

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

Interpretation of Human Biomonitoring Data: A Research Strategy



INTERNATIONAL
COUNCIL OF
CHEMICAL
ASSOCIATIONS

1. ICCA Global LRI Strategy and Biomonitoring

The *ICCA LRI Global Research Strategy* was approved by ICCA in October 2004. The ultimate goal of the LRI is to increase knowledge of the potential impacts that chemicals may have on the health of human and wildlife populations and the environment. The strategy recognized the growing global complexity of many of the issues the industry will face and sought to respond to this to move beyond coordination of regional activities to:

- Plan LRI activities on a global basis, thereby deepening the coordination, whilst continuing to carry out the bulk of the programs regionally;
- Link these global activities more closely to the ICCA priorities and in particular the execution of the Global Product Strategy and communications strategy;
- Execute global programs on topics for which there is a consensus and endorsement from the ICCA-LRI Steering Committee;
- Build rapport and dialogue with global agencies (e.g., WHO, OECD, UNEP) to ensure the industry is effectively addressing global concerns; and
- Provide a framework to which the industries of other countries or regions could contribute.

A pilot study on Biomonitoring was approved, with two initial implementation steps.

An industry meeting was held in Paris in June 2005 to review the Biomonitoring “issue” from the perspectives of:

- Product Stewardship, and the need for a responsible industry to understand the risks to health posed by the presence of environmental levels of chemicals in people;
- Advocacy, relating to the use of biomonitoring data within public health policy;
- Communication, to reassure and address public concerns over biomonitoring results; and
- Science gaps, in particular the difficulty of interpreting the presence of low levels of chemicals in terms of health risks. Health risk assessment is absolutely key to underpinning future product stewardship, advocacy and communications activity.

In September 2005, the ICCA LRI Steering Committee approved a science workshop to define a research agenda for ICCA LRI. This workshop was held in July 2006 against the backdrop of significant recent reviews of the needs for better risk interpretation of Biomonitoring data from the US National Academy of Sciences (presented to Congress), ECETOC and ILSI/HESI.

2. The Need and Scope for Industry Action

Identifying, controlling, and preventing population exposures to potentially hazardous agents in the environment are core parts of public health policy. Biomonitoring techniques which detect chemicals, or biomarkers for chemicals, are seen as very valuable in many regions of the world for monitoring exposure trends and assessing the effectiveness of public health interventions (e.g., monitoring blood lead levels following the removal of lead from gasoline). Governments are investing heavily in such monitoring and surveillance programs (US CDC, EC – SCALE) which are their primary interest. The industry can expect ever more data collection which will undoubtedly raise more questions, concerns, and uncertainties. CDC for instance is expanding their 2007 biomonitoring report to include 300 chemicals with the intention of measuring even more in the future.

Moving beyond surveillance to interpreting risk from Biomonitoring data poses fundamental challenges:

- There are very few reference levels against which to define what is normal or what is safe, and no agreed framework for when reference levels should be defined and how. Also occupational thresholds have limited relevance to chronic exposures at lower environmentally relevant levels.
- The detection of chemicals at very low levels (below 1ppb) is subject to poorly understood degrees of uncertainty and variability and highly demanding of analytical quality control and experimental design. Detection at 10^{-21} g/g was reported at the meeting – small numbers of molecules.
- There are very few chemicals for which the data exists for risk interpretation, exposure, pharmacokinetic, toxicological, or epidemiological data linking an internal dose to health response are rarely available

- The measurements are in people and carry with them deeply personal emotions and ethical concerns.
- The political environment for chemicals legislation is volatile and the fledgling science of risk interpretation of biomonitoring data is emerging at a time of contentious policy debate and potential litigation (chemical trespass).

These challenges frame neatly the issues ICCA will face increasingly as it pursues its commitments for Responsible Care® and the Global Product Strategy (GPS). The LRI meets Objective 7 of the GPS, which calls for constructive participation in scientific inquiry to address health and environmental issues and to improve product stewardship. As such, ICCA has expressed support for biomonitoring as an evolving approach to obtain exposure information. The industry has also committed to work with the scientific community and governments to develop the scientific foundation for risk-based decision making and to promoting the sciences and methodologies needed to interpret biomonitoring in a risk-based process. **Therefore, industry's role is to give a lead, to stimulate investment in the science to interpret biomonitoring data from a risk**

and health impact perspective, and to engage effectively with national and international agencies to promote this work and their involvement.

