere to study the relationships between environmental exposure and health outcomes in children. Obtaining exposure information from children is challenging, given inherent technical and ethical problems not encountered in adult populations.

Overcoming logistical problems of biomonitoring studies must be accompanied by rigorous ethical guidelines (Pedersen et al. 2007; Brody et al. 2007). Guidelines must address key elements likely to arise in biomonitoring research, including issues of informed consent, biobanking (storing biological samples for future research), participant incentives, information dissemination, and data and sample transfer. Multi-institutional collaboration is often hampered by differing requirements from each researcher's Institutional Review Board (IRB).

Harmonization of research protocols and IRB requirements from one institution to another, or from one country to another, to meet consensus ethical guidelines will help streamline the approval processes and will produce more comparable results.

### **2.3 International Perspectives**

In this session, speakers emphasized challenges in the application of biomonitoring data to risk evaluation and epidemiology, including in countries that have not historically used biomonitoring technology. In developed countries, emphasis has been placed on biomonitoring to investigate health outcomes from environmental exposures, especially with regard to children, infants, and pregnant women. Overcoming challenges posed by bureaucratic delays, IRB requirements, and population identification is paramount. Another priority has been the understanding of mechanisms of environmental degradation, to determine how chemicals interact from source to environment, before they reach the receptor.

In developing countries, environmental priorities are often sidelined in favor of more pressing public health issues. For instance, some countries continue to use banned and carcinogenic chemicals to increase crop output, because immediate needs (such as food production and economic growth) are seen as more pressing than environmental concerns or reduction of chronic health problems. Public and private organizations are partnering to apply basic biomonitoring research to developing areas, and to better quantify the impact of toxic chemicals on public health.

### **2.4 Looking Ahead: Perspectives on the Public Health Applications of Biomonitoring Data**

The closing session brought together different perspectives on the direction of biomonitoring research and its application to public health, and featured converging goals from representatives of government and NGOs. Speaker presentations focused on the past (previous successes as a guide for future success), the present (evaluation of current programs to improve effectiveness of new ones), and the future (planned studies that will move the science forward). Biomonitoring may provide information that could point to the causes of current diseases for which causal agents have not yet been identified. To accomplish these goals, the following elements should be incorporated into large-scale biomonitoring efforts:

- Upfront study design and strategy (e.g., standards and protocols for sampling, including timing and frequency);
- Coordination and cooperation between all parties on local and global scales (e.g., local, federal, regional government, industry, academia, media, and NGOs);
- A focus on multiple sources and cumulative risk; and
- Clear attention to social issues, including communication, perception, and privacy.

The National Children's Study (NCS), for example, is a long-term longitudinal study of children, families, and their environment. It proposes to collect data to make stronger inferences about the

links between environmental exposures (e.g., chemical, physical, behavioral, social, and cultural) and disease in the U.S. The NCS brings together six domestic agencies, including the National Institute of Environmental Health Sciences (NIEHS), the Centers for Disease Control and Prevention (CDC), and U.S. EPA, to provide scientific expertise and programmatic support for this collaborative effort. This major biomonitoring effort will attempt to overcome prior existing technological, ethical, and logistical barriers by tracking exposure and biological data from early pregnancy to late adolescence for a large population (100,000 children) and will be a comprehensive resource for future studies around the globe (NCS 2007).

### 3.0 PARALLEL SYMPOSIUM REPORTS

The parallel sessions each focused on one of three topic areas: (1) scientific advances in interpretation of biomonitoring data, (2) challenges faced in communication of biomonitoring information, and (3) the application of biomonitoring data to usefully characterize and prioritize vulnerable populations for public health tracking. The goal of the discussions in these sessions was to continue the dialogue between various interested parties while the science is still being developed to help interpret biomonitoring data and apply it to the public health domain. As biomonitoring continues to be a “hot topic” and is increasingly prevalent in the media, advancing the science and communicating knowledge (and knowledge gaps) to the public while developing policies that protect public health remains a challenge. The objectives and results of the group discussions are summarized in the sections that follow.

#### 3.1 Parallel Symposium 1: Scientific Advances in Interpretation of Biomonitoring Data

This session focused on scientific advances in the interpretation of biomonitoring data, including methods, technological advancements in measurement techniques and devices, and new challenges to interpretation of data. In this session, several speakers presented recent advances in the science of biomonitoring to help introduce the scientific interpretation of biomonitoring data, and the participants explored the topic by addressing the discussion questions presented in Exhibit 3. This session aimed to show how biomonitoring data have been used in practical (not theoretical) terms; to provide concrete examples of successful interpretation of biomonitoring data; and to discuss areas in which advances have been made, reasons leading to these advances, and possibilities to generalize to a broader context.

**Exhibit 3**  
**Parallel Symposium 1 Questions:**  
**Scientific Advances in Interpretation of Biomonitoring Data**

1. What is critical for effective interpretation of biomonitoring data?
2. What makes interpretation possible/impossible? What is missing (e.g. pharmacokinetic data, health based guidance values)? Is there progress? What is needed further? What makes it successful? What if critical data are missing?
3. Can results from one study (substance) be extrapolated to other situations/geographic locations, populations?
4. How do biomarkers of exposure and biomarkers of effect relate to existing biomonitoring data? How to design studies to investigate this?
5. How to deal with multiple exposures/causes (effect side)? What should our approach be towards multiple exposures (e.g. gene expression, receptor-binding, modeling)?
6. How do we deal with environmental exposure that is often difficult to quantify?
7. Do we use the appropriate biomarker related to the internal exposure and potential health effects? What about their predictive ability? How reliable are biomarkers? For current studies: are numbers sufficient (e.g. variability issues), were the right biomarkers selected for the context they are used in?

The primary objective of this parallel session was to address how biomonitoring data can be related to environmental concentrations and linked to health effects. Participants in this session identified and discussed the advances in science associated with biomonitoring data interpretation. The discussion centered on issues raised during the speaker presentations, and also touched on the questions presented in Exhibit 3 and on broader issues that spanned multiple related topics and disciplines.

