International Council of Chemical Associations (ICCA)
Long-Range Research Initiative (LRI)
Workshop

Making Sense of Human Biomonitoring Data

July 26 & 27, 2006
The Depot
Minneapolis, Minnesota

The Risk Assessment Paradigm. This framework summarizes the factors necessary to characterize a chemical's risk. Sources, environment, exposure, dose, and associated biological effects must be evaluated, as well as the relationships among them. The goal of the workshop was to identify emerging, relevant research in the area of biomonitoring that will provide methods to identify whether levels of chemicals in humans are associated with health risk.

Summary Report

International Council of Chemical Associations (ICCA) Workshop: Making Sense of Human Biomonitoring Data

July 26 & 27, 2006
The Depot
Minneapolis, Minnesota

Prepared for
American Chemistry Council
1300 Wilson Boulevard
Arlington, VA 22209

Prepared by
ICF International
9300 Lee Highway
Fairfax, VA 22031

October 2006

CONTENTS

Organizing Committee Members ii
List of Acronyms iii
1.0 INTRODUCTION 1
2.0 SESSION HIGHLIGHTS 2
2.1 Session I: Overview of Recent Efforts to Improve the Understanding of Biomonitoring Data 3
2.2 Session II: Policy and Decision-Making Perspective 4
2.3 Session III: Perspectives on Science and Related Needs 5
2.4 Looking Ahead: Translating Research Intent into Action 5
3.0 BREAKOUT GROUP REPORTS 6
3.1 Breakout Group 1: Exploration of the Link between Exposure, Dose, and Human Biomonitoring Data 6
3.1.1 Objectives of Breakout Group 1 7
3.1.2 Discussion of Breakout Group 1 Charge Questions 7
3.1.3 Recommendations from Breakout Group 1 9
3.2 Breakout Group 2: Computational Tools and Biomonitoring Data 11
3.2.1 Objectives of Breakout Group 2 11
3.2.2 Discussion of Breakout Group 2 Charge Questions 12
3.2.3 Recommendations from Breakout Group 2 13
3.3 Breakout Group 3: Relevance of human biomonitoring data to the design of toxicological studies 15
3.3.1 Objectives of Breakout Group 3 15
3.3.2 Discussion of Breakout Group 3 16
3.3.3 Recommendations from Breakout Group 3 17
4.0 References 19
APPENDIX A: ICCA BIOMONITORING WORKSHOP FINAL AGENDA 20
APPENDIX B: POSTER PRESENTATIONS 24

Organizing Committee Members

Dr. Dick Phillips, Co-Chair
ExxonMobil Chemical Company
Toxicology and Environmental Sciences

Dr. Tina Bahadori, Co-Chair
American Chemistry Council
U.S. Long-Range Research Initiative

Dr. Rick Becker
American Chemistry Council
Public Health Team

Dr. Ben Blount
Centers for Disease Control and Prevention
National Center for Environmental Health
Agency for Toxic Substances and Disease Registry

Dr. Laurent Bontoux
European Union
Joint Research Centre

Dr. Peter Boogaard
Shell Health Services - Shell International BV
Toxicology & Product Stewardship

Dr. Jim Bus
The Dow Chemical Company
Health & Environmental Research Lab

Mr. Bruce Caswell
Canadian Chemical Producers' Association
Environment, Health, and Safety

Mr. Harvey Clewell
CIIT Centers for Health Research
Division of Computational Biology

Dr. Akira Fukushima
Lion Corporation, Japan
Human & Environmental Safety Evaluation Center

Dr. Annette Guiseppi-Elie
Dupont Engineering, Corporate Remediation
Dupont Spruance Plant

Mr. Doug Haines
Health Canada
Health Impacts Bureau

Dr. Colin Humphris
Cefic (European Chemical Industry Council)

Mr. Masatoshi Kumamoto
Japan Chemical Industry Association

Mr. Chris Money
Exxon Mobil Petroleum & Chemical

Dr. Marsha Morgan
U.S. Environmental Protection Agency
Office of Research and Development
National Exposure Research Laboratory

Dr. Moiz Mumtaz
Centers for Disease Control and Prevention
Agency for Toxic Substances and Disease Registry
Division of Toxicology

Dr. Larry Needham
Centers for Disease Control and Prevention
National Center for Environmental Health
Division of Laboratory Sciences
Organic Analytical Toxicology Branch

Dr. Miles Okino
U.S. Environmental Protection Agency
Office of Research and Development
National Exposure Research Laboratory
Human Exposure & Atmospheric Sciences Division

Mr. Jim Quackenboss
U.S. Environmental Protection Agency
Office of Research and Development
National Exposure Research Laboratory
Environmental Sciences Division

Dr. Steven Robison
Procter & Gamble
Miami Valley Laboratories

List of Acronyms

ACC	American Chemistry Council
ADME	absorption, distribution, metabolism, and elimination
AUC	area-under-the-curve
CAFE	Clean Air for Europe
CDC	Centers for Disease Control and Prevention
Cefic	the European chemistry council
CTEPP	Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
EPA	Environmental Protection Agency
EU	European Union
HPV	high production volume
ICCA	International Council of Chemical Associations
ILSI/HESI	International Life Science Institute Health and Sciences Institute
JCIA	Japan Chemical Industries Association
LRI	Long-Range Research Initiative
MOE	margin of exposure
NGO	non-governmental organization
NHANES	National Health and Nutrition Examination Survey
NHEXAS	National Human Exposure Assessment Survey
NIOSH	National Institute for Occupational Safety and Health
NRC	National Research Council
OECD	Organisation for Economic Co-operation and Development
PBPK	physiologically-based pharmacokinetic
QSAR	Quantitative Structure Activity Relationships
QSPR	Quantitative Structure Property Relationship
REACh	Registration, Evaluation & Authorisation of Chemicals
RfD	reference dose
SCALE	Science, Children, Awareness-raising, Legal implementation tools & regular Evaluation

1.0 INTRODUCTION

A workshop was held on July 26 and 27, 2006 in Minneapolis, Minnesota to facilitate development of a coordinated research agenda for research to enable interpretation of human biomonitoring data. Ethical, legal, and regulatory issues and their influence on the direction and application of biomonitoring research were also discussed. The workshop was sponsored by 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 (the European chemical industry council), and the Japanese Chemical Industry Council (JCIA). It was attended by approximately 100 representatives from industry, academia, and various government agencies (see Exhibit 1).

