

COUNCIL OF STATE AND TERRITORIAL EPIDEMIOLOGISTS

BIOMONITORING IN PUBLIC HEALTH:

Epidemiologic Guidance for State, Local,
and Tribal Public Health Agencies



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ABOUT THESE GUIDELINES

In March 2010, the Association of Public Health Laboratories (APHL) requested assistance from the Council of State and Territorial Epidemiologists (CSTE) in building a national state-based biomonitoring system. APHL recognized that an effective national biomonitoring system requires a variety of skills and expertise and an infrastructure beyond those of the laboratory. These include epidemiologic aspects of conducting biomonitoring activities, such as study design, sample collection, and data analysis, and interpreting and communicating results.

These guidelines were developed collaboratively by a subcommittee of the CSTE Occupational and Environmental Health Committee in response to APHL's request. The subcommittee brought together state epidemiologists who have a broad range of biomonitoring experiences, from conducting projects to designing state programs.

The guidelines are intended to assist with biomonitoring activities, sometimes referred to as "programs" if they are ongoing and "studies," "projects" or "investigations" if they are episodic. These activities may be conducted for ongoing surveillance, epidemiologic investigation, and rapid response to protect public health. They are not intended to describe hypothesis-based research typically conducted by academic institutions. Epidemiologists, laboratorians, environmental health specialists, and others in state, territorial, tribal, and local health agencies may find these guidelines helpful in implementing biomonitoring programs and projects to inform public health decision making and actions.

INTRODUCTION

The Centers for Disease Control and Prevention (CDC) defines biomonitoring as the direct measurement of chemical contaminants in human specimens. The ability of public health laboratories to use biomonitoring to assess human exposure to environmental chemicals has steadily advanced during the past 30 years. Today, through its National Biomonitoring Program, the CDC Environmental Health Laboratory monitors on a regular basis (every two years) the US population's exposure to an increasing number of chemicals (currently more than 300). As public health laboratory scientists have developed and validated new analytical methods to measure internal doses of chemicals, the numbers of health research studies and public health or epidemiologic investigations that include biomonitoring have correspondingly accelerated. Research institutions now incorporate biomonitoring into major epidemiologic studies. For example, biomonitoring is a major component of the National Institute of Child Health and Human Development's National Children's Study.

However, state, territorial, tribal, and local public health agencies are just beginning to apply biomonitoring information and technology to environmental public health practice and disease prevention. The National Health and Nutrition Examination Survey (NHANES), which is used to collect specimens for the National Biomonitoring Program, does not allow for state- or local-level calculations of population exposure estimates. Yet, local concerns about chemical exposures continue to fuel public interest in biomonitoring, and some state legislatures have adopted legislation [1] to encourage or require state agencies to conduct biomonitoring at the state and local levels. As researchers and communities learn more about biomonitoring, the demand for this exposure measurement tool in public health settings is expected to grow.

In 2002, CDC began to fund planning and implementation grants to build biomonitoring capacity in state public health laboratories. In 2009, three states (California, New York, and Washington) were awarded funds to increase biomonitoring capability and capacity in their public health laboratories. This support will enhance the capability and capacity of these states to assess human exposure to environmental chemicals within their jurisdictions.

Biomonitoring in a public health context poses a number of challenges. These include study design and implementation, as well as ethical concerns, and unique methodologic issues that have yet to be fully appreciated. Understanding public perceptions and developing effective methods for communicating and interpreting results remain areas of interest and active research. According to the National Research Council's Committee on Human Biomonitoring for Environmental Toxicants, one of the greatest challenges "for public health agencies is to understand the health implications of the biomonitoring data and to craft appropriate public health responses" [2].

INTRODUCTION

These guidelines provide information about and help to guide decisions by public health officials and scientists about the design, conduct, interpretation, and application of biomonitoring activities. They address the major components for planning and implementing biomonitoring in a public health setting, including engaging stakeholders, developing protocols, addressing ethical considerations, selecting biomarkers, collecting biospecimens and other data, analyzing and displaying data, interpreting and communicating results, and using the findings to support public health action. A checklist of the key steps to developing a biomonitoring program or project appears at the end of this document (Appendix III). Along with state partners, CSTE hopes to build a foundation for biomonitoring that is scientifically rigorous, has broad public acceptance and support, and ultimately will best enable crafting appropriate public health responses to potential health effects of chemicals in our environment and our bodies.

PLANNING A BIOMONITORING PROJECT OR PROGRAM



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Setting priorities and uniform policies *a priori* is essential to guide planning decisions for biomonitoring programs and projects. Statutory authority may dictate many elements of a public health biomonitoring program. Other essential elements to consider during planning include establishing program goals and objectives; selecting the target population and chemical analytes; establishing methods for collecting biospecimens and epidemiologic and other data; identifying stakeholders and partners; engaging the community; developing a protocol; and addressing ethical considerations.

State Statutes, Administrative Rules, Legislative Directives, Funding Sources

State health departments have broad and powerful authority to protect the health of citizens. Building a biomonitoring program requires full use of these existing statutory authorities. Establishment of a public health biomonitoring program might begin with specific legislative directives. Although legislated bills include specific directives, more general directives, followed by development of administrative rules to guide implementation, are preferable; administrative rules are more easily modified than legislation if changes are needed. In general, a biomonitoring program will have a greater chance of succeeding if the administrative foundation builds on the existing public health and laboratory program structure and experience. Existing administrative rules for similar programs and activities can be used as templates for developing a successful biomonitoring program.

Legislation must be accompanied by dedicated and stable funding to ensure the sustainability of state and local public health biomonitoring programs. In the absence of adequate resources allocated in legislation, competitive applications may be submitted to organizations that support biomonitoring, such as CDC (National

Center for Environmental Health, Agency for Toxic Substances and Disease Registry), the National Institutes of Health (National Institute of Environmental Health Sciences), and nongovernment foundations.

Most states have mandatory disease reporting rules that may already include reporting of diseases that consider environmental chemical biomarkers (e.g., lead poisoning, pesticide poisoning, carbon monoxide poisoning). If these rules are comprehensive they can be a convenient means to require laboratories and health-care systems to report biomonitoring results. Even with enabling rules, however, ensuring consistent reporting from health-care entities is often labor intensive. Strategies to encourage more complete reporting include adding broad definitions for reportable conditions (e.g., “chemical exposures,” “suspected pesticide illness”) and requiring clinical laboratories to report targeted analytes (e.g., blood lead; measures of pesticide exposure, such as metabolites or other related tests). Adding broadly defined reporting requirements can authorize programs to obtain results already being collected by parties outside public health departments that would otherwise be protected from release by federal requirements, such as the Health Insurance Portability and Accountability Act (HIPAA).

Other programs might generate “remainder” biologic specimens that could be useful for biomonitoring. Examples include newborn screening requirements, maternal screening during pregnancy, childhood lead testing, and blood alcohol testing from persons involved in fatal highway incidents. It is imperative to understand the ethical, legal, potential social concerns, and scientific restrictions associated with programs that generate samples when considering the use of remainder specimens. Although their use seems cost efficient, the sensitivities associated with sample generation and use could make utilization impractical [3].

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Establishment of Goals and Objectives

As with any public health activity or program, the goals and objectives of biomonitoring programs and projects provide direction for planning the study design, data analysis, and results communication and thus must be clearly articulated. It is critical to note that goals and objectives are determined by the statutory authority under which the work is performed and by restrictions imposed by funding agencies.

The goals of a biomonitoring project can be broad or specific. For example, the broad goals of the NHANES Chemical Supplement are to conduct ongoing assessments of the US population's exposure to environmental chemicals by using biomonitoring methods (www.cdc.gov/exposurereport/) [4]. Specific goals include investigating chemical exposures in a specific community or population identified as at risk for exposure or evaluating worker exposures to chemicals at a specific worksite. Goals for other projects might be to develop or test particular laboratory methods for chemical analyses or to evaluate the efficiency and/or impact of an environmental health policy.

The public health goals of biomonitoring include the following:

- **Targeted Investigations:** Biomonitoring can be an investigative tool for measuring population exposures in response to a community health concern or discovery of chemical contamination. The community under investigation could be defined by geography or some other shared characteristic, such as occupation. The goals for targeted investigation could be to determine whether and to what extent a community is exposed and whether public health actions are needed to prevent exposure and protect health. For example, the purpose of the East Metro PFC Biomonitoring Study, conducted by the Minnesota Department of Public Health, was

to measure exposure to [perfluorochemicals](http://www.health.state.mn.us/biomonitoring) (PFCs) in adults living in a community where the drinking water is contaminated with PFCs (<http://www.health.state.mn.us/biomonitoring>) [5].

- **Population Surveillance:** The surveillance goals of biomonitoring are to monitor population exposures over time and space, identify exposure disparities and at-risk individuals and populations, and evaluate the progress and efficacy of public health actions aimed at reducing exposures. For example, the NHANES Chemical Supplement biomonitorers selected chemicals in blood, serum, and urine samples from random subsamples of participants from the larger NHANES program (www.cdc.gov/exposurereport/). The data are used to establish a reference population (or baseline) and to identify differences in the distribution of exposure across age, sex, and race/ethnicity. NHANES documented the dramatic decline in the US population's blood lead levels that corresponded with the removal of lead in gasoline. When gathered for surveillance purposes, biomonitoring data may be integrated with state environmental monitoring and disease surveillance data to evaluate and mitigate the sources of exposure in the environment.