In recent years, the amount of available human biomonitoring data has dramatically increased, driven in part by the improvement of the analytical methods that can now more accurately measure chemicals at very low levels. However, the ability to interpret these data has not kept pace with the availability. As raised by various participants throughout the workshop, one of the biggest hurdles in interpreting biomonitoring data is the “missing link” between exposure and response. Biomarker data can confirm whether humans were exposed to a chemical, but taken alone, they do not provide details about the concentration, route, duration, frequency, or source of exposure.

The critical question is whether the levels measured indicate a health risk. Because biomonitoring data can not alone answer this question, other scientific tools are needed. Some of the methods presented in this session that can help bridge the gap and make this critical link between exposure and effect include forward and reverse dosimetry (PBPK), biological equivalents (BE) approaches, and epidemiology studies. The group agreed that in order to advance the science in these areas, additional research needs to be performed to obtain a greater understanding of basic biology, including toxicology and disease causation (or definition). Many of the current approaches are only practical in the context of existing toxicity guidelines and pharmacokinetic understanding.

When considering these tools, users must acknowledge the tools’ limitations and appropriately match the tools for their intended applications. For example, it is important to understand that the BE concept should only be applied as a tool for prioritization. The values obtained using this approach are not health-based guidelines; rather, they are intended as a starting point to screen and prioritize chemicals for further evaluation (Hays et al. 2007). Therefore, participants noted that communication is an important component, and guidelines should be developed for clarity about the use of tools for interpreting biomonitoring data.

Following up on this point, participants discussed the importance of both communication and upfront coordination. Developing guidance for the interpretation of biomonitoring data is an important initial step in this process. A good example of where this was recently done is in the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) guidance document for the interpretation of biomonitoring data (ECETOC 2005). This document proposes a framework for the evaluation of biomonitoring data and includes an analysis of what is required for evaluation, depending upon the study. To analyze for trends in exposures, analytical integrity is needed. To characterize the exposures, both analytical and toxicokinetics knowledge are required. Adding to this knowledge about health effects enables a researcher to investigate health impacts and, with weight of evidence knowledge, to perform risk assessments and standard setting.



The group also discussed some of the common issues that arise during the interpretation of biomonitoring data and some of the critical components needed in this effort, which are listed below:

- **Toxicity data.** When linking internal dose to health outcomes, the lack of toxicity data is an issue. One potential solution, already being implemented, is U.S. EPA's ToxCast™ project, which is designed to enable scientists to predict or forecast a chemical's toxicity (U.S. EPA 2007a).
- **Timing of exposure.** Linking human biomonitoring data to exposure reveals problems that vary with the nature of the chemical. The timing of exposures and the window of susceptibility is often a challenge that arises when attempting to use biomarkers of exposure to quantitatively estimate human exposures, especially for non-persistent chemicals. There is a highly variable relationship between the actual exposure and the measured concentration, depending on when the sampling is conducted. Therefore, interpretations of data need to be assessed on the population level, not the individual level, and can perhaps be overcome with the use of probabilistic reverse dosimetry approaches (Tan et al. 2006).
- **Biomarker selection.** Issues when linking biomarkers to exposure and health outcome vary depending on the nature of the biomarker (e.g., what media is sampled, whether the parent chemical or active metabolite is measured). In many cases, good pharmacokinetic data are needed to help choose the appropriate biomarker. Participants suggested that panels or suites of biomarkers might be intelligently applied to overcome this challenge.
- **Study design.** Often human biomonitoring data is collected for detection of chemicals or their metabolites only, as is the case with the National Health and Nutrition Examination Survey (NHANES), which is a surveillance tool and should not be used alone for interpretation. Without having the pieces required for risk assessment as part of the study design, it is difficult to use the biomonitoring data for purposes beyond trend analysis. For example, studies should include the collection of environmental measurement data, which are vital in understanding the important sources, pathways, and routes of human exposures to chemicals. To effectively interpret biomonitoring data, knowledge about the mechanism, dose-response relationship, and mixture effects is required.
- **Standardized protocols.** The participants agreed that another important aspect of interpreting biomonitoring data from a study is ensuring upfront that there are standardized protocols. In addition to correctly designing the survey in which the data are collected, it is essential to have effective strategies for data collection, including those that address issues such as the timing of exposure. In some cases, data are collected extraneously, not because they improve the study or they are needed.

### 3.2 Parallel Symposium 2: Challenges Faced in Communication of Biomonitoring Information

This symposium focused on the challenges faced in the communication of biomonitoring information, on experiences and perspectives regarding the communication of these data, and on

how to address remaining challenges. The discussion focused on communicating biomonitoring information to three main audiences: individual study participants, the broader public and the media, and the medical community. The panelists included scientists conducting research in biomonitoring, communications specialists, and reporters. They were encouraged to bring their individual perspectives to the discussion, discuss their experiences, and identify potential approaches to facilitate effective communication. Discussion questions, presented in Exhibit 4, served as a springboard for panel deliberations.

**Exhibit 4**  
**Parallel Symposium 2 Questions:**  
**Challenges Faced in Communication of Biomonitoring Information**

1. All data collection, and particularly so with the current state of data collection of biomonitoring samples, typically requires caveats on the interpretation. How do you address potential for overinterpretation (or underinterpretation) of biomonitoring data? What caveats, if any, should be provided when providing conclusions about data?
2. What types of data do you think are appropriate to share and to what extent should the timing of such communication be considered?
3. Can you provide some specific recommendations on the type of information that can be provided that will allow for practical application from a public health perspective? For instance, how do you frame communication to allow a policymaker to make informed, rational decisions that may affect the general population versus communication at an individual or community level that could help with practical decisions in their daily lives?
4. Can you provide your insights into what specific aspects of biomonitoring data tend to evoke negative reactions?
5. Can you suggest effective communication strategies for putting these data in the context of risk and protection of public health that might mitigate some of these negative reactions?
6. What are good epidemiological practices in communicating results?
7. Discuss challenges faced when communicating biomonitoring data to an individual participant in a study, e.g., should individual results be returned when the results are not interpretable on an individual level?
8. What ethical issues should be considered (e.g., the role of IRB review) with respect to communication of biomonitoring information?