Exhibit 1
Affiliations of Participants and Observers Who Attended the ICCA Biomonitoring Workshop

American Chemistry Council
Arch Chemicals Corporation
Bayer
Battelle
Canadian Chemical Producers Association
California Environmental Protection Agency
Cefic (European chemical industry council)
Centers for Disease Control and Prevention
CIIT Centers for Health Research
Commonweal
Dow Chemical Company
DuPont
Emory University
Environmental & Occupational Health Sciences Institute
ExxonMobil
Harvard School of Public Health
Health Canada
Health & Safety Laboratory
Hercules Incorporated
HES Dow Corning Corporation
Honeywell International
ICF International
Imperial Oil
INERIS
Institute of Occupational Medicine
International Programme on Chemical Safety
Japan Chemical Industry Association
Johns Hopkins University
Lawrence Berkeley National Laboratory
Lion Corporation
McMaster University
Mickey Leland National Urban Air Toxics Research Center
Minnesota Department of Health
Minnesota Pollution Control Agency
Mitsui Chemical Inc.
Ohio State University
Pacific Northwest National Laboratory
Procter & Gamble Company
Rohm and Haas Company
Shell
Sumitomo Chemical Co., Ltd.
Summit Toxicology
Syngenta
University of Antwerp/VITO (Flemish Institute for Technological Research)
University of California
University of Leicester
University of Michigan
University of Minnesota
University of Montreal
University of North Carolina
University of Pittsburg
U.S. Environmental Protection Agency
World Health Organization

In 2005, the ICCA-LRI identified the interpretation of biomonitoring data as its highest priority research area. Specifically, this workshop was designed to develop a research agenda that will constitute a basis for planning at the ICCA-LRI level, to identify partnerships to better execute and develop such research, and to review the capacity and skills available to advance the

topic and identify how improved networking across stakeholders could serve to further improve resources.

The workshop agenda is provided in Appendix A. In summary, the morning of the first day and part of the second day of the workshop were devoted to presentations by invited speakers to provide a wide range of backgrounds and perspectives. A detailed discussion of research elements occurred in focused breakout sessions that met for several hours in the afternoon of the first day. On the second day, rapporteurs for breakout sessions presented a summary of their deliberations to all conference participants. Following these presentations, the breakout groups reconvened for further discussion and conclusion. The breakout group discussions each focused on one of three topic areas: (1) links between exposure, dose, and human biomonitoring data, (2) computational tools and biomonitoring data, and (3) the design of toxicological studies. The goal of these discussions was to identify options for the ICCA-LRI to consider as it develops a research strategy that incorporates further research into and use of human biomonitoring data. The workshop closed with presentations from each breakout group on their recommendations, followed by a final session on looking ahead.

These proceedings are a summary of the presentations, discussions, and preliminary research priorities from both the plenary and breakout sessions. This report is intended to capture the essence of the discussions and recommendations and is part of a process that will develop a more detailed and refined set of priorities for the chemical industry.

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 it 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.

Exhibit 2
What is Biomonitoring?

Human biomonitoring is the measurement of chemicals—or their biological breakdown products, known as metabolites—in biological media such as blood and urine. While biomonitoring can reveal whether exposure and absorption have occurred and whether levels are increasing or decreasing over time, it may not 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. Depending on the sources, certain chemicals leave fingerprints (e.g., dioxin-like compounds, volatile organic compounds), that help make the connections to exposures.

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
- Provide guidance to design of animal toxicology studies

2.1 Session I: Overview of Recent Efforts to Improve the Understanding of Biomonitoring Data

The general theme of the speaker presentations in Session I was to provide an overview of the national and international efforts in making sense of human biomonitoring data. Speakers presented a broad cross-section of select recent efforts to improve the understanding of biomonitoring data, including those carried out by the International Life Science Institute Health and Environmental Sciences Institute (ILSI/HESI) Biomonitoring Technical Committee, the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC), and JCIA. It was clear during the session that discussion regarding the interpretation and use of biomonitoring data must involve collaboration across all sectors (i.e., industry, government, academia) and countries.

The field of biomonitoring is rapidly evolving and is being heavily researched. In addition, the sensitivity of analytical methods to detect low levels of chemicals is improving dramatically. There are multiple national and international programs currently producing toxicity, hazard, and exposure data—for example, exposure data via the US National Health and Nutrition Examination Survey (NHANES); Organisation for Economic Co-operation and Development (OECD) information on high production volume (HPV) chemicals; and data from independent laboratories. However, despite the ability to detect very low levels of chemicals and the availability of toxicology and risk assessment information, biomonitoring has yet to be placed in a risk-based context. For this reason, groups such as the ILSI/HESI biomonitoring committee are attempting to identify and refine effective scientific uses of biomonitoring tools and/or biomonitoring data to characterize exposure to chemicals. ILSI/HESI also is interested in exploring mechanisms for integrating biomonitoring data and toxicology data into a robust risk assessment process. To achieve its goals, ILSI/HESI engaged in the following activities:

- Held a workshop to evaluate chemical case studies;
- Presented a poster at the 2005 Society of Toxicology meeting;
- Outlined common criteria for interpretation of biomonitoring;
- Produced a mini-monograph in *Environmental Health Perspectives* and a forum paper in *Toxicological Sciences*;
- Presented their findings to a National Academies of Science committee on biomonitoring; and
- Established four work groups to address various topics related to biomonitoring.

The European Union (EU) is also making advances in the field of biomonitoring. Three EU initiatives recently have been established and include Clean Air for Europe (CAFE), Registration, Evaluation & Authorisation of Chemicals (REACH), and Science, Children, Awareness-raising, Legal implementation tools & regular Evaluation (SCALE). Additionally, in 2005, ECETOC established a dedicated task force on biomonitoring with broad representation from academia, institutes, non-governmental organizations (NGOs), and industry and published a “white report” titled *Guidance for the Interpretation of Biomonitoring Data* (ECETOC 2005). The report includes a framework for the interpretation of human biomonitoring data that incorporates four principal considerations: analytical integrity, ability to describe exposure

(pharmacokinetics), ability to relate to effects, and overall evaluation (weight-of-evidence). The framework was validated by identifying the four principal considerations in peer-reviewed literature. Finally, the Cefic-LRI is sponsoring research in both the U.S. and the Europe to identify and address existing data gaps in human biomonitoring data. Some areas of research include quantitative relationships between DNA adducts and mutations, roles, applications, and state-of-the-science of biomarkers, background incidence of key biomarkers of chemical exposure in the general population, and intra- and inter-individual variation of key biomarkers in the general population.

In Japan, various biomonitoring studies have been conducted by the government, including studies on endocrine disrupting chemicals in blood, studies on the exposure to children, and studies on chemicals of concern. Presently, there has not been major concern or interest among either media or NGOs regarding biomontoring. However, JCIA is taking a proactive approach and has launched an introduction to biomonitoring on their website. Additionally, based on their experience with endocrine disruptors and the intensive dialogues with the Japanese government, JCIA has initiated contact with the government concerning the significance and future of biomonitoring. Current collaborative activities of the JCIA-LRI in relation to biomonitoring include research on phytoestrogens in cord blood and chemical sensitivity/sick building syndrome.