- **Rapid Response:** Biomonitoring can be part of rapid response to identify or confirm acute chemical exposures after an uncontrolled chemical release or other type of incident. Chemical exposures that require rapid response can occur through ingestion of contaminated food, uncontrolled releases to air and water, or chemical spills at work or in the community. In these instances, biomonitoring can be part of clinical evaluation of exposed persons for medical diagnosis and treatment, and public health agencies can collaborate with medical providers in accordance with established emergency response plans. For example, in

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response to a mercury spill in a school, the Massachusetts Department of Public Health conducted biomonitoring to provide assurance that children were not exposed at a level of health concern [6].

- **Resource for Research:** Although research is not generally a goal of public health practice, biomonitoring data and specimens collected by public health agencies might in some circumstances become an appropriate resource for research. Projects that begin as non-research could lead to substantive research questions that require a shift in project direction. Review and approval by Institutional Review Boards (IRBs) are required for research projects for the protection of human subjects. IRB review of projects with a public health focus may be sought to ensure that participants are treated ethically [7,8]. If research projects are anticipated in advance, the consent form may be able to adequately address prospective activities, such as the archiving of residual specimens for future projects. Local community preferences, standards and practices of the public health agency and appropriate IRB, and federal, state, and local laws will guide decisions on whether to include in the project research components such as the use of specimens to support the development of analytical methods in the laboratory or sharing of data and specimens with external investigators.

Selection of Target Population

The purpose of a biomonitoring project ultimately will determine the study design, which includes identification and selection of the target population. Factors to consider when choosing the population to be biomonitoring include:

- Purpose of project or program
- Population at risk for exposure and potential adverse health effects

- Ethical factors, such as age and ability to consent
- Resources required to access appropriate population
- Availability of an appropriate sampling frame

Depending on the study's purpose, goals, and objectives, the most appropriate study population might be the general population; vulnerable groups for adverse health effects, such as children, pregnant women, or elderly persons; or groups most likely to have higher exposure levels, such as sport and subsistence fishers and some occupational groups. The chemical exposures of interest, and whether biomonitoring will address past or only current/recent and ongoing exposures, should also be considered during selection of the study population. In some instances, existing biologic samples gathered as part of other programs or projects might be appropriate for study. In others, the population of interest may be studied only by gathering new samples and acquiring risk factor, exposure, and other information from personal interviews and/or questionnaires.

A critical planning consideration is choosing biological reference values that are appropriate for the study population as these are necessary for accurate interpretation of biomonitoring results and fulfilling the goals of the study. Demographic characteristics of the study population will dictate the choices for the reference population. For example, for a biomonitoring study in pregnant women, if reference ranges are available only for non-pregnant adults, the study planners could consider including a comparison ("unexposed") pregnant population as part of the sampling scheme for the project.

Finally, it is important to note that the choice of a study population may introduce ethical issues. Biomonitoring projects that limit the study population, for example by using existing samples collected as part of another study,

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may raise concerns regarding the project's lack of inclusiveness. As with any other public health program, the purpose of the study determines the populations for biomonitoring. By choosing appropriate methods for participant selection, planners can ensure that the study does not exclude people because of sex, age, race, ethnicity, language, culture, geography, socioeconomic status or other characteristics (See Ethical Considerations below).

Selection of Chemical Analytes

The purpose of the program, the target population, community concerns, local exposure factors, laboratory capability, resources, and considerations of feasibility and burden to participants are among the factors determining which analytes (or biomarkers) a biomonitoring program or project will include. The purpose of a project might be to collect biological specimens for a single chemical (for example, blood lead surveillance in children or working adults) or multiple chemicals (for example, the NHANES Chemical Supplement). Analyte selection during the planning phase will involve all partners (including epidemiologists, laboratorians, and toxicologists) and include general analyte selection considerations:

- **Sensitivity:** A sensitive limit of detection (LOD) or method detection limit (MDL) will measure lower levels of chemicals. Lower MDLs are often required to compare background or environmental exposure levels of an analyte with levels anticipated to occur from occupational exposure or community exposure to a known point source of contamination.
- **Specificity:** The analyte may indicate exposure to a class of chemicals or be specific to the chemical(s) of interest. This distinction is important to consider during planning if one of the intentions is to elucidate potential

pathways and sources of exposure. Certain metabolites may be common to several parent compounds. For example, 3-phenoxybenzoic acid (3-PBA) is a metabolite common to several pyrethroid insecticides, some of which are more commonly found in food, while others are usually found in residential-use pesticides. Furthermore, metabolites that are also environmental degradates can obfuscate interpretation of results. For example, both the environmental degradation of the insecticides chlorpyrifos and chlorpyrifos-methyl as well as human metabolism results in formation of the metabolite 3,5,6-trichloro-2-pyridinol (TCPy). By merely measuring TCPy in urine, exposures to chlorpyrifos, chlorpyrifos-methyl, or TCPy itself cannot be distinguished..

- **Practicality/Feasibility:** Factors relevant to selecting analytes include costs, laboratory precision and accuracy, ease of collection (e.g., 24-hour urine versus spot sample), invasiveness (e.g., blood versus urine/hair), volume of sample needed for analysis (which could preclude inclusion of children or other subgroups of interest), and stability of the compound. To ensure the integrity of laboratory analyses, it is important to consult with technical experts in specimen collection, handling, and laboratory methods. Involving the participating community will help to ensure that the sample collection plan complies with ethical and practical constraints, particularly if invasive sampling (e.g., drawing blood) or vulnerable subpopulations are included. As a practical consideration, samples collected noninvasively (e.g., urine) might have substantially lower collection costs, fewer risks to participants, and increased participation rates.
- **Results Interpretation:** The availability of reference ranges should be considered in the selection of analytes and sample media. Few clinical values exist to guide interpretation of biomarker levels; the best known examples

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are the guidelines for blood lead. In the absence of clinical comparison values, results can be compared with a reference range (e.g., those established by the NHANES Chemical Supplement or one that is specific to the study population). In order to make valid statistical comparisons, the reference population should be comparable with, and representative of, the study population. In some cases, risk-based interpretive approaches are also possible utilizing established dose-response relationships developed from epidemiology studies, experimental studies, and/or pharmacokinetic modeling. If biomonitoring is conducted on an emerging contaminant with no reference values, careful and honest discourse with the community and planning before implementation of the biomonitoring initiative is essential.

- **Pharmacokinetics:** Factors affecting the half-life, absorption, distribution, metabolism, and excretion of an analyte are key, practical considerations for choosing a biomarker. Pharmacokinetics also affects the choice of the matrix (e.g., whole blood, serum, or urine) and dictates sample management (e.g., analyte stability and storage temperatures).

Levels of substances with short half-lives (hours to days) can be difficult to interpret from a single collection, as they indicate exposures shortly before the sample was obtained. However, biomarkers of chemicals with short half-lives still can be reliably interpreted from a single collection if exposures are expected to be continuous or ongoing rather than intermittent. Thus, knowing how concentrations vary over time within the same person is useful.

Levels of chemicals with long half-lives (months to years) can be detected years after exposure. It is useful to collect information about factors that can affect interindividual variability in pharmacokinetics (e.g., age; body build; health

status; concurrent exposures; recent pregnancy or breastfeeding; and recent rapid weight change [for lipophilic chemicals]) as they may also impact biomarker concentrations.

- **Health Relevance:** If the purpose of analyte collection is to explore the association between internal dose or body burden with an adverse health effect, investigators must select analytes specific to the health outcome of interest. One must also consider whether the analyte has been measured at the appropriate time, during the critical life stage of interest, and characteristics of the disease's induction and latency period.

Other factors to consider when selecting analytes for public health biomonitoring projects include:

- Laboratory capability (the ability to reliably analyze levels of chemicals or metabolites)
- Laboratory capacity (the number of samples the laboratory is able to analyze)
- Anticipated prevalence of exposure in the target population at a level that is detectable
- Whether the chemicals are a priority concern for the public health jurisdiction (this may include such factors as the potential health effects and number of people potentially exposed)
- The public health benefits of biomonitoring
- Toxicity of the chemical/biologic relevance
- Ability to control excessive exposure

Planning for Collection of Biospecimens

During the project's planning or design phase, appropriate laboratory staff should participate in discussions about proper selection of biomarkers, biospecimens, and collection procedures that are in accordance with the specific purpose and goals of the project.

Collection procedures, storage, handling, and transport conditions affect analytical results and interpretation. Adequate protocols and quality

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Table 1. Biospecimen matrices, procedures, and relevant stages of life*

COLLECTION		STAGES OF LIFE					
Matrices	Procedure	Invasive Yes/No	Fetal Period	Delivery	Children 0-5 years old	Children 5-18 years old	Adults
Blood	Venipuncture or prick	Y	–	–	+	+	+
Cord blood	Drained into sterile container from cord after delivery	N	–	+	–	–	–
Urine	Collection cups or diapers	N	–	–	+	+	+
Saliva	Sterile plastic pipette or specially prepared cotton swab	N	–	–	+	+	+
Expired air	Spirometer attachment	N	–	–	+	+	+
Hair	In container after cut or falling out	N	–	–	+	+	+
Fingernails	Clippings in sterile container	N	–	–	+	+	+
Teeth	Collected in sterile container after loss or extraction	N	–	–	+	+	+
Meconium	Collected from diapers	N	–	+	–	–	–
Amniotic fluid	Amniocentesis (mother)	Y	+	–	–	–	–
Adipose tissue	Biopsy or postmortem collection	Y	–	–	+	+	+
Bone marrow	Spinal tap	Y	–	–	+	+	+
Breast milk	Breast pump	N	–	–	–	–	+
Semen	Cup	N	–	–	–	–	+
Feces	Container	N	–	–	–	–	+

*From the National Research Council, National Academies of Science. Table 4.2. In: *Human biomonitoring for environmental chemicals*. Washington, DC: National Academies Press; 2006:112.

assurance and control for biospecimen collection, storage, handling, and transport must be defined, tested, and finalized during the planning phase to maximize biospecimen integrity and prevent field contamination. Depending on the specific biomonitoring project, biospecimens can be collected expressly for a defined project or as an add-on to a current project or retrieved through an existing archive of previously collected biospecimens. For the latter, knowing whether biospecimens were collected and archived in a manner that ensures their integrity and

minimizes contamination, breakdown, or loss of the chemicals of interest is critical. Assessing whether the volume of stored biospecimens is adequate for desired analytical tests is another consideration during the planning phase.