The group discussed aspects of biomonitoring information that tend to evoke negative reactions. Human biomonitoring data are perceived as personal, emotional, and political. The scientific complexity and uncertainty of its implications for public health create challenges when presenting data to individuals or groups. Interpretation of biomonitoring data is in its infancy, so it is difficult to provide concrete information that is relevant and scientifically accurate to individuals, groups, and the general public. There are also concerns about the potential for discrimination against or loss of insurance coverage by study participants, whose results may not be kept confidential. For example, the Boston Consensus Conference on Biomonitoring expressed concern that communities or individuals could be stigmatized by results (BUSPH 2006). Some people are anxious when they learn that there are unpronounceable chemicals (e.g.,

phthalates) in their bodies. Mothers, in particular, worry about contaminants in breast milk, which many consider to be “sacred food.” Biomonitoring recently entered the political realm when the California Environmental Contaminants Biomonitoring Program bill passed through the state legislature and was signed by the governor in 2006 (California SB 1379), following an unsuccessful attempt to pass a similar program in 2004 (California SB 1168).

Many of the suggested communications practices are applicable across the range of audiences. The group discussed best practices for successful communication, which centered on the importance of developing the key messages that need to be conveyed. Successful messages must have several characteristics: they must be truthful, accurate, factual, and affirmative; they must be easily understood and presented in plain, conversational language, without acronyms; they must be repeated frequently; they must be relevant, compelling, and empathetic; and they must be sensitive to time limitations (e.g., many reporters file two to three stories a day).

The consensus conference model, such as that from the Boston Consensus Conference, engages stakeholders to understand potential concerns at an individual and community level, can inform communication strategies and demonstrates that the public can learn and understand complex scientific topics and articulate their concerns (BUSPH 2006). The group agreed that study participants should receive biomonitoring results at the study or group levels, though communicating at the individual-level data was debated. The group stressed the importance of communicating both the data and the uncertainty associated with that data responsibly and ethically. Medical ethics values should guide the development of a communication strategy (see Exhibit 5). For instance, respecting each study participant’s right to know (or right *not* to know) their biomonitoring results must be balanced with the medical ethic principle of non-maleficence. When the health significance of low concentrations in biological media is unknown, individual-level data could contribute to unnecessary anxiety, stress, or other negative impacts. The group agreed that it is acceptable to convey the lack of scientific knowledge about interpreting an individual’s biomonitoring results, and that further research is warranted to address this knowledge gap. The Boston Consensus Conference argued that action steps for

#### Exhibit 5

#### Medical Ethics Values to Consider When Communicating Biomonitoring Information

- **Non-maleficence:** avoiding and preventing or minimizing harm to persons
- Respect for the **autonomy** of persons: respecting the self-determination of individuals and protecting those with diminished autonomy
- **Beneficence:** giving highest priority to the welfare of persons and maximizing benefits to their health
- **Justice:** treating persons with fairness and equity, and distributing the benefits and burdens of health care as fairly as possible in society

Source: Merlo et al. 2007.

reducing exposure, where available, should accompany the human biomonitoring data reporting, and that data should remain completely confidential, lest it affect insurance coverage for participants (BUSPH 2006).

While some IRBs have discouraged the sharing of individual results with study participants, some research has encouraged such information transfer. For instance, in the Center for Health Assessments of Mothers and Children of Salinas (CHAMACOS) research effort, community organizations were involved in the planning of biomonitoring studies of women, children, and agricultural workers in the Salinas Valley in California. Stakeholders agreed that the center must share the results with the participants and the community, the research must be culturally sensitive, and intervention and community outreach must be conducted to reduce exposures. The CHAMACOS investigators designed a methodology in which the participants were able to “opt in” to receive their individual results. Individuals subject to suspected risk factors (e.g., high blood lead levels), as compared to official guidelines, were referred to their physicians for follow-up care.

An approach for reporting results of biomonitoring studies to study participants was recently introduced by Foster and Agzarian (2007). According to their methodology, the communication strategy depends on the understanding of the chemical’s health effects. Individual-level biomonitoring results should be communicated for chemicals for which there is credible evidence linking exposure with adverse health effects in the human population. Data should be supplemented with the mean exposure and range of exposure measured in the study. If a result is above an established safety level, then further information is provided to assist the study participant in reducing exposure. For chemicals for which human health risks and intervention levels are unknown, the individual biomonitoring results would not be communicated. However, all such studies should retain the data indefinitely should health risks be identified in the future and the study participants desire a re-evaluation of their exposure. If at a future time, evidence suggests a potential health risk at low levels of exposure, the biomonitoring data are available for reassessment to provide the study participants with appropriate intervention (Foster and Agzarian 2007).

Engaging the study community in the development of a communication methodology during the study design phase and addressing communications with the study participants during the consent process are among the solutions that have been proposed to the problem of inconsistency in protocols. Participants recommended that a compilation of best practices for communicating biomonitoring data should be prepared and disseminated to epidemiologists, exposure scientists, and other biomonitoring researchers, and that the IRB process should be harmonized globally.

In addition to the communication guidance provided above, media and public outreach strategies used for reporting results, such as those used for the National Reports on Human Exposure to Environmental Chemicals (CDC 2007), provide a useful example. Preparations for releasing information included internal and external meetings, media consultants to train scientists on interaction with media, and development of a “message palette,” which consisted of a single main message (“Better exposure information will help identify and prevent exposure problems.”) supported by four other clear messages (e.g., “Sharing information benefits everyone, the public most of all.”). Public services were provided, including a toll free number,

telephone triage, calls to experts, and report mailings. Upon publishing data, CDC held teleconferences and webcasts, briefed Congressional staff, and granted media interviews. Another successful strategy is reporting data for priority chemicals in peer reviewed journal articles and posting documents on the internet as the analyses are completed.