2.2 Session II: Policy and Decision-Making Perspective

The presentations in Session II focused on the perceived added value for interpreting biomonitoring data in regards to conducting risk assessments and making policy decisions. Biomonitoring has the potential to help inform individual and public health decisions. While biomonitoring has been used in the past to inform some policy decisions, a broader approach and additional understanding is necessary in order to realize the full potential of biomonitoring.

Prior to conducting any biomonitoring studies, it would be useful to determine how the resulting data will be utilized. Biomonitoring is a useful tool, but not a stand alone tool. It should be used in conjunction with exposure and health assessments. Linking biomonitoring data with dose, exposure, and environmental concentrations requires refined modeling tools (e.g., physiologically-based pharmacokinetic (PBPK) models, probabilistic source-to-dose models, and interfaces between exposure and PBPK models); advance statistical approaches; and information collection tools to improve interpretation of linkages and reduce uncertainties.

The ability to generate new biomonitoring data often exceeds the ability to meaningfully evaluate the source and pathway for exposure of a chemical, as well as how and if a chemical measured will pose a health risk to an individual or populations. Additionally, there are many challenges concerning biomonitoring, such as designing studies, interpreting what the data mean in terms of public health, and addressing ethical and communication issues. To address these elements, the National Research Council's (NRC) Committee on Human Biomonitoring for Environmental Toxicants published a report in July 2006 titled, *Human Biomonitoring for Environmental Chemicals* (NRC 2006). The report provides a reference guide for moving the field of biomonitoring forward from the design, to the conduct, to the reporting of biomonitoring results. The committee presents four research recommendations as follows:

1. Develop a coordinated strategy for biomarker development and population biomonitoring based on the potential for population exposure and public-health concerns.
2. Develop biomonitoring-based epidemiologic, toxicologic, and exposure-assessment investigations and public-health surveillance to interpret the risks posed by low-level exposure to environmental chemicals. Where possible, enhance existing exposure-assessment, epidemiologic, and toxicologic studies with biomonitoring to improve interpretation of results of such studies.
3. Advance individual, community, and population-based strategies for reporting results of biomonitoring studies.
4. Review the bioethical issues confronting the future of biomonitoring, including confidentiality, informed consent, reporting of results, and public-health or clinical follow up.

2.3 Session III: Perspectives on Science and Related Needs

The speakers in Session III focused on the use of biomonitoring data in risk assessments and the need for effective communication. Biomonitoring data can be used to provide exposure and risk information in order to inform public health decisions. Additionally, biomonitoring data could be used for screening purposes and prioritization of chemicals for further research or regulation. In order to effectively use biological data, researchers need to communicate the objectives when designing biomonitoring studies (e.g., analysis of trends, impact of mitigation strategies, contributing to risk assessment). In one example, biological testing was critical in directing the intervention efforts as a result of illegal pesticide application in the United States, and the early response resulted in removing the population, including the most vulnerable segment, from exposures.

Despite the fact that several data gaps exist in regards to interpreting biomonitoring data, this should not prevent the use of biomonitoring data in order to determine actions that are necessary to protect human health. Since there are still many data gaps in biomonitoring information, effective communication is critical. Public engagement has become an essential requirement for the advancement of science. Effectively engaging the public allows for more meaningful input, leads to better informed health/environmental decision-making, and results in greater understanding and acceptance of research studies, programs, and policies.

2.4 Looking Ahead: Translating Research Intent into Action

The closing session of the workshop looked towards the future. The scope of future biomonitoring activities includes supporting the design and evaluation of environmental health policy by focusing research on issues with the greatest impact to public health, defining population reference values for certain substances, and creating an early warning system for chemical risks. Additionally, as this field of science continues to evolve, biomonitoring will be increasingly requested and required for environmental health decision- and policy-making. For this reason, it is important to clearly define the scope of biomonitoring activities, to prioritize the issues to address, and to make uncertainties and limitations explicit. Finally, it is imperative to

establish a dialogue among all of the relevant stakeholders so that the advancement of biomonitoring is a coordinated effort that most effectively uses available resources.

3.0 BREAKOUT GROUP REPORTS

The breakout group discussions each focused on one of three topic areas: (1) links between exposure, dose, and human biomonitoring data, (2) computational tools and biomonitoring data, and (3) the design of toxicological studies. The goal of these discussions was to identify options for a research strategy that incorporates further research into and use of human biomonitoring data. Objectives, issues, and recommendations identified by the groups are summarized in the sections that follow.

3.1 Breakout Group 1: Exploration of the Link between Exposure, Dose, and Human Biomonitoring Data

This breakout session explored the link between external exposure, human biomonitoring data, internal exposure, and dose by addressing the charge questions presented in Exhibit 3. The focus was on understanding the types of data/information needed to interpret the relationship between biomonitoring data and external exposures, risk assessment, and ultimately risk management. Many health indices (e.g., reference dose (RfD), cancer risk) are in terms of external exposures. Insofar as we can relate biomonitoring data to external exposures, we can understand better the relationship between health risks to external exposures (e.g., is biomonitoring showing exposures above or below the RfD). Epidemiological studies are used to establish relationships between exposure and outcome measures, and may include a combination of environmental, biomonitoring, and questionnaire/survey data to assess exposures. These studies provide a direct link between levels measured in environmental and biological media and health outcomes, allowing for improved estimation of risks.

Exhibit 3
Breakout Group 1 Questions: Exploration of the Link between Exposure, Dose, and Human Biomonitoring Data

1. What are the characteristics of good biological markers of external and/or internal exposure?
2. How can we improve the designs of studies that collect/use biomonitoring (both exposure surveys and epidemiological studies)?
3. How can we better understand the linkages between biomonitoring and major sources of exposures?
4. What are major sources of uncertainty in linking biomonitoring results to external and internal exposures, and to sources?

3.1.1 Objectives of Breakout Group 1

The primary objective of this breakout group session was to identify (and to the extent possible, prioritize) research needs to relate human biomonitoring data to external exposures. This objective might be achieved by taking into consideration:

- Expanding or modifying the design of exposure studies (e.g., the National Human Exposure Assessment Survey (NHEXAS), the Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP) study) to address data needs for interpretation of biomonitoring data;
- Expanding or modifying the design of epidemiological studies to address data needs for interpretation of biomonitoring data; and
- Identifying other relevant linkages and research that will provide information and models needed to reduce uncertainties in the interpretation and use of biomonitoring data.

The focus of this session was on the interpretation of biomonitoring data relative to external and internal exposure, not health effects. The purpose was to look at the risk assessment paradigm from source to environment to exposure to dose and determine what additional information might be needed and used in combination with biomonitoring data to help identify the impact of sources (locations, pathways). The participants in this session considered the types of research studies that are needed to provide this information or that can help to identify/prioritize information that could address major sources of uncertainty in the interpretation and use of biomonitoring data.

3.1.2 Discussion of Breakout Group 1 Charge Questions

Breakout Group 1 identified and discussed the issues associated with biomonitoring data interpretation and its relationship to external exposures and risk assessment. The discussion centered on the four main charge questions, but also touched on broader issues that spanned the topics and disciplines.