The matrix (e.g., urine, serum, whole blood, or blood spot) for biospecimen collection should be selected during the planning phase. The appropriate matrix is determined by the pharmacokinetics of the chemical, validity of the method, and feasibility of collecting the specimens.

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A suggested sequence of planning steps relevant to biospecimen collection follows.

1. Determine the chemical analyte desired and the relevant biomatrix.
2. Confer with laboratory colleagues regarding the volume of biospecimens required for specific analyses and about collection materials, procedures, handling, storage, transport, and analytical cost.
3. Determine relative ranking of the chemical analyses by biomatrix in case the collected specimen is inadequate for all the desired tests.
4. Generate specimen collection diagram or flowchart (Appendix 1).

Planning for Other Data-Collection Activities and Instruments

Biological monitoring accounts for the uptake and metabolism of a chemical from all exposure sources and by all exposure routes. Many individual host factors can affect this uptake and metabolism. For example, genetic and demographic factors influence uptake and metabolism (as well as absorption and excretion), whereas dietary habits, use of consumer products, and cultural behaviors influence exposure. Data interpretation will need to take into account the timing of biospecimen gathering and the collection of other data. For example, whether environmental sampling or questionnaire administration occurs at the same time as biosample collection or separately will influence the interpretation of results. Depending on the purpose of the program, these activities or instruments can supplement biomonitoring to capture information about potential exposure sources and host factors. For example, questionnaires may be designed to gather information about timing or frequency of exposure (e.g., use of personal care products, food and beverage intake, cleaning habits, pesticide application). Environmental samples, such as dust or water, may contribute useful

information about exposure pathways and sources. Investigators can collect additional information by linking to previously collected data, such as administrative and health records and geographically coded datasets.

Unmeasured covariates (potential sources of exposure that are not measured) are of particular concern in biomonitoring when the most readily available and feasible biomarker is not specific to a particular exposure source. For example, a current proposed biomarker for exposure to disinfection by-products (DBPs) in drinking water is trichloroacetic acid (TCAA). TCAA can be measured in urine, but its presence in drinking water is not the sole determinant of biomonitored levels. Individual behaviors, including the amount of water consumed at home and elsewhere and swimming in chlorinated pools can affect exposure to DBPs that would be measured by TCAA levels. Additional sources of exposure, such as dry cleaners and gas stations, may also increase exposure to volatile organic compounds that could affect TCAA levels in urine. Careful consideration of the impact of these additional exposure determinants and the validity and specificity of the selected biomarker is needed to properly interpret measured levels and communicate biomonitoring results.

Additional data that are useful to consider as part of biomonitoring projects include the following:

- **Surveys:** Biomonitoring studies commonly include survey information from participants who provide biological samples. As in other types of epidemiologic studies, use of a self- or interviewer-administered questionnaire or interview depends on the complexity of the questions, factors related to balancing accuracy and efficiency, and privacy concerns (for example, adolescents will answer drug-use questions more honestly in a self-administered format than in an interview). Because exposures might occur at the household level (e.g.,

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through residential pesticide use), investigators need to determine whether a household, individual, or combination questionnaire is most appropriate. Using questions that have been validated by others can help ensure data accuracy. However, not all questions that have been used in other studies have been adequately assessed for reliability and validity. Interview questions should be selected that account for the timing of biospecimen collection relative to pharmacokinetics and/or the timing of exposure. For example, spot urine samples of bisphenol A reflect only exposure during the previous 4–6 hours [9].

- **Demographics:** As in most epidemiologic studies, information about age, sex, income, education, and race/ethnicity may be collected as part of biomonitoring projects through questionnaires or interviews. Even though demographic information might be useful for determining exposure conditions, it more commonly serves as a marker for individual or cultural covariates that cannot be measured directly and provides information about whether environmental risks are shared equally across groups. Since age and gender often affect exposure levels and potential for adverse health effects, information about these covariates is needed for proper data analysis. This information is also helpful for comparisons with known clinical values or reference ranges. Use of standard definitions and metrics facilitates comparisons across jurisdictions and with other studies, such as the NHANES Chemical Supplement.

- **Diet:** Investigators often are interested in knowing what people eat and drink because samples obtained for biological monitoring can reflect dietary habits and intake. Dietary information is most commonly collected by questionnaire as a food frequency, 24-hour recall, or diet diary. For some chemicals, diet

is the major source of exposure among the general population. However, obtaining valid information about dietary intake is complex and is best accomplished in consultation with epidemiologists, toxicologist, nutritionists, and others with expertise in physiologic pathways and collection of dietary data. To gather information over the correct time period, investigators must understand the pharmacokinetics of the chemical of interest in relation to the biological matrix in which the chemical is measured. For example, because arsenic passes through the body relatively quickly, it is appropriate to collect dietary intake information over the past 2 or 3 days. In contrast, lipophilic compounds, such as dioxins, accumulate in fatty tissues over years, and biomonitoring levels could represent historical, rather than current, dietary exposures. Similarly, levels of metals in urine could represent relatively recent dietary exposures, but the same metals in hair might represent diet (or other) exposures from a more distant period.

- **Administrative Records:** In certain instances, data can be collected from administrative records, such as medical or employment records. Use of administrative datasets generally is most meaningful when the biological specimen is collected for the same general purpose as the administrative records. For example, employment health records may be considered when biomonitoring in an occupational setting. Investigators should collaborate with the organization that collects the information to determine whether legal or regulatory constraints exist on the organization's ability to release data and, if so, whether these constraints can be addressed through such procedures as IRB review.

- **Geographic Factors:** For potential exposures that are geographically determined and for

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which location information (e.g., residential address or census block) is available, it may be efficient to link participant location to datasets with potential exposure information, especially when self-report is likely to be inaccurate or incomplete. For example, geographically based pesticide use data could be linked to residential location when biomonitoring for pesticide metabolites. Demographic information may also be accessed in this manner. For example, if asking participants about their income is not feasible, information from the American Community Survey on area-based poverty levels could be used to characterize participants based on their areas of residence. For geographically-based exposures, area-based demographic measures may be more pertinent than individual-level data.

- **Environmental and nonhuman biological samples:** Levels of contaminants in the indoor and outdoor environments in conjunction with biomonitoring can offer information relevant to potential sources of internal exposure. Timing of sample collection is crucial with respect to persistence of the contaminant in the environment or nonhuman biological sample. For example, a metal will either remain in the surface soil or migrate downward, depending on the soil type and the specific metal; surface soil sampling will not detect a metal that is more likely to be found in subsurface soils. Isolating chemicals in water and air can be more problematic, given the movement of contaminants through these media. Although some contaminants persist in their original form, others break down or change as they react with other substances or are metabolized by living organisms. Selecting the correct environmental medium, plant, or other living organism for sampling is complex and requires the same rigor as collecting the human biological sample to ensure the integrity of the sample from field collection

through laboratory analysis. Thus, as for human samples, investigators may need to consult with toxicologists, laboratory personnel and other experts to develop protocols for collecting, processing, and transmitting the sample to the laboratory; laboratory handling of the sample; and maintaining a chain of custody and quality assurance procedures.

Identification of Stakeholders and Partners

The success of a biomonitoring project/program depends on support from individuals and organizations outside the agencies or departments conducting the activities. Therefore, partners and stakeholders need to be defined and identified early in the planning phase to establish decision-making processes, form organizational structures, and aid in setting and managing expectations.

DEFINITIONS, ROLES, AND RESPONSIBILITIES

A **stakeholder** is an individual, group of individuals, or organization whose interests are affected by decisions about the biomonitoring project/program of interest. Possible stakeholders include the following:

- Study participants and their families
- Community members, leaders, and organizations
- Health-care professionals
- Local and state elected officials, policy makers;
- Local or state health departments and other public health programs (e.g., offices of multicultural health, children's health, nutrition, breastfeeding programs)
- Collaborators of local or state health departments
- Regulatory agencies (e.g., environmental, occupational)
- Industry groups or parties responsible for pollution

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- Health, environmental, and environmental justice advocacy groups
- Academic researchers and the wider public health community
- News media

Stakeholders are most likely to be interested in day-to-day details of the project/program only as they directly affect them or their organizations. They might want to be informed or consulted about overarching themes and strategies but not be involved in the execution of activities.

A **partner** is an individual, group of individuals, or organization who shares responsibility for making decisions and conducting the day-to-day work of the biomonitoring project/program. They will be heavily invested in the protocol and overarching themes, strategies, and design. Possible partners include the following:

- Chemists from the analyzing laboratories
- Toxicologists
- Health care providers and medical consultants
- Health educators and communicators
- Representatives of the community

The design and work of the project/program determines whether a person, group, or organization is a stakeholder or a partner; for example, a community can be either or both. Funding allotment also helps distinguish stakeholders from partners. Because a partner has responsibilities in completing the project, a proportional amount of funding will be allocated for those responsibilities. On the other hand, a stakeholder's much smaller degree of responsibility still will be reflected in funding allotment. However, stakeholders will be personally or financially invested in the project results; thus, their interests must be considered carefully during planning.

