

Limitations and Uncertainties of Biomonitoring Surveys Conducted With Small Populations

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Biomonitoring, the measurement of environmental chemicals in human tissues and body fluids, can provide useful data for estimating environmental exposures to naturally occurring and synthetic chemicals. The U.S. Centers for Disease Control and Prevention (CDC) has collected biomonitoring data in conjunction with the National Health and Nutrition Survey (NHANES) to determine both population exposures to various chemical substances and national exposure trends, and to judge whether public health interventions have been successful in reducing exposures to toxicants, such as lead and secondary smoke.¹

The CDC National Reports on Human Exposure to Environmental Chemicals have increased public awareness and concern that various environmental chemical substances can be found in body fluids (blood and urine) and tissues throughout the U.S. population. However, there should be no cause for alarm since the very low levels reported by the CDC are not necessarily synonymous with adverse health consequences. CDC has emphasized in the July 2005 Report that the mere detection of a chemical substance in urine or blood should not be misinterpreted to indicate a health risk or potential disease in individuals or the U.S. population.

“...for many environmental chemicals, we need more research to assess health risks from different blood or urine levels. The results shown in the *Third Report* should help prioritize and foster research on human health risks that result from exposure to environmental chemicals...the presence of a chemical does not imply disease. The levels or concentrations of the chemical are more important determinants of the relation to disease, when established in appropriate research studies, than the detection or presence of a chemical.”

Assessment of biomonitoring results can be used to evaluate prior exposures but the study design, study conduct and data analyses must adhere to rigorous scientific standards in order to evaluate potential health implications. When evaluating human biomonitoring investigations and reports, it is also important to consider the extent to which these meet scientific standards of practice.

Following is a list of many, but not all, of the critical elements needed for a scientifically sound biomonitoring investigation.

Minimum requirements for a scientifically credible biomonitoring study

1. Includes a clear statement of objectives
2. Provides an overview of the state of knowledge in relation to the study objectives
3. Lists those factors affecting levels and groups that might have different exposure levels
4. Plans for communication to study participants, stakeholders and the general public on state of knowledge and what the study can and what it cannot determine
5. Utilizes a sample size that has substantially similar characteristics to the target population and sufficient statistical power for detecting differences
6. Employs and documents use of validated sampling procedures and validated analytical methods and adherence to appropriate laboratory quality assurance and quality control programs
7. Presents all, not a selective listing, of the results
8. Uses appropriate statistical analyses and provides a balanced interpretation of the data, indicating strengths and weaknesses of the study
9. Subjects findings to an independent peer-review before the results are published

The July 25, 2006 National Academy of Sciences (NAS) National Research Council (NRC) Committee on Human Biomonitoring for Environmental Toxicants report “Human Biomonitoring for Environmental Chemicals” extensively evaluates the state of the science and provides recommendations for study design, data interpretation, communications and research needs to advance the field

The NAS has concluded that

“The ability to generate new biomonitoring data often exceeds the ability to evaluate whether and how a chemical measured in a population may cause a health risk or to evaluate its sources and pathways for exposure.”

The NAS also cautioned that not all biomonitoring surveys should be equated to the CDC NHANES evaluations.

“Because not all biomonitoring studies are conducted with the same rigor, it is important that the guidelines presented be followed to ensure, to the extent possible, that biomonitoring studies will lead to the identification of chemicals that are causing risk or health effects, will provide information on exposure pathways and health effects to guide future control efforts and will avoid anxiety or apathy about chemicals where personal or societal risks appear not to warrant that reaction.”

Table 3.1 page 54 of the NAS Report outlines a continuum of risk assessment and management activities related to exposure biomonitoring comprised of four key elements:

- Scoping: screening; exploratory investigations; source investigations and societal-hazard identifications

- Status and Trends: exposure surveillance; population research; pathway research; decision validation and health surveillance
- Exposure: epidemiology research; toxicological research; pharmacokinetic and pharmacodynamic research and community and occupational investigations
- Risk Assessment: population risk characterizations; clinical applications and individuals risk characterizations.

Some non-governmental biomonitoring surveys may be so limited in design that they do not meet any of the NAS risk assessment continuum criteria^{3, 4, 5, 6} or have been conducted on such a small scale so as to only meet the specifications for a scoping study. The NAS has stated that for biomonitoring, scoping is a basic activity that “may provide the first indication of a potential problem.” Thus, by their very nature, most small-scale studies cannot provide scientifically meaningful, quantitative data on trends, epidemiology or conclusions about health risks.

Small sample size and non-random selection of biomonitoring survey participants also precludes the possibility of making scientifically supportable, unbiased comparisons among various subpopulations. Potential confounding factors, such as age, weight, diet, health issues, work place, and genetic factors should be considered when assessing environmental exposures.

The detection of a chemical, or its metabolites in urine or blood, however, is not a stand-alone means to evaluate individual or population risk. Scoping generally only determines whether a chemical is detected in the biomonitoring sample but not what it means. Conversely, the presence of other more toxic substances, either natural or synthetic, may be overlooked because they were not analyzed. Few, if any, small-scale biomonitoring surveys of this type will meet the NAS standards for use in trends, epidemiology or health risk assessment. Moreover, interpreting the results from small biomonitoring surveys directly to population risk assessment skips over key exposure analyses. It is important to both consider and integrate all the available data from animal toxicology studies, epidemiology, pharmacokinetics (how a chemical substance is absorbed, metabolized and eliminated from animals and humans) and genetic factors that are essential to determining the significance of exposures.

The NAS also identified ethical considerations and communications, interpretations and use, as high priorities. The protocols and study designs of biomonitoring surveys, involving any number of participants, should undergo evaluation by Institutional Review Boards (IRBs) before the studies are initiated (at the design stage). Biomonitoring survey results should be independently peer-reviewed before reports are either published or made public. Since human subjects are involved, it is essential that scientifically responsible and clear reports be issued that explain the results to the public. Failure to take into account the ethical issues of communicating biomonitoring data in the context of public health risk may raise undue concerns and fear in study volunteers and the public.

To summarize, biomonitoring is an important tool that can be applied to better understand exposures to chemicals in our environment. The recommendations in the July 2006 NAS report provide comprehensive scientific and ethical guidance to conduct and interpret biomonitoring surveys and to communicate their result. Small-scale biomonitoring surveys, that do not follow the NAS guidance, often cannot reach scientifically valid conclusions because they may involve too few individuals and lack scientifically robust study designs.

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