Characteristics of good biological markers of exposure. In order to determine what characteristics are most essential for biological markers of exposure, the breakout group considered several criteria for collection and use of biomonitoring data, including the:

- Persistence of the chemical being measured;
- Time period represented or the timing of exposure vis-à-vis the time samples were collected;
- Sensitivity and specificity (relative to target chemicals);
- Characteristics of the analytical methods;
- Feasibility for collection/analysis; and
- Whether/how the data have been validated (e.g., efforts to evaluate whether and/or how biological measurements reflect the target chemical).

The answer of what characteristics determine a good marker of exposure is complex and depends on why the data are being collected. The researcher needs to ask what the biomonitoring data are being used for. The goal of the study and the paradigm that it fits under should be clearly identified upfront (e.g., will the data be used to make risk management decisions?). As part of this, the null hypothesis also needs to be defined whenever studies are undertaken.

Improving the design of studies. Several issues were discussed in relation to the improvement of study design. An initial concern was the identification of other types of information that should be collected to facilitate the interpretation of biomonitoring results relative to exposure and/or risk assessment, exposure/response relationships, and risk management. In order to design future studies, lessons learned from prior exposure and/or epidemiology studies (and their analyses), including those conducted in occupational settings, need to be considered. Also, additional information (e.g., efforts to "validate" biological measurements relative to target chemicals), may need to be collected to improve our ability to interpret biomonitoring results relative to external and internal exposure.

The group agreed that a key issue to the design of studies is how to effectively deal with variability – both in the exposures (inter- and intra-individuals), the population, and endpoints such as gender, age, population/race, diet, medication, and alternative medicines. Once biomonitoring measurements are taken outside of the occupational setting, the variability greatly increases. The design needs to balance the number of samples, number of subjects, and types of media (e.g., blood, hair) that should be measured with the objectives, resources, and other issues (e.g., ethics) surrounding the study.

Understanding the links to sources of exposures. In conjunction with better understanding the links to major sources, the group initially discussed how to use biomonitoring, in conjunction with other information, to reduce exposures. To understand this issue, the group discussed what other information and/or assumptions would be needed to relate biomonitoring results to important media and pathways contributing to exposures. Some of the considerations included kinetics/metabolism, personal behaviors relative to exposure and uptake, timing and types of exposures (e.g., intermittent vs. continuous), and locations and environmental concentrations (measured, unmeasured). The group agreed that pharmacokinetics can help with understanding the linkages and is a very useful tool.

Major sources of uncertainty. Some of the issues related to uncertainty that were briefly discussed included whether uncertainty could be addressed and reduced through additional information collected during study, the use of more specific/relevant information (factors, assumptions) about the population, and/or improvements in models and analytical approaches.

The group discussed studying target tissue levels as a possible means to reduce uncertainty when linking biomonitoring results to external and internal exposures and to sources. To do this, target tissue levels should be collected concurrently with available exposure information (e.g., diet, blood and/or urine samples). In addition, the formation of adducts (e.g., for organophosphates) could be studied to help reduce uncertainty when looking at exposure to parent compounds versus their metabolites.

3.1.3 Recommendations from Breakout Group 1

Based on the issues the group identified earlier in the discussion, Breakout Group 1 generated the following list of recommendations, in approximate order of priority:

- **Integration of pharmacokinetics**. To better predict and/or characterize exposures and sources, pharmacokinetics should be integrated with other approaches that are currently used, such as statistical and PBPK modeling.
- **Characterization of population exposures**. Biomonitoring data can be used to better characterize population exposures in epidemiological studies. This can be done in several ways. For example, following the definition in the null hypothesis of where and/or why biomonitoring creates "value," researchers could create a library of case examples. Biomonitoring data can also be used instead of traditional approaches to better define exposed versus non-exposed populations. In addition, effects biomarkers can be used as a reflection of the extent to which relevant mechanistic understanding exists.
- **Biomonitoring guidance values**. Develop additional guidance values beyond those effect/risk indicators (e.g., RfDs, cancer unit risks) that we have and formulate a consistent process for their development. Guidance values are important in that they provide context for biomonitoring measurements (e.g., what do the levels mean?).
- **Improved methods**. Develop better methods (in terms of specificity, sensitivity, and reliability) for some key chemicals. When methods are developed or revised, they should indicate where "multiple monitoring" is appropriate (i.e., monitoring for more than one substance using the same method) and keep specificity in mind (e.g., some methods measure metabolites that are a result of the body's metabolism of a parent chemical exposure plus the same degradation product that occurs in environmental media and does not represent exposure to the parent chemical). Also, there was general recognition among the group that biomonitoring methods that are not invasive are preferred.
- **Library of research and results**. Compile a library of past, recent/current or planned biomonitoring research and results. This will enable the research and regulatory community to assess what we have learned already in the field of biomonitoring from measurement techniques to interpretation to applications. In this area there may be potential for pooled or meta analyses. This type of research, which is not data collection like some of the other ideas proposed, is very important to ensure that future work is not duplicated unnecessarily, key gaps in information are identified, and research can be prioritized based on current knowledge and needs. The group acknowledged that while this information would ideally be very useful, it would also be a very costly and time-intensive endeavor.
- **Library of analytical methods**. Similar to the library of research results, it would also be useful to compile a library of validated analytical methods or standards. This library would be a repository or reference collection similar to CDC or NIOSH libraries, but for all existing and emerging new compounds.

- **Pathway analysis**. There can be many pathways between emissions and exposure. For example, a person may be exposed to a pesticide via a food pathway, a surface-to-hand pathway, or an air pathway. Pathways are very important if biomonitoring data are to be correctly interpreted and used to mitigate exposure (e.g., by reducing exposure via the pathway resulting in the greatest dose). For environmental exposures, we often don't know the pathway(s) or sources. In some cases, lifetime accumulation may be a source (e.g., remobilization from body fat or bones). And in most cases, information on bioavailability is often lacking.
- **Collection protocols**. Create model protocols for human biomonitoring collection as part of the study design, including when and how often to collect. Protocols should also consider whether it is more advantageous to collect multiple biomarkers or multiple samples when resources are limited. When developing basic validity protocols, it is essential to ensure the wider availability of biomonitoring standards.
- **Identify exposed groups and trends**. Make better use of biomonitoring data to identify exposed groups, especially those who are highly exposed, and determine trends. When determining groups or trends, it is important to consider the impacts of interventions, such as those laid out by human subject committees in the Stockholm Convention or the U.S.-equivalent Common Rule (NRC 2004). Also, improved guidance on study power, size, and variability will be crucial.
- **Sharing of chemical use information**. There is a need to share chemical use information. Better sharing of information, such as product use registers and time diary databases, will help to break down the barriers of institutional ownership, highlight the gaps in current biomonitoring data, and promote research that will improve the science and understanding of biomonitoring data and its interpretation.