COMMUNICATION BETWEEN GROUPS

Communication with partners will be much more frequent and detailed than communication with

stakeholders. Some stakeholders will want to provide input on specific issues or aspects of the project; others simply will want to remain informed of project progress and results. Thus, the method(s) and frequency of communication should be addressed and tailored to the specific individual or group before the project/program activities begin.

Community Engagement [10]

Public engagement and participation provide an avenue for health departments and communities to exchange information, resources, and knowledge. The “varying degrees of community and health department involvement, decision-making and control” depend on the purpose, goals, and resources available for community engagement [11]. These factors, combined with the considerable complexities and uncertainties of biomonitoring data, make consideration of community engagement necessary throughout a biomonitoring study.

GOALS OF COMMUNITY ENGAGEMENT

Overall project/program goals will influence activities for and scope of community engagement. For example, California's biomonitoring program has broad goals: to determine levels of environmental chemicals in a representative sample of the state's population, establish trends in the levels of these chemicals over time, and help assess the effectiveness of public health efforts and regulatory programs to reduce exposures to specific chemicals. The Minnesota program was established with a narrower goal of conducting four pilot studies on specific chemicals and providing recommendations for establishing a broader biomonitoring program in the state. However, goals of both states are similar for community engagement and public involvement [5,12,13]:

- Build public awareness and understanding of the program

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- Provide opportunities for stakeholders to contribute to program design implementation, and evaluation
- Achieve high participation rates within the target population(s) to be biomonitoring
- Communicate biomonitoring results in an understandable manner

Some other goals of community engagement include increasing public acceptance and support for biomonitoring programs; increasing use of biomonitoring data to guide policies and public health actions or interventions; and supporting the principles of environmental justice and democracy [14].

LEVELS OF COMMUNITY ENGAGEMENT

Community engagement and public participation occur on a continuum (Appendix II). The level of community engagement depends in part on the orientation of the biomonitoring program (Figure 1). A community-based orientation places most control and decision-making power with the health department and tends to fall in the “inform and consult” area of the spectrum. This orientation might be appropriate for population-level surveillance systems or rapid response situations. A community-based participatory orientation places some measure of power and control in the hands of the community and falls in the “involve and collaborate” area of the spectrum. This orientation can be used for targeted investigations, particularly those that are initiated by community concerns or require high-level buy-in from the community.

Regardless of a project’s/program’s orientation or approach, a biomonitoring study is likely to require more planning and resources for community engagement than traditional public health investigations. Establishing a community advisory committee may help to build consensus and provide guidance on community- or culture-specific values and ethical issues, such as who can participate, how results should be communicated, and how specimens should be disposed of after analysis.

CORE NEEDS FOR STAFF CONDUCTING COMMUNITY ENGAGEMENT

- Familiarity with human subjects protection and IRB requirements
- Training and experience in risk communication and message development
- Training and experience in cultural competency
- Access to translation services
- Facilitation skills for meetings (e.g., with community, advisory group, technical staff)
- Ability to refer study participants to health educators or health-care providers if needed
- Materials that describe the purpose, goals, and activities of the project/program (e.g., fact sheets, websites, forums, reports)

Protocol Development

Decisions made by the team charged with planning a biomonitoring project should be thoroughly documented in a written protocol. The protocol is a guide and reference for ensuring that each phase of the work is conducted according to the design and intent. Design and methods

Figure 1. Orientation, resource needs, and community engagement of a biomonitoring project/program

ORIENTATION	COMMUNITY-BASED	COMMUNITY-BASED PARTICIPATORY	COMMUNITY-LED*
RESOURCES/TIME NEEDED	Less More		
LEVEL OF CONTROL	Health-Department	Shared	Community

**Often conducted for advocacy; local or state public health agencies may be less likely to be involved with these types of studies.*

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are critical to appropriate interpretation of results. Any changes in these elements during the project should be documented as amendments to the protocol. The protocol also forms a basis for the development of applications submitted for approval by IRBs and training materials for field staff. It can be easily adapted or modified for subsequent projects and grant applications.

Elements documented in a biomonitoring protocol include the following:

- Purpose and objectives of the project
- Study investigators and partners and their roles and contact information
- Target population (including eligibility and exclusion criteria) and sampling frame
- Chemical analytes and selection rationale
- Data collection methods:
 - Participant recruitment and enrollment
 - Informed consent
 - Specimen collection, transport, and storage
 - Other data collection and parameters
 - Laboratory analysis
 - Laboratory quality and control measures
- Data entry, management, and protection of data privacy
- Data analysis, statistical methods, and sample size calculation
- Dissemination, notification, and reporting of results
- Risks and benefits and methods to minimize risks
- Medical counseling and clinical referrals
- Community engagement and results communications methods
- Storage or destruction of specimens
- Appendices:
 - Contact letters with participants;
 - Consent documents;
 - Data-collection instruments;
 - Protocols submitted to the IRB and approval letters; and
 - References.

ELIGIBILITY CRITERIA

After the appropriate target population has been selected, participant eligibility and exclusion criteria must be defined and a sampling strategy developed. If the study's goal is to generalize from the results of the participants and draw conclusions about a larger population, a population-based sampling strategy with a defined sampling frame and randomized participant selection will allow selection of a representative sample. Consultation with a statistician with expertise in sampling methods can help to design a sampling plan that minimizes bias and allows results to be generalized.

For some discrete targeted projects, the exposure scenario may define the target population and constrain its size. In such cases, it may be possible to invite the entire target population to participate in the biomonitoring study. Convenience samples are appropriate for pilot studies, where the purpose is exploratory or designed to test a particular method, but do not allow reliable generalization of the findings to the entire population from which the sample is drawn. Convenience samples may also be considered if limited resources do not allow for a representative sample.

With any sampling strategy, eligibility and/or exclusion criteria need to be developed for recruitment from the study population. These can include exposure criteria, such as residential location, membership in a particular community, occupation, years of exposure, and timing of exposure. Eligibility and/or exclusion criteria may also include individual characteristics, such as age, sex, or medical conditions, or other potential confounders. For example, confounding exposures (e.g., tobacco use) might exist that could result in exclusion of a participant for a study of environmental benzene or second-hand smoke exposure.

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Another consideration for recruitment is the difficulty of enrolling a sufficient number of participants to obtain a representative sample. Sampling statisticians can develop power calculations to estimate the appropriate sample size for achieving project goals. Depending on the goals of the study, population or exposure subgroups of particular interest may be oversampled to achieve sufficient numbers to allow generalization to the larger population. If multiple, diverging approaches exist to acquiring participants, resource considerations and the costs and benefits of various approaches should be addressed during planning. Depending upon the project, it may be important to include potential participants and other stakeholders in planning eligibility criteria. If information about the project is widely disseminated, careful communication about participant eligibility criteria and a clearly described selection process will help the community have realistic expectations and reduce confusion or disappointment during project implementation.

PROTOCOL DEVELOPMENT SPECIFIC TO STUDY POPULATION

Decisions about the study population and sampling strategy will influence many aspects of the study protocol, including informed consent, recruitment, incentives, communication, and outreach. A study team that includes various areas of expertise, such as epidemiologists, environmental toxicologists, risk communicators, cultural advisors and translators, and medical counselors, will help to develop protocols that are appropriate for the study population. Characteristics of the target population will also guide choices about incentives for participation.

Before the first contact with potential participants, the study protocol needs to incorporate plans for communicating findings to the project's target population and to the public so that everyone receives accurate and appropriate messages about

the project's purpose and limitations. The study protocol also should include plans for providing information to participants about the project results; such plans are particularly necessary if the project will take place over a long period because participants could relocate before receiving results. As with other applied public health activities that produce findings of interest to multiple audiences and stakeholders, the special status and specific needs of participants as the primary audience and the possibility that their interests might differ from those of the general public and other stakeholders need to be recognized.

Ethical Considerations

Like all investigations that involve human subjects, ethical issues in human biomonitoring will be addressed mostly through careful assessment and minimization of risks to participants (e.g., physical or psychological risks) and communities (e.g., risk for public stigma), an informed consent process, and protection of privacy and confidentiality. Human biomonitoring in public health practice poses unique ethical challenges, such as those associated with specimen banking and results return.

Biomonitoring of human populations is similar to environmental monitoring in that it can describe population exposure to a contaminant. However, like medical screening, it can describe body burden of a potentially harmful chemical and possibly predict individual risk for adverse health outcomes. This dual role of biomonitoring creates unique ethical challenges. Some issues can be addressed through the informed consent process; others are more complex and need to be considered during other phases of a study. Although these challenges have yet to be fully resolved, human subjects and privacy protection training modules available online provide some guidance. At a minimum, all project staff who will have access to individually identifying information should be required to complete

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this training through their own institutions or through the National Institutes of Health [15].

INFORMED CONSENT AND HUMAN SUBJECTS PROTECTION

In order to ensure that participants' rights are protected and that the study is conducted in an ethical manner, it is prudent to submit all biomonitoring project protocols to an IRB. It is the role of the IRB to determine if a particular project is exempt from IRB review. While IRB review is critical if children or other vulnerable groups are involved, most biomonitoring projects will require IRB review and approval.

A project might involve more than one IRB review; for example, if partnering with a university, if receiving federal funding, or if working with a tribe (which could include a tribal IRB and/or an Indian Health Services IRB). Because biomonitoring is an emerging field, IRB members might not be fully familiar with all its ethical ramifications and might need education on biomonitoring; the state of the science; its relevance to environmental public health; and the risks, benefits and limitations, particularly of reporting results for chemicals that have unknown health effects and mitigating actions.

Some IRBs might determine that data gathering for public health practice, not research, is exempt from review [16]. However, most biomonitoring projects in which participants are asked to provide specimens will not be exempt. The line between research and public health practice is subject to interpretation, and each IRB will classify biomonitoring activities and requirements for informed consent differently.