To facilitate their message delivery and retention, scientists can invest in providing background and context to reporters, readily available information for a story. For example, organizing a symposium at the Society for Environmental Journalists Conference provides an opportunity for educating journalists about biomonitoring (or any other complex scientific issue). It was also agreed that scientists would benefit from communications or media training. Since credibility of the source is always an issue for reporters, when speaking with the media, scientists should be open and transparent with regard to conflicts of interest, should not attempt to vet questions, and they should avoid topics that are “off the record.”

The group discussed the power of humanizing a complex science story to make it compelling and understand its impact, as is accomplished in David Duncan’s *National Geographic* article (2006). Such stories help reporters and scientists engage with one another and motivate science reporters to pursue community-oriented stories. Biomonitoring studies are receiving media attention, as is the case for the C-8 Health Project blood biomonitoring and health assessment study.

The group acknowledged that physicians and other health practitioners are not attuned to biomonitoring issues. The medical community has little time to learn about biomonitoring and they tend to avoid discussing it with patients given the uncertainties in the interpretation of the data and that biomonitoring is considered a non-clinical issue that does not fit into the diagnostic framework. Some physicians feel that discussing biomonitoring information with patients would elicit unnecessary worry or panic. However, in the absence of medical community engagement, non-evidence based medicine assumes the role otherwise occupied by discussion of biomonitoring data. The following approaches were suggested to engage the medical community:

- Identify objectives and value of engaging the medical community, key messages, and media to best reach it, using focus groups to test messages and develop strategies.
- Find creative ways to deliver message (e.g., webcasts/podcasts, storylines in popular medical television shows, local citizen club presentations, public radio features).
- Review case studies or existing guidance such as the consensus conference model, the Institute of Medicine’s Roundtable on Evidence-Based Medicine (IOM 2007), and environmental health questionnaires from the Agency for Toxic Substances and Disease Registry (ATSDR 1992).
- Improve curricula in medical school to include biomonitoring. For example, Boston University School of Public Health hosts neurotoxicology training and case studies for students in the medical school.
- Host symposia at medical society meetings.

- Find the “thought leaders” and convince them of the importance.

It may require that patients ask their medical providers about the issue to spur the medical community to learn more about biomonitoring.

### **3.3 Parallel Symposium 3: Application of Biomonitoring Data to Usefully Characterize and Prioritize Vulnerable Populations for Public Health Tracking**

This parallel symposium explored how human biomonitoring data can be applied to usefully identify, characterize, and prioritize vulnerable populations. A number of presenters provided case studies that identified specific vulnerable populations and highlighted measures being employed to better characterize and protect these populations. Additionally, the group addressed discussion questions, presented in Exhibit 6, that focused on issues that exist for defining the boundaries around vulnerable populations and using biomonitoring data to identify vulnerable populations.

In order to demonstrate how human biomonitoring data can better be applied to usefully characterize and prioritize vulnerable populations for public health tracking, presenters in this symposium identified specific vulnerable populations, discussed in the following paragraphs, and highlighted potential measures being taken, or to be taken, to better characterize these populations and identify measures to reduce their exposures.

#### **Exhibit 6**

##### **Parallel Symposium 3 Questions: Application of Biomonitoring Data to Usefully Characterize and Prioritize Certain Vulnerable Populations for Public Health Tracking**

1. Can biomonitoring be used to define what vulnerability means (e.g. 95<sup>th</sup> percentile, 4 standards deviations above the mean, etc.)?
  - For example, given anecdotal evidence of a differentially exposed population, how can biomonitoring be used to characterize that population’s vulnerability? What would be some issues to consider when collecting biomonitoring information in that setting?
  - Given a biomonitoring data set, how can those data be used to characterize a particular vulnerable population? What data characteristics must be considered?
2. If a population is deemed vulnerable based on lifestyle and activities or susceptible based on lifestage and genetics, how can biomonitoring data be used to prioritize policy decisions?
3. How can biomonitoring data from a vulnerable population be used to inform the science for establishing causal relationships between exposure and health outcomes?
4. Can you provide an example where biomonitoring data has been used to inform public policy, public health interventions, or demonstrate a public health outcome in a vulnerable population?
5. Can biomonitoring data be used in lieu of other health-based standards, e.g., reference doses (RfDs)?

One example of a population vulnerable to toxicant exposure is the Northern Aboriginal population of Northern Canada. Levels of mercury and persistent organic pollutants (POPs) measured in Aboriginal people in the Arctic region were in some cases higher than those found in people from more temperate Canadian regions, despite the fact that there are no industries in the region. These body burdens are accumulated through exposures from the Northern Aboriginal people's traditional diet, which consists of marine mammals such as seals, whales, walrus or polar bears that may contain elevated levels of contaminants (INAC 2006). To address this issue, the Northern Contaminants Program has completed a number of dietary surveys which included both traditional foods and market foods, so the overall contribution to nutrient intakes and contaminant exposure could be assessed (INAC 2006).

Children also represent a population that is considered to be vulnerable to exposure from a variety of external factors. For example, prenatal children are vulnerable to ethanol exposure, which can result in fetal alcohol syndrome or some prenatal alcohol damage. However, there is a lack of clinical tools for assessing levels of alcohol consumption in pregnant women and for identifying newborns who may have been exposed to alcohol (Bearer et al. 2003). Identifying a biological marker for risk levels of drinking during pregnancy would allow for earlier identification and intervention for affected infants. Additionally, a biomarker would enable recognition of women at risk for drinking during their next pregnancy. Bearer et al. (2003) have investigated the use of fatty acid ethyl esters (FAEEs) measured in meconium (newborn stool) as a potential biomarker for identifying prenatal ethanol exposure. They have determined that FAEEs measured in meconium may prove to be a useful biomarker that is readily available, since a large amount of meconium is passed during the newborn's initial hospitalization (Bearer et al. 2005).