In addition to these recommendations, the group identified several related considerations that include some overarching issues. For example, researchers should adopt or follow the guidance that already exists for biomonitoring data collection (e.g., through the International Programme on Chemical Safety). Similarly, all involved parties should make an effort to cooperate better internationally (e.g., OECD initiatives). And finally, there is a need to recognize that biomonitoring research needs often differ between scientific research applications and policy implementation, and this should be kept in mind when developing a strategy for research.

3.2 Breakout Group 2: Computational Tools and Biomonitoring Data

This breakout session explored how available computational tools (e.g., PBPK modeling) can be used to relate human biomonitoring data to measures of external (environmental) and internal (target tissue) exposure/dose both in human and animal studies by addressing the charge questions presented in Exhibit 4. The focus was on describing the requirements for meaningful applications of computational models to characterize the exposures that would be consistent with measured biomonitoring data, to estimate target tissue dosimetry for comparison with animal dosimetry, to evaluate biomarkers used in human biomonitoring studies, and to address the impact of variability in both exposures and receptors.

Exhibit 4
Breakout Group 2 Questions: Computational Tools and Biomonitoring Data

1. What are the kinds of data/parameters needed for the computational tools identified – at the population, study, and individual chemical levels?
2. How can we use PBPK and other models to assist in the design of biomonitoring studies?
3. How can we use PBPK and other models to assist in the design of toxicology studies?
4. How can modeling relate measures of internal exposure (e.g., biomonitoring data on blood or urine concentrations of a chemical or stable metabolite) to measures of target tissue dose (e.g., amount metabolized in the target tissue) in both humans and bioassay animals?
5. What data should be collected in biomonitoring studies to be able to consider multiple chemicals/mixtures or cumulative exposure?
6. How can PBPK/PD models be used, in conjunction with biomonitoring data, to either verify or falsify alleged cumulative or synergistic effects of combined exposure to substances with a similar pharmacological effect?
7. How do we foster a continuing dialogue between modelers, toxicologists, and those who collect biomonitoring data so that the needs of all groups are met/considered?
8. Can we identify key areas for evaluation based on lessons learned from PBPK modeling when going forward to examine biomarkers of interaction (e.g., hemoglobin adducts) and biomarkers of effect (e.g., acetylcholinesterase inhibition)?
9. How can modeling assist a risk assessment paradigm based on internal biomarker versus external dose?

3.2.1 Objectives of Breakout Group 2

The primary objective of this breakout group was to identify (and to the extent possible, prioritize) research needs to provide better quantitative interpretation of human population biomonitoring data. To achieve this objective, efforts will likely be needed in:

- Identifying the various available computational modeling tools that could be applied in the interpretation of biomonitoring data (e.g., PBPK modeling, environmental exposure modeling, empirical dosimetry, Monte Carlo analysis), discussing the capabilities and limitations of each, and recommending approaches for evaluating their region of applicability.

- Identifying data needs to evaluate and expand the applicability of PBPK and other models for interpretation of human biomonitoring data, considering issues such as,
    - Animal to human extrapolation (target tissue dosimetry)
    - Human to animal extrapolation (exposure/dose comparisons)
    - Characteristics of biomarkers used in human biomonitoring studies
    - Exposure variability
    - Sampling variability
    - Inter-individual pharmacokinetic variability
    - Life-stage-specific exposures
- Identifying deficiencies in biomonitoring studies that hinder the interpretation of the resulting data, and recommending approaches to improve them.
- Identifying deficiencies in animal toxicity studies that hinder the interpretations of human biomonitoring data and recommend approaches to improve them.
- Identifying lessons learned from PBPK modeling of biomarkers of exposure that can inform the development and use of biomarkers of interaction (e.g., adduct data) and biomarkers of effect (e.g., genomic response).

3.2.2 Discussion of Breakout Group 2 Charge Questions

This breakout group identified and discussed the issues associated with biomonitoring data interpretation and its relationship to external exposures and risk assessment. More specifically, the discussion centered on the need to develop additional methodology that would allow for a better understanding of the relationship between biomarkers of exposure and biomarkers of effect, and their subsequent relationship to adverse health outcomes. The group noted that there is a general lack of knowledge regarding the significance of biomarkers, and the detection of a compound in the body doesn't always indicate the presence of a risk.

The discussion focused on the identification of existing computational tools, and how available computational tools can be used to relate biomonitoring data to external measures, and internal exposure/dose in human and animal toxicity studies. The group identified the following existing computational tools:

- PBPK models. The group noted that PBPK models are useful, but tend to be data intensive. Moreover, data are not available for many chemicals of interest. For example, according to the NRC there are only approximately 25 of 148 chemicals on the CDC Exposure Report list that have "consensus" toxicity data (e.g., RfDs, cancer unit risks). Additionally, the group indicated that a mechanism to rationally prioritize chemicals for further PBPK development is necessary and suggested the use of Quantitative Structure Property Relationship (QSPR) models.

- "Simple" models. The group discussed the use of "simple" models as an alternative model that can be used to screen/evaluate large numbers of chemicals similar to the pharmaceutical industry experience that looks at hazard identification and Quantitative Structure Activity Relationships (QSAR).
- Bioinformatics (and multi-factorial analyses). The group indicated that bioinformatics and other multi-factorial analyses are useful tool(s) to link environmental information with internal dose. However, the field is still developing and there is a need to need to learn more about these techniques for specific application.
- Distributional analysis (e.g., Monte Carlo simulations)
- Exposure pathway analysis

The breakout group then suggested that determining the necessary approach (e.g., epidemiologically-based models, forward dosimetry, reverse dosimetry, exposure analysis) will dictate what data are needed and identify which computational tool should be utilized.

Additionally, the group identified several key information needs that should be addressed for chemicals to allow for the prioritization of chemicals according to their public health impact. Obtaining this data would also result in the continued development and effective implementation of computational tools with biomonitoring and toxicology data. Biomonitoring studies and the use of computational tools for interpretation of data could be improved with additional research into the effect of "timing." This research would include obtaining knowledge regarding the half life of various chemicals in the body, the persistence of chemicals in relevant medium (external and internal), the persistence of biomarkers of response, the exposure frequency/duration, and the timing of sampling (i.e., how sampling relates to potential exposures and whether there is variability due to multiple timeframes). Additionally, there is a need for validation of computational tools in human subjects, with special attention focused on choosing the appropriate analyte, measuring the concentrations in the appropriate medium, and relating the dose to target tissues. Toxicology studies and the use of computational tools for the interpretation of data could be improved by considering biomarkers of exposure and effects and the toxicology of mixtures, conducting additional research into the effect of timing on toxicological results, obtaining data on chemical co-existence in the environment, developing/using alternatives to animal testing, and incorporating the use of "omics."