Even when public health projects are exempt from IRB review, participation requires informed consent so that participants know the voluntary nature of the project and how they will be involved in the study. The informed consent

process should explicitly detail participants' role, risks and benefits of participation, limitations to interpreting the data, and how the data can and cannot be used.

Participants' individual information also needs to be protected in accordance with IRB and HIPAA requirements. For biomonitoring, this protection generally involves labeling specimens and other personal data with a study identification code, and investigators maintain personal identifiers separately to link findings to individual participants on a need-to-know basis for reporting results or conducting exposure source and exposure pathways investigations.

Anonymization of specimens, i.e., permanent separation of identifiers from specimens so results cannot be traced to an individual, is not recommended for public health studies. Anonymization limits use of the data for understanding possible health effects, prevents informing participants of their results, and prevents exposure-related intervention that might protect individuals at risk for excessive exposure—all fundamental goals of public health practice. Anonymization may be acceptable for a project investigating the technical feasibility of a new laboratory method.

IRB approval does not ensure recognition and consideration of the values of an organization, community, or culture. An open and transparent process, which identifies and engages all community stakeholders, is the best assurance that community values will be addressed. For communities to have realistic expectations of what can be achieved through biomonitoring, they need to clearly understand the limitations of biomonitoring and that biomonitoring alone might not identify sources of exposure or predict community health risks. Communities also must understand what, if any, public health actions can be taken in response to the findings.

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SPECIMEN BANKING

Unlike many other types of studies, biomonitoring can provide opportunities—and accompanying concerns—for storing or banking specimens collected. Banked samples could be particularly beneficial in public health settings for developing laboratory methods and screening for emerging contaminants. The informed consent process should allow participants to choose whether their individual specimen can be stored to test for additional analytes not specified in the consent.

If at the time of initial informed consent broad permission to analyze additional chemicals has not been obtained, participants who agree to further contact should again provide consent before additional analyses are conducted and should be given the choice to opt out. Without specific consent for banking, specimens must be destroyed at the end of the project and secondary analysis disallowed.

Even though researchers other than those who collected the samples might want access to these biospecimens for research unrelated to the initial study, access should be granted to the specimens only in accordance with informed consent. This secondary access to biospecimens should exclude access to individual identifying information.

RESULTS RETURN

Many ethical concerns about biomonitoring pertain to communicating individual results and the availability of mitigating action to participants. The benefits of biomonitoring to individual participants might include individual access to exposure and health information and, in some cases, an opportunity for individual counseling or follow-up to identify individual behaviors that might reduce or eliminate sources of exposure. Often, however, the health consequences of a given chemical concentration are unknown, and information about sources of exposure may be incomplete. Knowing the concentration of

a chemical in one's body, but not knowing the exposure source, the possible health effects of a certain level of that chemical, or ways to reduce or eliminate exposure, may cause anger, anxiety, and feelings of helplessness. Unless results are returned with sensitivity and by appropriate personnel, participants may experience feelings of a loss of privacy. Prior to enrolling in a study, participants should be given clear information about the benefits and risks of participation and limitations of biomonitoring data with respect to diagnosis, treatment, and prevention of clinical disease so they can make informed decisions about involvement.

Biomonitoring communications research has only recently begun to examine how knowledge about chemicals affects participants' health behaviors. Informed consent alone may not be effective in educating people about the ramifications of participating, including how to make reasonable judgments about exposure and health, preventing disease, and medical treatment decisions based on the findings. Biomonitoring has the potential to result in adverse consequences if participants make scientifically unwarranted efforts to remove the measured chemicals from their bodies (e.g., by chelation, purported antidotes, sweat lodges). In addition, participants who seek further medical testing or make attempts to identify exposure sources could experience additional expenses. Identifying real estate as a source of exposure also can have economic implications. For example, if remediation is conducted or property values decrease as unintended consequences of biomonitoring, both participants and other property owners may be affected financially. Therefore, investigators should consider the ramifications of providing individual medical counseling for participants who receive their biomonitoring results and ensure that recommendations are scientifically valid.

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Data Management

Data management is a critical component of biomonitoring. As with any public health surveillance activity, data should be collected, managed, and stored by using the least amount of identifiable public health information necessary to achieve the program goals. The use of participant identification and barcodes can help preserve confidentiality during collection, processing, and development of analytic results. Similarly, a database containing questionnaire or key confounding variables can be maintained by using a unique participant identifier and by maintaining the most sensitive identifiable information, such as name and address, in a separate administrative database that limits access to individuals who may need this information to track and communicate with participants.

Data systems must uniquely identify participants and also allow questionnaire and other information to be later linked to the biomonitoring results. Because most laboratories are accustomed to using de-identified specimens and barcode systems, attaching barcodes that can be scanned to biomonitoring samples and all other participant information might offer an efficient way to pre-label material or tag information in the field. Systems need to ensure that the correct barcode is consistently used for a participant. In addition to unique codes, if the study includes more than one person from a unique location, a system to link all participants from that location might be needed. For example, if all members of a household provided urine samples and the study includes exposure information related to the house, all individual members need to be linked to the same residence.

Investigators often keep a key to link de-identified data to names and addresses. To maintain confidentiality, investigators need to store the

key so that it can be used only when authorized. Investigators should also consider possible needs for re-identifying data to determine how long they want to keep the key. IRBs often need to approve plans for maintaining a key and may require informing participants about the key as part of the informed consent process.

Biospecimen Collection

BIOSPECIMEN COLLECTION, HANDLING, TRANSPORT, AND STORAGE PROTOCOLS AND PROCEDURES

As in other types of epidemiologic studies, most quality assurance occurs before study implementation. Clearly defined and tested protocols and procedures for biospecimen collection, labeling, handling, processing, transport, storage, and tracking are essential and can be defined through laboratory standard operating procedures. Proper collection, handling, and storage protocols will help ensure that biospecimen integrity is maintained and field contamination is avoided. Collaboration with laboratory colleagues is critical for developing protocols and procedures to ensure use of appropriate collection vessels (e.g., prescreened batches), correct field processing (e.g., serum separation), and proper storage and shipment of samples to the laboratory. Field blanks, spikes, and duplicates should be included in the analytic batch of specimens as part of quality assurance for sample-handling.

Biospecimen collection and transport methods must be documented. For biospecimen collected in the field, collection logs should document, at a minimum, participant number, sample identification, date, time, volume collected, and storage conditions. Time between sample collection and processing also needs to be considered; serum usually must be separated within 24 hours after collection. If blood samples are processed for serum separation, the number

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of tubes processed, appearance and volume, and other information also should be documented. Information that could affect biospecimen integrity or stability, such as storage temperature or freeze–thaw cycles, also should be noted. Timing of processing, temperature, addition of stabilizing chemicals and buffers, and sterility also are important.

A laboratory system for labeling, receiving, and tracking biospecimens is usually handled through an automated laboratory information management system. Labels can contain barcodes and include the participants' unique coded identifier, sample type, and aliquot as needed. Shipping of samples from the field to the laboratory should follow acceptable standardized procedures for diagnostic clinical samples. General requirements include use of an insulated container, absorbent material, double bagging with an outer bag that can be sealed to contain a pressure of 95 kPa, and use of proper labels (e.g., dry ice, biohazard) on the outside box. Chain-of-custody forms and shipping information (e.g., receipts, tracking numbers) that track movement and location of samples also will be required.

Examples of biospecimen collection, labeling, and shipping instructions are available from CDC [17,18].

BIOREPOSITORY/LONG-TERM STORAGE

As biospecimens are collected, aliquots of the specimens may be stored for later analyses. Reference materials from the International Society for Biological and Environmental Repositories contain comprehensive information about handling blood, urine, nail clippings, saliva, breast milk, and other human biospecimens [19].

Other issues that need to be addressed in the planning stages of a project include ownership of samples; how decisions will be made about use and disposition of biorepository specimens;

and standard procedures for review of requests from external and internal investigators for secondary uses of stored specimens, such as for research studies or laboratory methods development. Inappropriate use or release of stored specimens (not in accordance with legal and ethical guidelines) by a public health agency can have serious negative consequences for future biomonitoring.

Laboratory Analysis

Laboratory analyses need to be addressed jointly with partnering laboratories. Costs, feasibility, quality control procedures, and consistency of analyses across laboratories need to be considered. Consistency of methods with other laboratories is important so that results may be compared to other studies and populations. For public health surveillance activities in which results will be compared with reference values or with national estimates (e.g., NHANES), epidemiologists and partners should collaborate to identify and develop standard laboratory analytical methods that are consistent with national standards. This collaboration may require consultation with CDC laboratories and APHL.

Statistical Analysis

As with most environmental exposure studies, special statistical analyses of the data will be required. These analyses usually will describe the population characteristics, assess the range and distribution of the measured exposures, and assess relationships between covariates. Most biomonitoring data do not follow a normal distribution, which is required for using standard parametric statistics. Therefore, exposure results from the laboratory must be log transformed, or nonparametric statistics and geometric mean values used for data analysis.

The choice of appropriate statistical approaches depends on the study design and goals. For

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population comparisons using aggregate results, geometric and arithmetic means can be utilized. Descriptive and exploratory estimates using box plots, histograms, or scatterplots can be used to explore distributions, identify significant outliers, and determine which participants are above or below reference values. Stratification can help identify differences between and disparities within populations. When adjusting values for covariates, investigators can use regression-based methods if exposure data are normally distributed or log-transformed. All results must be kept and maintained by using the same units of analysis (e.g., milligram vs. microgram, liter vs. milliliter).