Children are also considered vulnerable as a result of exposures from their biological and physical environment, chemical exposures, genetics, and psychosocial factors. Not much is known, however, regarding the linkage between exposure and health outcomes, and researchers are currently conducting studies to help address this knowledge gap and to better protect children. For example, as discussed in the closing plenary session, the NCS plans to be the largest long-term study of children's health and development to be conducted in the U.S., and may potentially identify not only what is harmful but also what is helpful to children's health and provide a national dataset linking source to exposure to effect (NCS 2007). Another example is the Mechanistic Indicators of Childhood Asthma (MICA) study, which is a study of childhood asthma and parallel rodent study that combines and integrates biomarkers of exposure effects and susceptibility in the context of clinical measurements and disease (asthma) outcome (U.S. EPA 2007b).

Following the presentations, the group began to address how biomonitoring can be used to determine the difference between a highly exposed (i.e., vulnerable) population and the general population. However, the group noted that the first step should be to focus on the difficulties associated with defining the boundaries around a vulnerable population. Currently, multiple definitions exist for the terms *vulnerable* and *susceptible*; this may lead to confusion since these definitions mean different things to different people. The group identified one possible set of definitions for the terms: a *vulnerable* individual is one that is highly exposed, and a *susceptible* individual is one that, once exposed, is more likely to experience health outcomes. While these definitions proved to be a good starting point, the group also recognized that

vulnerability is not always defined by actual exposure, but may be influenced by public perception. Moreover, the group noted that an exposed population is often defined based on the study setting (e.g., 95<sup>th</sup> percentile, four standard deviations from the mean).

Additionally, the group discussed the difficulties in characterizing exposure, which adds to the difficulty in defining the boundaries around vulnerable populations. One issue the group focused on is whether a single or multiple measurements are necessary to adequately characterize exposure. The group determined that linking exposure to health outcomes requires substantial data, and a single measurement at one point in time may not adequately capture an exposure. Additionally, they noted that even at the 0<sup>th</sup> percentile, an exposure may be present. For these reasons, the group suggested that multiple measurements may help address the temporal variability associated with human health exposure.

Finally, the participants concluded that it would be helpful to form a multidisciplinary team (similar to the one that attended this symposium) to assemble a package of lessons learned. This package would include common terminology and definitions (e.g., for vulnerable and susceptible), and a discussion of the ethics involved in characterizing vulnerable populations. This action would provide a basis to move forward in defining boundaries around vulnerable populations, using biomonitoring data to identify vulnerable populations, and incorporating biomonitoring data into policy decisions to adequately protect public health. The group noted that multidisciplinary teams are beneficial because they provide a wide range of perspectives and they can work effectively to make decisions that incorporate science, social factors, and ethics to better understand the relationship between dose and exposure.



#### 4.0 REFERENCES

- Albertini R, Bird M, Doerrer N, Needham L, Robison S, Sheldon L, and Zenick H. 2006. The use of biomonitoring data in exposure and human health risk assessments. *Environ Health Persp* 114(11): 1755-1762.
- Agency for Toxic Substances and Disease Registry (ATSDR). 1992. Taking an exposure history, exposure history form. Available online at: [http://www.atsdr.cdc.gov/HEC/CSEM/exphistory/exphist\\_form.html](http://www.atsdr.cdc.gov/HEC/CSEM/exphistory/exphist_form.html). Last accessed on October 23, 2007.
- Bahadori T, Phillips RD, Money CD, Quackenboss JJ, Clewell HJ, Bus JS, Robison HS, Humphris CJ, Parekh AA, Osborn K, and Kauffman RM. 2007. Making sense of human biomonitoring data: Findings and recommendations of a workshop. *J Expo Sci Env Epid* 17 (4): 308-313.
- Bearer CF., Jacobson JL, Jacobson SW, Barr D, Croxford J, Molteno CD, Viljoen DL, Marais AS, Chiodo LM, and Cwik AS. 2003. Validation of a new biomarker of fetal exposure to alcohol. *J Pediatr* 143:463-9.
- Bearer CF, Santiago LM, O’Riordan M, Buck K, Lee SC, and Singer LT. 2005. Fatty acid ethyl esters: Quantitative biomarkers for maternal alcohol consumption. *J Pediatr* 146:824-30.
- Boston University School of Public Health (BUSPH). 2006. Measuring Chemicals in People—What Would You Say? A Boston Consensus Conference on Biomonitoring. Consensus Statement. December 11. Available online at: <http://www.biomonitoring06.org/>. Last accessed on October 24, 2007.
- Brody JG, Morello-Frosch R, Brown P, Rudel RA, Altman RG, Frye M, Osimo CA, Pérez C, and Seryak LM. 2007. “Is it safe”: New ethics for reporting personal exposures to environmental chemicals. *Am J Public Health* 97(9):1547-1554.
- California Senate Bill 1168. 2004. Available online at: [http://www.leginfo.ca.gov/pub/07-08/bill/asm/ab\\_1151-1200/ab\\_1168\\_bill\\_20071013\\_history.html](http://www.leginfo.ca.gov/pub/07-08/bill/asm/ab_1151-1200/ab_1168_bill_20071013_history.html). Last accessed on October 24, 2007.
- California Senate Bill 1379. 2006. Available online at: <http://www.dhs.ca.gov/ps/deodc/ehlb/BPP/PDF/SB1379.pdf>. Last accessed on October 24, 2007.
- Centers for Disease Control and Prevention (CDC). 2007. National report on human exposure to environmental chemicals home page. Division of Laboratory Services. Available online at: <http://www.cdc.gov/exposurereport/default.htm>. Last accessed on October 24, 2007.
- Duncan DE. 2006. Chemicals within us. *National Geographic Interactive Edition* (October). Available online at: <http://www7.nationalgeographic.com/ngm/0610/feature4/index.html>. Last accessed on October 24, 2007.