3.2.3 Recommendations from Breakout Group 2

Based on the issues the group identified earlier in the discussion, Breakout Group 2 generated the following list of recommendations regarding research priorities:

- **Case Studies**. Developing case studies on the interpretation of biomonitoring data based on existing health data/guidelines is imperative to demonstrate the appropriate approach to take.
- **Alternatives to PBPK Modeling**. Deriving alternatives to the "gold standard" PBPK modeling is needed. This will depend on the desired approach for a study (e.g., epidemiologically-based models, forward dosimetry, reverse dosimetry, exposure

analysis). Alternative screening-level approaches (e.g., single compartment models, correlations) that are less intensive than PBPK models should be explored for the purpose of addressing large numbers of chemicals in a timely manner or identifying priority chemicals.

- **Human PK Data**. Approaches/methods for obtaining (realistic) human PK data rapidly on chemicals for use in PBPK modeling (e.g., microdosing, non-invasive methods) should be derived.
- **QSPR/QSAR Approaches**. Quantitative methods, such as QSAR and QSPR, are based on the assumption that biological activity is correlated with a chemical's structure or properties. Consequently, biological activity can be modeled as a function of a chemical's physiochemical properties. The breakout group recommended using QSPR approaches for developing human models and human kinetic data for various chemicals and QSAR approaches for potentially obtaining potency information on new chemicals.
- **Modeler Involvement**. Computational modelers should be involved early in the research process to determine the appropriate analyte and medium to be used in a specific biomonitoring study, which would make interpretation of biomonitoring data as straightforward as possible.
- **Template Human PK Descriptions**. There are several classes of chemicals that have little or no PK data available. Currently, there are PBPK models for only a few chemicals, mostly for volatiles, ethers, and organophosphorus pesticides. Template descriptions could help guide modelers regarding what PK information would be most helpful for different classes of chemicals.
- **Focused Proof of Concept Analyses**. Additional focused proof of concept analyses should be used to apply advanced statistical methods and other novel computational approaches (e.g., combine spatial statistical and mechanistic models) to interpret biomonitoring data and environmental data and public health information.

In addition to these recommendations, the group identified considerations that include some overarching issues. For example, researchers should create protocols or guidance for identifying appropriate chemical parameters and addressing multiple values for "basic" data. Additionally, researchers should recognize that the field of bioinformatics is evolving and there is a need to determine best practice for the application of bioinformatics in biomonitoring.

3.3 Breakout Group 3: Relevance of human biomonitoring data to the design of toxicological studies

This breakout session addressed how human biomonitoring data can better inform design of animal toxicology studies and improve our ability to extrapolate effects in animals to human biomonitoring data by addressing the charge questions presented in Exhibit 5.

3.3.1 Objectives of Breakout Group 3

The primary objective of this breakout group session was to identify (and to the extent possible, prioritize) research needs to relate better human biomonitoring data to toxicology studies. In addition, other objectives included:

- To identify how human biomonitoring data can best inform design of animal studies.
- To identify how animal toxicology studies can help improve the design, sampling strategies, and interpretation of human biomonitoring studies.
- Identify information or endpoints useful for further development and enhancement of PBPK models.

Exhibit 5
Breakout Group 3 Questions: Relevance of Human Biomonitoring Data to the Design of Toxicological Studies

1. Can routine toxicology studies (e.g., 90-day studies, 2-year bioassays, 2-generation reproduction studies) be modified to collect pharmacokinetic data that provides improved links to human biomonitoring data, e.g., collection of internal dose estimates of parent compound or relevant metabolite(s)? What are barriers to collection of such data and how can they be overcome? What research is necessary to support implementation of such data collection? What are the implications of new animal sampling approaches for future standardized pharmacokinetic guidelines?
2. Can internal dose evaluations be linked to human risk assessments (e.g., refined approaches for evaluating Margin of Exposure estimations between animal toxicity studies and results from human biomonitoring evaluations)?
3. Can animal test models be used to refine sampling strategies for human biomonitoring studies, particularly for short and intermediate half-life substances?
4. Can animal toxicology studies be used to refine approaches to “reverse dosimetry” approaches for defining potential human exposures from biomonitoring evaluations? Can potential external dose exposures be estimated from biomonitoring samples? And, vice versa, can potential “internal dose” estimates be derived from external biomonitoring samples (e.g., urine, hair, saliva)?
5. Can animal toxicology studies be used to evaluate potential for age, genetic variation, disease presence, etc. on potential confounders for interpretation of human biomonitoring studies?
6. Can human biomonitoring findings facilitate improved design of toxicology studies (e.g., selection of appropriate study doses and/or most relevant animal species)?

3.3.2 Discussion of Breakout Group 3

This breakout group addressed how human biomonitoring data can better inform design of animal toxicology studies and improve the ability to extrapolate from animals to humans. They agreed that toxicology studies can and should be modified to collect PK data to provide improved links to human biomonitoring data. The group noted linking toxicology studies to biomonitoring data has the following advantages:

- The ability to develop Margin of Exposure (MOE) comparisons based on internal dose (animal)/internal dose (human) ratios, which will help reduce uncertainties in human health risk assessments.
- Such comparisons are made routinely in pharmaceutical assessments.
- Animal toxicology studies are important in the development of biomarkers for chemical exposure and are a first step in the identification of potential biomarkers and of the conditions under which they can be used.
- Animal studies are also a necessary step for the biomonitoring of substances for which human volunteer studies are considered by some to be unethical.
- Collecting data in this way is easier than reconstructing the administered dose.
- Data might be more valuable for public health communications than for risk assessment, but social research may be necessary to determine whether the message is helpful.

The group cited the following challenges for modifying toxicology studies to collect PK data and linking them to human biomonitoring data:

- Pharmacokinetic samples must be collected without compromising results of core toxicity evaluations (e.g., for rats, no more than three samples over 24-hour period).
- Regulatory guidelines for absorption, distribution, metabolism, and elimination (ADME) studies encourage oral gavage pharmacokinetic evaluations. There are existing oral gavage toxicology data that need to be supported by gavage ADME studies, but to the extent more recent toxicology tests involve other exposure routes (e.g., dietary, drinking water, inhalation), ADME data should be collected under the same conditions as the bioassay.
- Real-world exposure varies greatly over time, but dose is constant in toxicology studies. The role of time must be reconsidered in toxicology. Additional shorter-term studies may be needed depending on anticipated exposure scenarios. Also, the timing of the collection of biological samples must be evaluated (e.g., when is the time to reach max excretion).
- Diet can impact metabolite excretion (e.g., observed quantitative impact of fiber diet comparable to differences due to enzyme polymorphism).
- Information on mechanism and dynamics (e.g., “resident effect” versus “damage/repair”) and kinetics (e.g., rapid elimination, slow, accumulation) is necessary because

interpretation of biomonitoring data will differ for classes of chemicals that vary in these parameters.