Use of methods for imputation, or substituting a value for missing data, should be considered if the data include a large number of values that are missing or below the LOD or MDL [20–25]. Standard methods for analyzing chemical concentrations below the MDL include using the value $LOD/\sqrt{2}$ or other method for imputation of mean values or adjusted mean values of all the results. If missing data are substituted, the methods used should be fully documented, the impact on the results considered, and the validity of comparison with reference data (e.g., NHANES) provided.

The methods for reporting individual results to participants should be determined prior to data analysis. A recommended approach is to report actual measured values and units of analyses. If an individual's result is below the LOD, the results should be explained in lay language to recipients of the data.

For studies that collect supplemental health and environmental data, several analytic approaches can be used to determine associations between exposure sources, biomonitoring results, and/or measures of disease outcomes or to evaluate whether an intervention has made a substantial difference in the public's health. Such methods as correlations, analysis of variance, and regression are applied in the same way as in other epidemiologic studies.

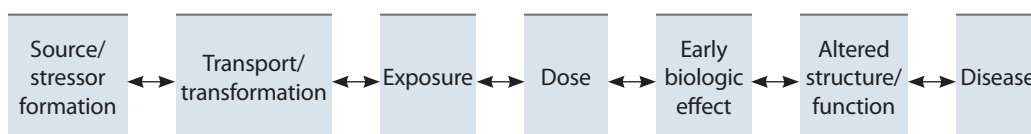
Results Interpretation: Methods and Comparisons

Epidemiologists interpret data by drawing valid inferences from data using their knowledge of study design and conduct and analytical methods used. They must also place the analytical results from biomonitoring studies into context so that health officials, policy makers, and community members can take appropriate actions to protect and promote health.

Interpreting data from biomonitoring studies presents unique opportunities and challenges. The internal dose of a chemical or metabolite at a point in time lies along the environmental public health continuum (Figure 2) and has the potential to provide valuable information about both upstream exposures and downstream effects on human health [26].

Continued advances in technology enable laboratories to measure more chemicals at increasingly lower levels in the body. However, as the National Research Council notes, “our technical ability to generate new biomonitoring data has essentially exceeded our ability

Figure 2. Environmental public health continuum



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to interpret them” [2]. Some of the major considerations for interpreting biomonitoring data are outlined below.

ATTRIBUTION OF EXPOSURE TO A PARTICULAR SOURCE

Measuring the internal dose of a substance does not enable the investigator to pinpoint the source of exposure, especially for chemicals that are widely used, found in the environment, or enter the body through multiple pathways [27]. For example, inorganic arsenic is widely distributed in the earth’s crust and occurs naturally at high levels in water and soil in some parts of the world. Inorganic arsenic also is used in human-made products, such as wood preservatives, pesticides, and herbicides; environmental releases of these products are another potential source of arsenic exposure. Thus, attributing arsenic levels in the body to a particular source is difficult, especially for low-level exposure, without collecting and analyzing data from a variety of possible sources.

HALF-LIFE AND PHARMACOKINETICS

Information about a chemical’s half-life and how it is metabolized, distributed in, and eliminated from the body is critical to interpreting biomonitoring results. Individual differences in these processes partially explain the variability in biomonitoring data. Chemicals with half-lives of hours or days (e.g., metals, volatile organic chemicals) can be eliminated and undetectable in the body within a few days after exposure. Biomonitoring data on these chemicals can be used to confirm recent exposure to chemicals (e.g., inhalation exposure from a chemical spill in a workplace or recent dietary consumption).

Chemicals that accumulate or persist in the body (e.g., lead, dioxins, polychlorinated biphenyls) have relatively long half-lives. These chemicals sometimes can be measured many years after

exposure, and the data can provide an estimate of the level of exposure over time. However, ascertaining with certainty the source, timing, and frequency of exposure for these chemicals is complex because processes for metabolism, storage, and excretion of the chemical over the same period, which can vary with individuals, also must be considered.

DETERMINATION OF RELEVANCE TO HEALTH

At the individual level, study participants and medical providers often want to know whether chemicals measured in a person’s body could be linked to previous or existing health conditions or pose future health risks. Policy makers, health researchers, and public health practitioners want to know the burden and risks to population health so they can prioritize and evaluate public health interventions, policies, and research.

The scientific evidence between internal dose and health effects is strong for only a few environmental chemicals. Lead, mercury, and cadmium are among the chemicals with health-based reference values that can be used to screen measurements in blood or urine. Even for these chemicals, the health-based reference values used should be relevant to the population of interest. For example, for lead, the level of concern for men differs from that for children and pregnant women. For most environmental chemicals, many questions remain unanswered about the chemicals’ toxicity and mechanism of action in humans, critical health endpoints at different levels of exposure, and possible risks from very low concentrations in the general population. Public health practitioners need to consider information in addition to published scientific studies to interpret and communicate information about a biomarker’s relevance to health.

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POPULATION TRENDS AND COMPARISON WITH A REFERENCE

The most common method for interpreting biomonitoring results is to describe trends or distributions of exposure to chemicals in a population and compare them with an appropriate reference population. Data on reference populations can come from national or statewide biomonitoring surveys (e.g., NHANES), surveys from other regions, historical measurements on the same population, or measurements from a known unexposed population. Use of reference populations also can be used to gain perspective on individual-level data, especially in the absence of clinically relevant health-based reference values. These comparisons provide information about whether the biomarker levels in a study population differ from the levels in a comparison population. However, they cannot be used to determine population- or individual-level health risks.

Comparing data from a study population with data from a reference population requires consideration of several factors, including the following:

- **Data Collection:** Were the biomarkers, laboratory test methods, LODs, quality assurance/quality control requirements, population sampling frame, and recruitment methods, and other factors comparable between the two populations?
- **Population:** Were the study and reference populations comparable in terms of age, sex, ethnicity, lifestyle, occupation, relative levels of exposure, and other factors?

Table 2 shows four options for reference data that have been identified in the scientific literature and guidance documents on biomonitoring [2,26-28].

Table 2. Options for reference data in biomonitoring studies

DATA SOURCE	INFORMATION PROVIDED	LIMITATIONS
CDC: <i>National Report on Human Exposure to Environmental Chemicals</i> (based on NHANES data)	■ Data on environmental chemicals measured in blood or urine ■ Data collected from a representative sample of the US population every 2 years ■ The most recent report (published in 2009 and 2010) provides data on 212 chemicals [29]	■ Data not representative of environmental exposures in all US regions/states ■ Data not available at the city, state, and regional levels ■ Data possibly not available on a biomarker of interest ■ Time lag between collection and release of data ■ Limited stratification of data
Occupational studies	■ Data from biomonitoring studies conducted in workers exposed to a particular chemical or industrial process	■ Studies usually on highly exposed workers with recent/ongoing exposures; might not be comparable with low-level community exposures ■ Biomarkers, sample collection, and laboratory methods possibly not comparable ■ Occupational safety standards that should be considered possibly not appropriate for community exposures

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Table 2. Options for reference data in biomonitoring studies (*Continued*)

DATA SOURCE	INFORMATION PROVIDED	LIMITATIONS
Risk assessment–based values or guidelines	■ Information about health effects observed in toxicological studies (in laboratory animals and/or humans) and epidemiologic studies ■ Published risk-based values or guidelines (e.g., no observable adverse effect levels, lowest observed adverse effect levels, permissible exposure limits, minimal risk levels, reference doses, biomonitoring equivalents) [30]	■ Risk-based guidelines have high degree of uncertainty and might not be based on effects observed in humans ■ Human data usually based on occupational studies or exposures in a highly exposed population ■ Generally not recommended for comparisons with biomonitoring data in general population
Internal comparison (for interpreting individual-level data)	■ Comparison of an individual's result to the distribution within the study population	■ Cannot be used to interpret or communicate risk to health ■ No clinical relevance

INTERPRETATION OF AGGREGATE AND INDIVIDUAL DATA

Factors that need to be considered and included to ensure accurate interpretation of aggregate and individual level data include the following:

- Information about possible sources of error in the data, including issues with data quality. For aggregate results, the sources of error or bias that might have been introduced during participant selection, recruitment, and sampling should be discussed.
- Statistics for the study that are comparable with the those from reference populations. For example, CDC reports NHANES data by using the geometric mean, and the 50th, 75th, 90th, and 95th percentiles.
- Data reported in a manner that meets requirements to protect confidentiality.

COMMUNICATING BIOMONITORING RESULTS



COMMUNICATING BIOMONITORING RESULTS

Effective results communication remains one of the greatest challenges for biomonitoring programs in public health settings. Most likely, programs will need to interpret and communicate both the aggregate and individual-level biomonitoring data. Research evaluating biomonitoring communications methods is slowly emerging [31-33] and should be reviewed for guidance, but much remains to be learned as public health officials determine the most appropriate and informative ways to explain results to multiple audiences. For guidance on reporting biomonitoring research results for scientific audiences, see the statement on molecular epidemiology by the STROBE initiative [34]. (STROBE stands for STrengthening the Reporting of OBservational studies in Epidemiology.)

Results communication is most effective when methods are considered during the planning phase of a biomonitoring project or program. To be most effective, biomonitoring projects should include a health educator or public communications specialist as a member of the project team at the earliest stages of planning.

The purpose of the study or program will dictate to whom information is communicated, the content of the message, and the methods used. Legislative or other mandates will further influence the audience, content, and methods. Possible audiences include

- Biomonitoring study participants
- The affected community (if the project is community based)
- Scientific or community oversight panels
- Policy officials, such as the legislature and political appointees
- Scientific peers and public health professionals;
- The general public
- Health-care providers, including clinics and professional societies
- Other stakeholders

Although the language and details need to be tailored to each audience, the overall message or interpretation of the findings should be consistent across all groups. Use of communication tools, such as message maps, can help clearly and concisely organize information for multiple audiences [35].