These issues are being recognized by others. The US National Academies report notes; *"The ability to generate new biomonitoring data often exceeds the ability to evaluate whether and how a chemical measured in an individual or population may cause a health risk or to evaluate pathways for exposure."* It goes on; *"The challenge for public health officials is to understand the health implications of the biomonitoring data, to provide the public with appropriate information, and to craft appropriate public-health responses."*

Given this growing public health interest, the time is therefore right for coordinated ICCA action and leadership. The Science workshop was a good example of this. ICCA LRI successfully achieved engagement with national and global agencies, industry, academia, and NGOs to build a measure of consensus on research priorities.

3. The Biomonitoring Research Agenda

The workshop in Minneapolis aimed to facilitate development of a coordinated research agenda 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. 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 progress such research, and to review the capacity and skills available to progress the topic and identify how improved networking across stakeholders could serve to further improve resources.

The workshop focused on three primary areas for which research is needed to close the significant gap between biomonitoring data and external exposures, and which the ICCA LRI may be able to address. Highlights of the recommendations been abstracted below from a report of the workshop (being prepared for publication).

- **Linkages between biomonitoring data, external exposures, and dose:** This area focuses on collecting the types of data needed to interpret the relationship between biomonitoring data and external exposures, risk assessment, and ultimately risk management. It will aim to improve methods to characterize biological markers of exposures, collect relevant and concurrent multi-pathway exposure information, and better characterize human behaviours, activities and other factors that influence exposures.
- **Computation methods to relate measured concentrations to dose and to exposure for use in risk assessment:** This area focuses on how available computational tools (e.g., physiologically based pharmacokinetic modelling) can be used to relate human biomonitoring data to measures of external (environmental) and internal (target tissue) exposure/dose in the animals exposed in toxicity studies. Meaningful applications of computational models will be developed 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.
- **Relevance of human biomonitoring data to improved design of toxicological studies:** This area focuses on improving the design of traditional toxicological studies to enhance interpretation of human biomonitoring studies. It will aim to improve methods to collect relevant pharmacokinetic data during toxicology studies (e.g., 90-day studies, 2-year bioassays, 2-generation reproduction studies), to provide improved links to human biomonitoring data (e.g., collection of internal dose estimates of parent compound or relevant metabolite(s)), and to develop methods to link internal dose to human risk assessments (e.g., refined approaches for evaluating margin-of-exposure estimations between animal toxicity studies and results from human biomonitoring evaluations.)

Existing LRI commitments in the three regions to date equate to an investment of \$6.5 million. This work addresses:

- A global database of biomarker developments;
- What constitutes normal levels of synthetic and natural chemicals, including phytoestrogens; and
- Biomarker methodologies, health significance and statistical techniques.

The ICCA Biomonitoring pilot project will build on these regional activities, and we anticipate the need to step up investment over the next 5 years to approximately \$15 million targeted within the priority areas. Specific expenditures will be justified through the current regional research calls for proposals and related processes. This level of expenditure should be seen in the context of governments investing hundreds of millions in research programmes for biomonitoring data collection in US and Europe, but with virtually no effort to interpret such data exists. **The industry investment is therefore intended to be not only affordable within current projected LRI activity, but material enough to give the lead to governments and other agencies to devote more resources to data interpretation.**

4. Biomonitoring Pilot Project Action Plan

After endorsement by the ICCA LRI Steering Committee and the Board, with information to the ICCA Steering Committee, the Action Plan envisages a number of steps by the ICCA LRI Planning Group:

- a. Development of a detailed, coherent research agenda for industry built on the Minneapolis proceedings;
- b. Review of regional priorities and opportunities for specific engagement with regional and global agencies;
- c. Agreement of the focus of each regional LRI programme, with each region issuing calls for proposals starting in late 2006/2007;
- d. Establishment of a global project monitoring and tracking process for ICCA with suitable linkage to GPS; and
- e. Maintaining a series of public workshops over the next five years (~\$130K or €100K /workshop). These will complement and coordinate the implementation of the regional biomonitoring research programs, build on the engagement with the public authorities already achieved, keep the industry's commitment increasingly in the public eye, and provide a leadership forum.

ICCA LRI Planning Group
18th September 2006

The ICCA LRI Biomonitoring Strategy was endorsed by the ICCA LRI Steering Committee and ICCA Board in their September 2006 meetings.