- Additional information is necessary regarding animal-to-human extrapolation:
  - Need to confirm that the animal's metabolic profile is relevant to humans.
  - Humans typically ingest food more intermittently than rodents and human diets are extremely heterogeneous.
  - There is still uncertainty for human susceptibility if direct animal-human comparisons of area-under-the-curves (AUCs) are made.
  - Ironically, urine is easier to collect from humans but not animals, while blood is easier to collect from animals, but not humans.
- With human-to-human extrapolation, polymorphisms and exposure factors need to be considered. For example, a study of styrene found occupational effects observed due to short intense exposures, even though biomonitoring data showed workers were consistent with "background" non-worker populations.
- A general lack of knowledge about mixtures and how they interact in the body and with each other and effect human health is also an issue.
- There is an overarching concern that it that it takes so much study (resources) to understand just one or two chemicals.

3.3.3 Recommendations from Breakout Group 3

Based on the issues the group identified earlier in the discussion, Breakout Group 3 generated the following list of recommendations:

- **Design of Studies**. Animal and human studies need to be designed and conducted to address the impacts of fundamental differences between species dosimetry and dose rates on the interpretation of biomonitoring data. The significance of these differences needs to be quantified. Occupational monitoring can support these studies. Some specific suggestions included:
  - Encouraging the collection of dosimetry data when animal studies are conducted. High quality data sets of both PK and toxicology will contribute greatly to the interpretation of biomonitoring data.
  - Following all ethical guidelines (e.g., Common Rule or its international equivalents, NRC 2004), encouraging human volunteer PBPK case studies as a bridge between biomonitoring data and toxicology. The studies will be necessary to make progress on improving the interpretation of biomonitoring data.
  - Developing better models or methods for estimating anticipated human exposure, so that this information can be used to design laboratory animal studies with realistic dose levels and conditions (time, route, dose rate). The design of toxicology studies needs to consider also whether the peak concentration or the AUC is important for a chemical. Research is needed to improve or develop guidance for study design that addresses all of these concerns/challenges.

- ***In Vitro* Metabolism Screens**. Early assessment *in vitro* metabolism screens with animal and human hepatocytes should be encouraged because they will provide information on the metabolic relevance of different animal models to humans, support selection of relevant metabolites to measure, and inform cross species extrapolation. *In vitro* screening and QSAR for tissue distribution pose opportunities for research because 1) it isn't known how applicable currently-available *in vitro* tissue distribution models are for non-volatile organic compounds, and 2) cross-species models for predicting urinary excretion have not yet been developed. Therefore, there is a need to evaluate whether PK models can predict urine outputs (or from urine data to blood).
- **Tiered Framework for PK Data Collection**. A tiered framework should be developed for PK data collection for chemicals depending on toxicology screening results. More routine PK testing should be conducted during initial screens and then more refined PK evaluations if concerns are found and more specific tests are conducted. Perhaps short half-life chemicals could be the focus, given that persistent bioaccumulative chemicals are already studied extensively.
- **Update of OECD Guideline for ADME Studies**. Efforts to update the OECD guideline for ADME studies to promote the collection of dosimetry data under the exposure conditions of animal bioassays should be encouraged. EPA is the lead organization for this effort. Similarly, toxicology studies should be designed to take into account anticipated/potential exposure scenarios/patterns. For example, it is unknown whether rodents' "grazing" ingestion patterns result in internal doses that will be useful for evaluating human episodic ingestion exposures.
- **Refinement of Risk Assessment Process**. Methods for using internal dose implications for refinement of risk assessment should be derived. Additionally, national/international risk assessment methods to encourage use of dosimetry comparisons in risk assessment should be refined. Research is also needed to describe how best to make internal dose comparisons.

- **Case Studies**. Working through a case study (or a small number of case studies) on relatively data rich substances would help to identify and sort out the best characteristics to select and prioritize substances for the type of additional research needs.

In addition to these recommendations, the group identified some secondary recommendations. For example, researchers should consider studying natural chemicals (e.g., methyl eugenol). Such compounds may provide data more relevant to humans, and support testable hypotheses for assessments of other chemicals. Additionally, approaches for addressing biomonitoring data for chemicals that have complex metabolic pathways should be developed. Furthermore, it would be beneficial to explore the role of "non-routine" toxicological studies (e.g., study of transgenic animals) to evaluate susceptible sub-populations. Finally, researchers should consider using the "duplicate diets" approach used in epidemiologic studies, but administer human diet samples to laboratory animals and measure biomarkers to see if they produce the same metabolites.

4.0 References

European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC). 2005. Guidance for the Interpretation of Biomonitoring Data. Document number 44. November 30, 2005.

National Research Council (NRC). 2006. Human Biomonitoring for Environmental Chemicals. NRC Committee on Human Biomonitoring for Environmental Toxicants. July 2006.

NRC 2004. Intentional Human Dosing Studies for EPA Regulatory Purposes: Scientific and Ethical Issues. NRC Committee on the Use of Third Party Toxicity Research with Human Research Participants. Science, Technology, and Law Program. Policy and Global Affairs Division. Washington, DC: The National Academies Press.

APPENDIX A: ICCA BIOMONITORING WORKSHOP FINAL AGENDA

Wednesday, July 26

7:00 – 8:00 AM	Registration and Continental Breakfast Room: Winter Garden
8:00 – 8:15 AM	Welcome Room: Great Hall • **Judy Graham**, American Chemistry Council • **Dick Phillips**, ExxonMobil
8:15 – 8:30 AM	Workshop Objectives and Expectation of Outcome Room: Great Hall • **Colin Humphris**, Cefic (European Chemical Industry Council)
Plenary Session I: Overview of Recent Efforts to Improve the Understanding of Biomonitoring Data	
8:30 – 10:00 AM	Activities of the International Life Science Institute Health and Sciences Institute (ILSI/HESI) Biomonitoring Committee, National Research Council (NRC) Committee on Human Biomonitoring, European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC), and Japan Chemical Industries Association (JCIA) (30 min each, including Q&A) Room: Great Hall *Session Chair:* **Rick Becker**, American Chemistry Council • **Steve Robison**, Procter & Gamble • **Peter Boogaard**, Shell • **Akira Fukushima**, Lion Corporation
10:00 – 10:30 AM	**Break** (Posters will be available/attended for viewing in the Winter Garden)
Plenary Session II: Policy and Decision-Making Perspective	
10:30 – 12:30 PM	The Perceived Added Value on Risk Assessment and Policy (30 min each, including Q&A) Room: Great Hall *Session Chair:* **Tina Bahadori**, American Chemistry Council • **George Gray**, US Environmental Protection Agency • **Tom Burke**, Johns Hopkins University and Chair of NRC Committee on Human Biomonitoring • **Doug Haines**, Health Canada • **John Cocker**, UK Health and Safety Laboratory
12:30 – 1:30 PM	**Lunch** Room: Winter Garden