Results communication might involve returning individual-level data to specific participants and/or reporting aggregate data to participants and to other audiences. Factors to consider include ethical issues, how the program will respond to results that may be worrisome to participants or the community, the need for confirmatory or repeat sampling, and the possibility of legal or economic ramifications.

METHODS OF COMMUNICATING RESULTS TO PARTICIPANTS

- **Results of laboratory analysis only:** This method may be appropriate when clinical reference values and medical consultation to interpret the results are readily available to participants and their health care providers.
- **Results of analysis plus interpretation of data, and possible health effects:** If resources allow, this communication could recommend discussion of results with a health-care provider and offer to help participants locate a provider if needed. This option is likely to be the most informative to participants and other audiences and is also resource-intensive.
- **If available, information about the potential health effects of a chemical and/or known and practical methods or interventions to reduce exposure:** ATSDR's Toxicological Profiles may be a good resource for basic toxicological and epidemiologic information about particular chemicals or biomarkers and can be helpful for results communication (www.atsdr.cdc.gov/substances/index.asp). Since these profiles are available for a limited set of chemicals and may not have been updated, recent reviews or studies should also be consulted.

COMMUNICATING BIOMONITORING RESULTS

If health risks and effective exposure reduction measures are unknown or controversial, the benefits of full communication must be weighed against the risks of providing incomplete or misleading information (see Ethical Considerations above).

SPECIFIC ISSUES REGARDING RETURN OF INDIVIDUAL RESULTS

Triggers for communicating results to individual participants

- **Mandates:** Some state mandates require that individual results be returned to participants, regardless of the level or whether the clinical relevance is known.
- **Alert Values:** When biomonitored levels exceed established levels of concern (for example, the blood lead level of concern in children), investigators have ethical and clinical obligations to inform participants and/or health care providers so that appropriate follow-up care or prevention action can be taken (http://www.cdc.gov/nceh/lead/ACCLPP/Lead_Levels_in_Children_Fact_Sheet.pdf).
- **Clinical Relevance:** For the few biomonitored chemicals for which clinically relevant values exist, information about expected health effects possibly associated with specific chemical levels may be included in the communications materials. For example, information about the correlation of elevated blood lead levels in adults with specific health effects may be appropriate to include in results communication materials, especially if the blood lead levels are elevated (www.health.state.ny.us/publications/2584/).
- **Right to Know:** Individuals might believe they have the right to know about the presence of chemicals detected in their bodies. Even when established health-based reference values do not exist, the decision to return individual results may be based on prior agreement with participants or communities and be

documented in the informed consent process.

- **Workplace Testing:** If biomonitoring is conducted in workers, employers might need to be notified if levels exceed occupational standards. Workers are typically concerned that employers not discriminate on the basis of biomonitoring results. Employers might be concerned that biomonitoring findings could trigger workers' compensation issues. Biomonitoring results might be impacted by non-occupational exposures; without detailed information about exposure sources (including industrial hygiene monitoring), differentiating between these and occupational exposures may not be possible. Results of biomonitoring conducted for public health purposes should be kept separate from the workers' employment and medical records and should be addressed in the study protocol and informed consent process.
- **IRB determination:** An IRB may determine that results that cannot be interpreted or cannot be clinically correlated can cause anxiety in or harm to the participant and therefore should not be returned. This issue is more likely to occur with IRBs in academic and other research institutions than in public health agencies.

Communications should restate information about the limitations of interpreting and using the data, which was explained to participants during the informed consent process and before data collection.

Written results may be presented in numeric, graphical, or pictorial format or a combination of these methods. To maximize comprehension and minimize alarm and concern, the following additional steps should be part of the communication plan:

- Incorporate best practices for results communication regardless of the method used.
- When possible, conduct usability testing of communication materials with an audience

COMMUNICATING BIOMONITORING RESULTS

that is similar to the eventual intended recipients. Materials can be modified on the basis of findings. Adequate monetary and personnel resources for the planning, development, testing, and implementation of a communications plan and materials should be incorporated into the project.

Timing of results communication

Biomonitoring results might not be available for months after recruitment and specimen collection. Results that are elevated or of clinical concern—especially if they indicate a need for medical follow-up—should be returned within a short time.

Most IRBs require investigators to inform participants at recruitment when they can expect to receive results. If the time between recruitment and return of results is expected to be long, investigators need to collect contact information from participants. As with other types of studies with long follow-back times, one approach is to ask participants for contact information of people who are likely to be in stable living situations and to know the participants' whereabouts. Another approach is to acquire participants' email addresses, which are less likely to change during a move, for the sole purpose of contacting them (i.e., not for sending results, which could violate HIPAA regulations). Participants also can be encouraged to notify investigators about changes of addresses.

When establishing a program or designing a study, the timing of communicating individual results to participants relative to presenting results to the community, general public, stakeholders, or scientific peers needs to be determined. In public health settings, communication of results to affected individuals and their communities is expected first and supersedes rapid publication of scientific findings and analytical techniques. However, if one purpose of a study is to test or develop laboratory analytic methods, project

partners may decide that publication of a novel laboratory method will precede notification of participants about results.

As part of communicating results, programs can consider offering a way for participants to contact program staff beyond contacts listed on the informed consent form. Physicians can be included among key project partners so that participants who wish to further discuss the health implications of findings can be referred to a knowledgeable and interested health care provider. Partnering with health care providers who are trusted members of the community is an additional option because participants might be more comfortable obtaining counseling from their own providers, rather than those associated with the study.

RESULTS AND RISK COMMUNICATION MESSAGE FOR COMMUNITY

Interpretation and communication of results should be defined in the original study design and addressed during the informed consent process. Timelines for communicating results should be identified in advance. If community partners are involved, a communication plan should be developed jointly with them. The cost of regular communication with the community must be factored into the project plan.

Communication with community members should include the following, written in plain language:

- Clear delineation of study objectives, e.g., what questions the study aims to answer;
- Explanation of study methods, e.g., how study participants will be chosen, how data are collected and analyzed;
- Report of findings, e.g., what we found, what we learned; and
- Interpretation of findings:
 - o Comparison with other appropriate biomonitoring data, e.g., other studies of

COMMUNICATING BIOMONITORING RESULTS

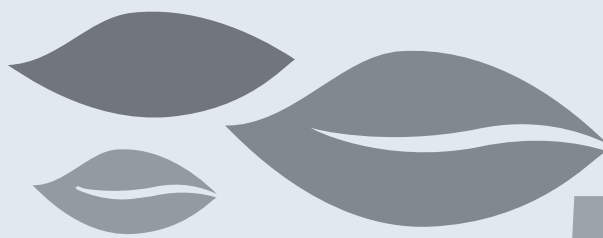
comparable populations. If applicable, how do data for the study population differ from data for the general population as reported by CDC or other reference populations?

- o What do biomonitoring results mean to the individual's health? To the family's health? To the community?
- o What actions can individuals take to reduce exposure? What actions can communities and public health agencies take? Are these actions recommended?

The following messages need to be delivered in plain language in biomonitoring communications:

- The measurement of an environmental chemical in a person's body tissues or fluids, such as blood or urine, provides an estimate of how much of a chemical is present in a person but cannot necessarily predict what health effects, if any, could result from that exposure. The presence of a chemical in the body does not mean the person will get sick.
- The level of a chemical does not by itself indicate
 - o Whether the exposure occurred recently or over a long period of time.
 - o How the exposure occurred. Presence in blood or urine alone does not tell the source or route of exposure.
 - o Whether the chemical potentially causes disease or an adverse health effect at the level measured.

USING BIOMONITORING TO INFORM PUBLIC HEALTH ACTION



USING BIOMONITORING TO INFORM PUBLIC HEALTH ACTION

The ultimate goal of biomonitoring in the context of public health practice is to produce results that provide information for public health action. Although these actions might take different forms—from targeting interventions to reduce exposure to harmful chemicals to confirming that past public health actions have successfully done so—they are essential to the concept of public health surveillance and to the mission of protecting public health. By documenting human exposure to environmental chemicals, biomonitoring is uniquely positioned to provide valuable information for policymaking and programmatic activities.

Complicated questions exist about how such policies should be developed, primarily because knowledge about the possible health outcomes of exposure to numerous chemicals has lagged behind the capability to conduct biomonitoring. The answers to these questions depend on the purpose of the biomonitoring program or project (e.g., Is the investigation of exposures in a specific community or for population tracking?) and on the chemicals in question (e.g., Are health-based action levels available? How well understood are sources of exposure to the chemical?). These questions need to be addressed during planning, and measures must be in place to ensure that results can be assessed for their public health significance and responded to as rapidly as possible.

USE OF BIOMONITORING RESULTS TO INFORM NEW POLICIES

Targeted exposure reduction actions from New York City's Health and Nutrition Examination Survey (NYCHANES)

NYCHANES, a community version of CDC's NHANES, was conducted in 2004 by the New York City Department of Health and Mental Hygiene. It included a biomonitoring component. Blood and urine from 1,811 adult participants were analyzed for different forms of mercury and

pesticide metabolites. Results from this survey led directly to a series of targeted public health actions [36].