- ESBIO European Human Biomonitoring. 2007. European human biomonitoring homepage of the implementation group and ESBIO. Available online at: <http://www.eu-humanbiomonitoring.org/>. Last accessed on October 24, 2007.
- European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC). 2005. Guidance for the interpretation of biomonitoring data. Document 44. November.
- Foster WG and Agzarian J. 2006. Reporting results of biomonitoring studies. *Analytical and Bioanalytical Chemistry* 387:137-140. Available online at: <http://www.springerlink.com/content/j2w4766178904771>
- Hays, SM, Becker RA, Leung HW, Aylward LL, and Pyatt DW. 2007. Biomonitoring equivalents: A screening approach for interpreting biomonitoring Results from a Public Health Risk Perspective. *Reg Tox Pharm* 47(1):96-109.
- Indian and Northern Affairs Canada (INAC). 2006. Human health – Canadian arctic contaminants assessment report II. Available online at: [http://www.ainc-inac.gc.ca/ncp/pub/heltsum\\_e.html](http://www.ainc-inac.gc.ca/ncp/pub/heltsum_e.html). Last accessed on October 18, 2007.
- Institute of Medicine (IOM). 2007. Roundtable on evidence-based medicine. Available online at: <http://www.iom.edu/CMS/28312/RT-EBM.aspx>. Last accessed on October 24, 2007.
- Kim S, Vermeulen R, Waidyanatha S, Johnson BA, Lan Q, Rothman N, Smith MT, Zhang L, Li G, Shen M, Yin S, and Rappaport SM. 2006. Using urinary biomarkers to elucidate dose-related patterns of human benzene metabolism. *Carcinogenesis* 27(4):772-81.
- Kim S, Lan Q, Waidyanatha S, Chanock S, Johnson BA, Vermeulen R, Smith MT, Zhang L, Li G, Shen M, Yin S, Rothman N, and Rappaport SM. 2007. Genetic polymorphisms and benzene metabolism in humans exposed to a wide range of air concentrations. *Pharmacogenet Genomics* 17(10):789-801.
- Lin YS, Vermeulen R, Tsai CH, Waidyanatha S, Lan Q, Rothman N, Smith MT, Zhang L, Shen M, Li G, Yin S, Kim S, and Rappaport SM. 2007. Albumin adducts of electrophilic benzene metabolites in benzene-exposed and control workers. *Environ Health Perspect* 115(1):28-34
- Merlo DF, Knudsen LE, Matusiewicz K, Niebrój L, and Vähäkangas KH. 2007. Ethics in studies on children and environmental health. *J. Med. Ethics* 33:408-413.
- National Children's Study (NCS). 2007. The National Children's Study. Available online at: <http://www.nationalchildrensstudy.gov/index.cfm>. Last accessed on October 24, 2007.
- Needham L, Calafat AM, and Barr DB. 2007. Uses and issues of biomonitoring. *Int J Hyg Environ Health* 210: 229-238.
- Paustenbach D and Galbraith S. 2006. Biomonitoring: Is body burden relevant to public health? *Reg Tox and Pharm* 44(3): 249-261.

- Pedersen M, Merlo DF, and Knudsen LE. 2007. Ethical issues related to biomonitoring studies on children. *Int J Hyg Environ Health* 210(3-4): 479-82.
- Reis, MF, Tedim J, Aguiar P, Miguel JP, Casteleyn L, Joas R, and Van Tongelen B. 2007. Online integrated solution to collect data, generate information and manage events in the human biomonitoring field. *Int J Hyg Environ Health* 210(3-4): 403-406.
- Staessen JA, Nawrot T, Den Hond E, Thijs L, Fagard R, Hoppenbrouwers K, Koppen G, Nelen V, Schoeters G, Vanderschueren D, Van Hecke E, Verschaeve L, Vlietinck R, and Roels HA. 2001. Renal function, cytogenetic measurements, and sexual development in adolescents in relation to environmental pollutants: a feasibility study of biomarkers. *Lancet* 357(9269): 1660-1669.
- Tan, Y-M, Liao KH, and Clewell HJ. 2006. Reverse dosimetry: interpreting trihalomethanes biomonitoring data using physiologically based pharmacokinetic modeling. *J Expo Sci Environ Epidemiol* doi:10.1038/sj.jes.7500540.
- U.S. EPA. 2007a. ToxCast™ Fact Sheet and FAQ. August 1, 2007. Available online at: [http://www.epa.gov/comptox/toxcast/files/ToxCast\\_FactSheet\\_and\\_FAQ\\_01aug2007.pdf](http://www.epa.gov/comptox/toxcast/files/ToxCast_FactSheet_and_FAQ_01aug2007.pdf). Last accessed on October 24, 2007.
- U.S. EPA. 2007b. A systems biology approach to improve the predictive value of biomarkers for assessing exposure, effects, and susceptibility in the Detroit children's health study. Available online at: [http://www.epa.gov/NCCT/new\\_start/detroit.html](http://www.epa.gov/NCCT/new_start/detroit.html). Last accessed on October 18, 2007.

## APPENDIX A: ICCA BIOMONITORING WORKSHOP FINAL AGENDA

### Workshop Co-Chairs:

Kacee Deener, US Environmental Protection Agency  
Tina Bahadori, American Chemistry Council

### Monday, September 24

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7:00 – 8:30 AM

#### Registration and Continental Breakfast

Room: EPA-RTP Main Campus, Building C, Atrium

8:30 – 9:05 AM

#### Welcome

Room: Auditorium (C111)

- Carol Henry, American Chemistry Council
- George Gray, US Environmental Protection Agency

9:05 – 9:15 AM

#### Workshop Objectives and Expectation of Outcome

- Janet Mostowy, Bayer Corporation
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### Plenary Session I: Setting the Stage for the Meeting

9:15 – 10:15 AM

Session Chair: Lawrence Reiter, US Environmental Protection Agency  
30 min each, including Q&A

Human Biomonitoring Activities and the Vision for Europe

- Ovnair Sepai, UK Health Protection Agency

Using Biomarkers to Characterize Human Benzene Metabolism

- Stephen Rappaport, University of California, Berkeley

10:15 – 10:45 AM

#### Break

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### Plenary Session II: Applications of Biomonitoring in Public Health