Breakout Group Discussions

1:30 – 1:45 PM	Setting the Stage for the Breakout Sessions and Introduction of Breakout Session Leads and Rapporteurs Room: Great Hall • **Dick Phillips**, ExxonMobil
1:45 – 5:00 PM (15-20 min Break at 3:15 PM)	Session 1: Exploration of the Link between Exposure, Dose, and Human Biomonitoring Data Room: Great Hall *Lead*: **Jim Quackenboss**, US Environmental Protection Agency *Speakers*: • **Marsha Morgan**, US Environmental Protection Agency • **Tye Arbuckle**, Health Canada • **Lesley Onyon**, International Programme on Chemical Safety
	Session 2: Computational Tools and Biomonitoring Data Room: Rink/Promenade *Lead:* **Harvey Clewell**, CIIT Centers for Health Research *Speakers*: • **Peter Farmer**, University of Leicester • **Sean Hays**, Summit Toxicology • **Tom McKone**, Lawrence Berkeley National Lab
	Session 3: Design of Toxicological Studies Room: AJ Earling *Lead*: **Jim Bus**, Dow *Speakers*: • **Jim Bus**, Dow • **Kim Travis,** Syngenta • **Claude Viau,** University of Montreal
6:00 – 7:00 PM	**Reception and Poster Viewing** Room: Winter Garden
7:00 – 9:00 PM	**Group Dinner** Room: Great Hall

Thursday, July 27

7:00 – 8:00 AM	**Continental Breakfast** Room: Winter Garden
8:00 – 8:20 AM	Human Biomonitoring Data—Industry Perspective Room: Great Hall • **Myron Harrison**, ExxonMobil

Plenary Session III: Perspectives on Science and Related Needs

8:20 – 10:20 AM	How Biomonitoring Data Are Actually (or Should Be) Used (30 min. each, including Q&A) Room: Great Hall *Session Chair:* **Bruce Caswell**, Canadian Chemical Producers' Association • **Larry Needham**, Centers for Disease Control and Prevention • **Sharyle Patton**, Commonweal • **Bette Meek**, Health Canada • **Joan Scott**, Johns Hopkins University
10:20 – 10:45 AM	**Break** Room: Winter Garden

Breakout Session Reports

10:45 – 12:15 PM	Session Reports and Recommendations (30 min. each) Room: Great Hall *Session C*hair: **Chris Money**, ExxonMobil ➢ Session 1: Exploration of the Link Between Exposure, Dose, and Human Biomonitoring Data • *Rapporteur:* **Chris Money**, ExxonMobil • *Recorder:* **Rebecca Kauffman**, ICF International ➢ Session 2: Computational Tools and Biomonitoring Data • *Rapporteur:* **Annette Guiseppi-Elie**, Dupont • *Recorder:* **Ami Parekh**, ICF International ➢ Session 3: Design of Toxicological Studies • *Rapporteur:* **Bob Krieger**, University of California - Riverside • *Recorder:* **Kimberly Osborn**, ICF International

12:15 – 1:15 PM	**Lunch** Room: Winter Garden
1:15 – 2:15 PM	Breakout Sessions Reconvene ➢ Session 1: Exploration of the Link Between Exposure, Dose, and Human Biomonitoring Data Room: Great Hall ➢ Session 2: Computational Tools and Biomonitoring Data Room: Rink/Promenade ➢ Session 3: Design of Toxicological Studies Room: AJ Earling
2:15 – 3:15 PM	Breakout Sessions: Report on Final Prioritized Recommendations (15 min each) Room: Great Hall
Looking Ahead	
3:15 – 4:00 PM	Translating Research Intent into Action (20 min. each, including Q&A) Room: Great Hall *Session Chair*: **Carol Henry**, American Chemistry Council • **Roberto Bertollini**, World Health Organization • **Phil Lewis**, Rohm & Haas

APPENDIX B: POSTER PRESENTATIONS

Principal Investigator	Affiliation	Title
Stuart Batterman	University of Michigan, U.S.	Design and Evaluation of a New Breath Monitoring System for Volatile Organic Compounds
Deborah Bennett	University of California – Davis, U.S.	Influence of Basements, Garages, and Common Hallways on Indoor Residential VOC Concentrations
		Contribution to Total Personal Exposure of VOCs from Shopping and Dining Microenvironments
Karen Brown	The Biocentre, Cancer Biomarkers and Prevention Group, University of Leicester, UK	Measurement of Endogenous and Exogenously Derived N7-(2-hydroxyethyl)-2'-Deoxyguanosine Adducts in Ethylene Oxide Treated Rats using LC-MS/MS
John Cocker	Health & Safety Laboratories, Buxton, UK	Analysis of Inter and Intra-Individual Variation in Key Biomarkers of Chemical Exposure Within the General Population
Noel Cressie	Ohio State University, U.S.	From Sources to Biomarkers: A Hierarchical Bayesian Approach for Human Exposure Modeling
Warren Foster	McMaster University, Canada	Serum Levels of Perfluorinated Compounds in Human Maternal and Umbilical Cord Blood Samples
Seymour Garte	University of Medicine and Dentistry of New Jersey, U.S.	Lack of Benzene Induced Hematoxicity in Bulgarian Petrochemical Workers with Exposures Below 1 ppm
		Benzene Genotoxicity and Metabolism in Humans is Strongly Affected by Genotype at Loci Involved with Metabolic Pathways
Panos Georgopoulos	Computational Chemodynamics Laboratory at EOHSI, U.S.	Modeling Exposures to VOCs through the Individual-Based Exposure Modeling Implementation of MENTOR/SHEDS-1A
Marek Jakubowski	Nofar Institute of Occupational Medicine, Lodz, Poland	Kinetics of Urinary Excretion of Unchanged Volatile Organic Compounds
Len Levy	Institute of Environment and Health, Cranfield University, UK	Key Biomarkers of Chemical Exposure within the UK General Population – Background Levels in a Pilot Study
Leena Nylander-French	University of North Carolina-Chapel Hill, U.S.	Biomarkers of Exposure to Hexamethylene Diisocyanate
James Quackenboss	Environmental Protection Agency, U.S.	Exposure Assessment for the National Children's Study: Integrating Biomonitoring with Environmental Measures

Principal Investigator	Affiliation	Title
Miles Okino	Environmental Protection Agency, U.S.	Urinary Biomarker Interpretation using Pharmacokinetic Models
Stephen Rappaport	University of North Carolina-Chapel Hill, U.S.	Statistical Methods for Evaluating Exposure-Biomarker Relationships
Louise Ryan	Harvard School of Public Health, U.S.	Biomarker analysis using Structural Equations Models (SEMs)
Greet Schoeters	VITO (Flemish Institute for Technological Research), Belgium	Human Biomonitoring in Different Areas of Flanders, Integration of Biomarkers of Exposure with Biological Effect Data
		Intra- and Inter-individual Variations in Key Biomarkers within the General Population