10:45 AM – 12:45 PM

Session Chair: Hugh Tilson, US Environmental Protection Agency  
30 min each, including Q&A

Applications of Biomonitoring in Environmental Decision Making

- Linda Sheldon, US Environmental Protection Agency

The Flemish Environmental Human Biomonitoring Program: 2002-2006

- Greet Schoeters, VITO (Flemish Institute for Technological Research)

Biomonitoring and Children's Health: Global Perspectives

- Ondine von Ehrenstein, National Institute of Child Health and Human Development

Biomonitoring in Europe: Ethics

- Lisbeth Knudsen, University of Copenhagen
-

12:45 – 2:00 PM

**Lunch** (on your own)  
Room: EPA cafeteria

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## **Parallel Symposia**

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2:00 – 5:00 PM

### **Session 1: Scientific advances in interpretation of biomonitoring data**

(30 min Break)

Chair: Peter Boogaard, Shell  
Rapporteur: Chris Money, ExxonMobil  
Recorder: Rebecca Kauffman, ICF International

Description of Parallel Symposia and Charge to Participants (15 min)

- Peter Boogaard, Shell

Speakers (30 min each with 1 hr for discussion and Q&A):

Interpretation of Human Biomonitoring Data Using A Forward Dosimetry Approach:  
Permethrin A Case Study

- Marsha Morgan, US Environmental Protection Agency

The Application of Probabilistic Reverse Dosimetry for Interpreting Human  
Biomonitoring Data

- Harvey Clewell, The Hamner Institutes for Health Sciences

Interpretation of Human Biomonitoring Data in a Public Health Risk Context Using  
Biomonitoring Equivalents

- Sean Hays, Summit Toxicology
- 

### Session 2: Challenges faced in communication of biomonitoring information

Chairs: Peggy Geimer, Arch Chemicals  
Rapporteur: Annette Guiseppi-Elie, Dupont  
Recorder: Kimberly Osborn, ICF International

Description of Parallel Symposia and Charge to Participants (15 min)

- Dana Barr, Centers for Disease Control and Prevention

Speakers (30 min each with 1 hr for discussion and Q&A):

Communication of Biomonitoring Information

- Robert Zachariasiewicz, US Environmental Protection Agency

The Boston Consensus Conference on Biomonitoring: Process, Findings and  
Recommendations

- Madeleine Scammell, Boston University School of Public Health

Challenges in Communicating: One Reporter's Perspective

- Pat Rizzuto, BNA, Inc.
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**Session 3: Application of biomonitoring data to usefully characterize and prioritize certain vulnerable populations (for public health tracking)**

Chair: Larry Needham, Centers for Disease Control and Prevention

Rapporteur: Judy Graham, American Chemistry Council

Recorder: Ami Parekh, ICF International

Description of Parallel Symposia and Charge to Participants (15 min)

- Larry Needham, Centers for Disease Control and Prevention

Speakers (30 min each with 1 hr for discussion and Q&A):

Human Health Implications of Arctic Environmental Contaminants

- Jay Van Oostdam, Health Canada

Biomarker for Prenatal Ethanol Exposure: Identifying a Vulnerable Population

- Cynthia Bearer, Case University

CDC's Environmental Public Health Tracking Network and Biomonitoring

- Beverly Kingsley, Centers for Disease Control and Prevention

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5:00 – 6:30 PM

**Reception and Poster Viewing**

Room: Atrium

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6:30 – 8:30 PM

**Group Dinner**

Room: EPA cafeteria

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**Tuesday, September 25**

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7:00 – 8:00 AM

**Continental Breakfast**

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**Parallel Symposia Breakout Sessions**

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8:00 – 10:00 AM

**Session 1: Scientific advances in interpretation of biomonitoring data**

Chair: Peter Boogaard, Shell

Rapporteur: Chris Money, ExxonMobil

Recorder: Rebecca Kauffman, ICF International

Speakers (30 min each):

Biomarkers in Epidemiology: The best thing since sliced bread or just another tool?

- Jane Hoppin, National Institute of Environmental Health Sciences

Biomarkers of Exposure and Effect to Environmental Carcinogens, and Their Applicability to Human Molecular Epidemiological Studies

- Peter Farmer, University of Leicester

Panel discussion (including speakers above and panelists listed below):

- Brenda Weis, National Institute of Environmental Health Sciences
  - Marsha Morgan, US Environmental Protection Agency
  - Harvey Clewell, The Hamner Institutes for Health Sciences
  - Sean Hays, Summit Toxicology
- 

**Session 2: Challenges faced in communication of biomonitoring information**

Chair: Peggy Geimer, Arch Chemicals

Rapporteur: Annette Guiseppi-Elie, Dupont

Recorder: Kimberly Osborn, ICF International

Speakers (30 min each):

Balancing Act: Communicating Information about Biomonitoring and Surviving to Tell the Tale

- Dorothy Sussman, Centers for Disease Control and Prevention

Reporting Biomonitoring Results to Individuals and Medical and Public Audiences: Challenges and Opportunities

- Asa Bradman, University of California, Berkeley

Panel discussion (including speakers above and panelists listed below):

- Cheryl Hogue, Chemical & Engineering News
  - Pat Rizzuto, BNA, Inc.
  - David Ewing Duncan, National Geographic
  - Robert Zachariasiewicz, US Environmental Protection Agency
  - Madeleine Scammell, Boston University School of Public Health
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**Session 3: Application of biomonitoring data to usefully characterize and prioritize certain vulnerable populations (for public health tracking)**

Chair: Doug Haines, Health Canada

Rapporteur: Larry Needham, Centers for Disease Control and Prevention

Recorder: Ami Parekh, ICF International

Speakers (30 min each):

Opportunities for Linking Biomonitoring Data to Risk Assessment and Public Health in the National Children's Study

- Jim Quackenboss, US Environmental Protection Agency

Mechanistic Indicators of Childhood Asthma (MICA) – Integrating Environmental, Clinical and Susceptibility Markers to Improve the Impact of Human Air Pollution Studies

- Jane Gallagher, US Environmental Protection Agency

Panel discussion (including speakers above and panelists listed below):

- Cynthia Bearer, Case University
- Beverly Kingsley, Centers for Disease Control and Prevention
- Lisbeth Knudsen, University of Copenhagen

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10:00 – 10:30 AM

**Break**

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10:30 – 11:30 AM

**International Perspectives**

Chair: Elaine Cohen-Hubal, US Environmental Protection Agency

20 min. each, including Q&A

Challenges Faced in the Less Industrialized Regions of the World

- Paul Erhardt, International Union of Pure and Applied Chemistry

Maternal - Infant Biomonitoring: The Epidemiological Challenges

- Tye Arbuckle, Health Canada

Challenge to Improving the Precision of Risk Evaluation Systems for Humans

- Fumiaki Shono, Japan Chemical Industry Association

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11:30 AM – 12:30 PM

**Parallel Symposia Report Back**

Chair: Judy Graham, American Chemistry Council

20 min. each, including Q&A

- Chris Money, ExxonMobil
- Annette Guiseppi-Elie, Dupont
- Doug Haines, Health Canada

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12:30 – 1:30 PM

**Lunch** (on your own)

Room: EPA cafeteria

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**Looking Ahead: Perspectives on the Public Health Applications of Biomonitoring Data**

1:30 – 3:00 PM

Chair: Jerry Blancato, US Environmental Protection Agency  
30 min. each, including Q&A

The POPs Global Monitoring Plan under the Stockholm Convention

- Katarina Magulova, United Nations Environment Programme

Biomonitoring: A Public Interest and Public Health Perspective

- John Balbus, Environmental Defense

Children's Environmental Health: Biomonitoring and the National Children's Study

- Duane Alexander, National Institute of Child Health and Human Development
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**APPENDIX B: ICCA BIOMONITORING WORKSHOP  
LIST OF POSTER PRESENTATIONS**

<b>Presenter</b>	<b>Affiliation</b>	<b>Project Title</b>
Karen Brown	University of Leicester, UK	Assessment of the relative contribution of endogenous versus exogenously derived N7-(2-hydroxyethyl)guanine adducts in rats treated with 14C-labelled ethylene oxide
Kate Calder	Ohio State University, U.S.	Arsenic exposure pathways in subpopulations: Bayesian inference from NHEXAS data
Christine Chaisson	The LifeLine Group, U.S.	Determination of aggregate and cumulative exposures of perfluorinated compounds consistent with biomarkers of the compounds using simulation modeling of exposure and pharmacokinetics
Harvey Clewell	Hamner Institutes for Health Sciences, U.S.	Development of a PBPK model for interpreting biomonitoring data on carbaryl and other n-methyl-carbamates
Seymour Garte	University of Pittsburg, U.S.	Genetic susceptibility to benzene toxicity in humans
Yue Ge	U.S. EPA	Using proteomics to monitor protein expression in human cells exposed to carcinogens
Dale Hattis	Clark University, U.S.	Use of biomarkers and physiologically based pharmacokinetic (PBPK) modeling in risk analysis for developmental effects of chlorpyrifos
Brooke Heidenfelder	U.S. EPA	Integration of animal and human gene expression data to improve the predictive value of exposure, effects, and susceptibility biomarkers in asthmatic children
Erin Hines	U.S. EPA	Brominated flame retardant levels in human milk and serum from North Carolina residents in the US EPA MAMA study
Yong Joo Chung	U.S. EPA	Qualitative measurements of IgE and IgG in human asthmatic serum for mold reactivity
Lisbeth Knudsen	University of Copenhagen, Denmark	European network on children's susceptibility and exposure to environmental genotoxicants
		A better environment for the children - proposed courses of actions in Denmark
		Biomonitoring of pregnant mothers
		Danish questionnaires used for the mother-child biobank
		Transport of substances across the human placenta: placenta perfusion system
		Micronuclei in families exposed to air pollution: a pilot study in the Czech Republic
Michael Madden	U.S. EPA	Lipidomics: a possible tool for the biomonitoring of specific air pollutants

<b>Presenter</b>	<b>Affiliation</b>	<b>Project Title</b>
Rocio Monroy	McMaster University, Canada	Serum levels of perfluorinated compounds and brominated flame retardants in human maternal and umbilical cord blood samples
		Effects of maternal smoking in the placenta vasculosyncytial membrane thickness
Jessica Nelson	Boston University, U.S.	Boston Consensus Conference on Biomonitoring: lay findings and recommendations
Leena Nylander-French	University of Carolina at Chapel Hill, U.S.	Biomarkers of exposure to hexamethylene diisocyanate
James Olson	University at Buffalo, U.S.	CYP-specific PBPK/PD models to interpret biomarkers for organophosphate pesticides
Cherie Pucheu-Haston	University of Carolina at Chapel Hill, U.S.	Early biomarkers of acute respiratory allergen exposure
Brad Reisfeld	Colorado State University, U.S.	An integrated computational framework for the interpretation of organophosphorus pesticide biomarkers
Greet Schoeters	VITO (Flemish Institute for Technological Research), Belgium	Linking emission and air quality data with biomarker measurements in Flemish adolescents
		Inter-individual variability in serum PCBs in adolescents and adults from the Flemish environment and health study
Ovnair Sepai	Health Protection Agency, UK	UK contribution to a pan-European human biomonitoring programme – focus on children’s health
Ken Sexton	University of Carolina at Chapel Hill, U.S.	Innovative experimental techniques to help understand exposure to volatile organic air toxics
Warren Strauss	Battelle, U.S.	Development of statistical sampling strategies and optimal design considerations for complex environmental epidemiology studies
Tim Wade	U.S. EPA, National Health and Environmental Effects Research Laboratory	Salivary antibody responses as an indicator of waterborne infections: pilot community study before and after installation of UV treatment