- New Yorkers born in the Dominican Republic had strikingly higher urine levels of inorganic mercury, with the 95th percentile for this group above the reportable level of 20 ug/L [37]. Follow-up interviews were conducted, and the elevated levels were attributed to the use of mercury-containing skin-lightening creams. As a result, inspectors visited stores possibly selling these products, products were embargoed, and an extensive public education campaign was conducted in Spanish and English.
- Blood levels of total mercury were higher in New Yorkers than in the US population, particularly in Asian New Yorkers, nearly 50% of whom had above the reportable level of 5 ug/L. Fish consumption was the strongest predictor of mercury levels. These findings led to the conclusion that past emphasis on sport fishing as a source of mercury exposure was inadequate and that more attention should be given to consumption of commercially purchased fish. Actions resulting from the findings included increased sampling of commercial fish, clinical guidance to health providers, and development of the New York City health department's first educational campaign on fish consumption.
- Preliminary analysis of urine organophosphorous and pyrethroid pesticide metabolites showed that levels were 4–14 times higher in New Yorkers than in the US population and that exposures were higher in women and people who had recently had a pest control professional in their homes. These findings, combined with other information, led to increased awareness and concern about urban pesticide exposures. In response, NYC restricted local government use of pesticides and implemented a program for reporting and public disclosure of pesticide use.

USING BIOMONITORING TO INFORM PUBLIC HEALTH ACTION

For the two mercury examples, biomonitoring identified elevated exposures in subpopulations of participants, and public health officials were able to compare results to reportable levels that New York State had established. Public health action—product embargoes, public education campaigns, and further investigation—was taken to reduce exposures. In the pesticide example, public health action was taken not on the basis of exceedence of a reportable value, but on the revelation from biomonitoring that exposures to potentially harmful chemicals were higher than expected. Furthermore, biomonitoring identified that women, a subpopulation more vulnerable to the possible reproductive effects of pesticides, were more highly exposed.

Regulatory and market-driven actions on polybrominated diphenyl ethers and perfluorochemicals

Polybrominated diphenyl ethers (PBDEs) and PFCs are classes of chemicals used as flame retardants and in the manufacture of nonstick and stain-resistant products, respectively. Early biomonitoring results indicated that these compounds were present at detectable levels in humans, that concentrations were increasing over time, and that chemical levels (of PBDEs) were higher in persons residing in states requiring their use. Even though harm to human health from exposure had not been definitively established and reference doses or similar health-based values did not exist, increased awareness about levels in humans, combined with existing information about animal toxicity and persistence in the environment and in humans, led to a variety of public health actions. Certain PBDEs and PFCs have been subject to voluntary phase-outs by industry and, for PBDEs, to regulatory action by government entities. Biomonitoring results were critical to spurring public health action and bringing public, government, and industry attention to health concerns about these chemicals.

USE OF BIOMONITORING RESULTS TO EVALUATE EXPOSURE-REDUCTION ACTIONS

Documenting reductions in exposure to lead, environmental tobacco smoke, and legacy pesticides

The most widely discussed example of the usefulness of biomonitoring data in assessing the effectiveness of exposure reduction measures is that of blood lead levels and the phase-out of leaded gasoline. As the use of leaded gasoline in the United States decreased during the late 1970s, biomonitoring results from NHANES documented a dramatic decline in population blood levels during 1976–1980, a decline that tracked lead used in gasoline [38]. Even though modeled estimates had predicted that the removal of leaded gasoline would not have a major impact on blood lead levels, the biomonitoring data showed the opposite. This information was instrumental in the US Environmental Protection Agency's decision to further restrict and ultimately ban the use of leaded gasoline.

Decreased exposure to environmental tobacco smoke and legacy pesticides resulting from public health actions also have been confirmed by biomonitoring results. Since enactment of smoking bans and other antismoking campaigns, NHANES biomonitoring results have documented dramatically reduced cotinine levels (a marker of exposure to environmental tobacco smoke) in children and adults; during 1988–2000, serum cotinine levels in nonsmokers declined by 70% [39]. Similarly, the use of certain organochlorine pesticides, including DDT, was banned in the United States (but not in other countries) during the late 1970s. Results from NHANES and other biomonitoring studies have since shown a continual decline in serum levels of these compounds in the US population (CDC fact sheet). Some subpopulations, such as non-Hispanic Blacks and casino workers, continue to be more highly exposed and might be further targeted for exposure reduction.

USING BIOMONITORING TO INFORM PUBLIC HEALTH ACTION

Evaluating exposure reduction in a community context

Biomonitoring can document the effectiveness of exposure-reduction measures in communities. In Minnesota, drinking water in communities east of Minneapolis–St. Paul was discovered to be contaminated by certain PFCs that resulted from disposal of PFC-containing wastes. Exposure-reduction measures, such as additional filtration of public water supplies and provision of water filters, bottled water, and connections to municipal water for people using private wells, began in 2005. A biomonitoring pilot project conducted by the Minnesota Department of Health in 2008 indicated that residents of two communities in the area had elevated serum levels of certain PFCs compared with US national estimates [40]. Even though residents' exposure to contaminated drinking water had presumably been substantially reduced starting in 2005, levels 3 years later remained elevated because the compounds have serum half-lives of 3–7 years. During 2010–2011, the Minnesota Department of Health conducted a follow-up biomonitoring study to measure changes in serum levels in the same persons over a 2-year period to determine whether efforts to reduce exposure were effective.

As these examples illustrate, public health actions can be taken in response to biomonitoring results. These actions include targeted exposure-reduction programs, regulatory measures, broad public education campaigns, and assessment of the success of past exposure-reduction efforts. Although policy decisions are in many cases complicated by a lack of conclusive data on specific biomonitoring levels that could be related to human health impacts, biomonitoring is clearly useful for shaping public health action.

FUTURE CHALLENGES

As described previously, these guidelines are intended to help inform and guide decisions made by public health officials and scientists about the design, conduct, interpretation, and application of biomonitoring activities. They support efforts by APHL, the Association of State and Territorial Health Officials, the CDC Environmental Public Health Tracking Program, and others to advance the science and practice of biomonitoring for public health.

Major challenges remain in achieving this goal. These include limited resources (monetary and personnel) and optimal management and interpretation of data is an emerging field. With continued building of state capacity and partnerships for biomonitoring, in the laboratory and among environmental epidemiologists, successful strategies for meeting these challenges can be developed. As the field evolves, the practices and guidance described here will be updated in an iterative process. Because of the personal and politically sensitive nature of measuring toxic chemicals in humans, environmental epidemiologists, in collaboration with others, should engage in best practices and appropriate uses of biomonitoring. Avoiding the challenge could have potentially serious consequences, such as failing to proactively protect public health. Public health agencies need to expand their understanding and experience with this powerful new tool for advancing environmental public health practice and policy.

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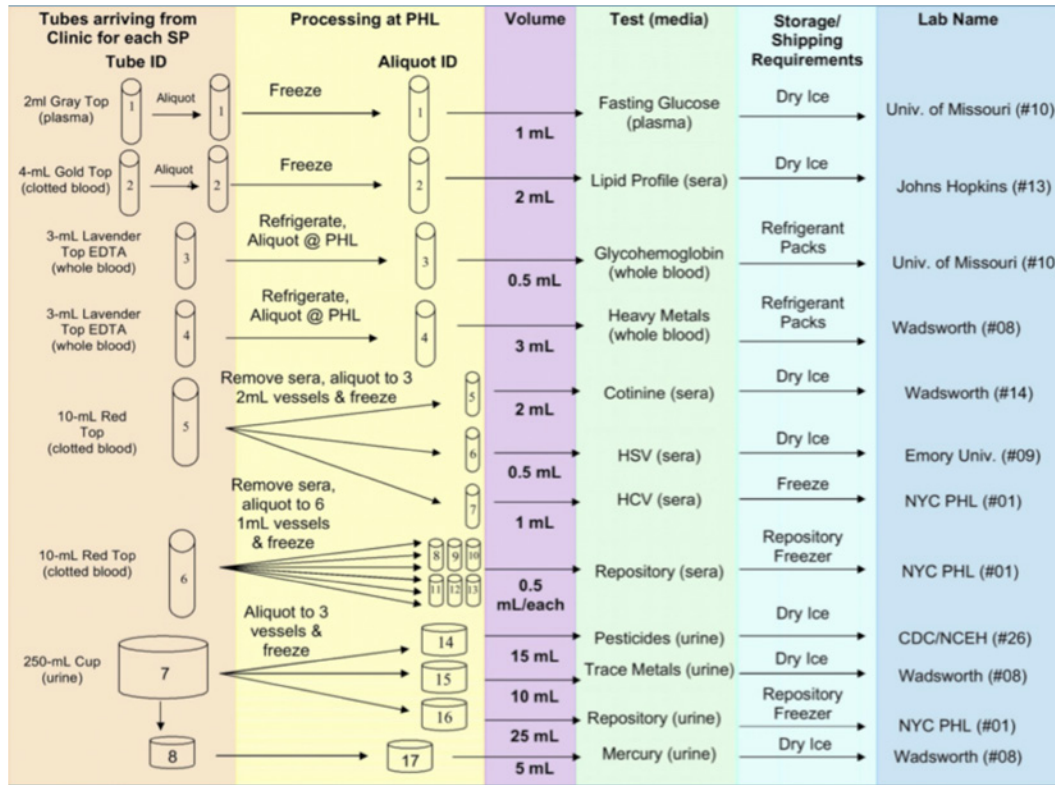
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APPENDICES



APPENDIX I

Specimen Flowchart NYC Hanes Specimen Processing Flowchart



APPENDIX II

IAP2 Public Participation Spectrum (used with permission)

International Association for Public Participation Australasia INCREASING LEVEL OF PUBLIC IMPACT				
INFORM	CONSULT	INVOLVE	COLLABORATE	EMPOWER
Public Participation Goal:	Public Participation Goal:	Public Participation Goal:	Public Participation Goal:	Public Participation Goal:
To provide the public with balanced and objective information to assist them in understanding the problems, alternatives, opportunities and/or solutions.	To obtain public feedback on analysis, alternatives and/or decisions.	To work directly with the public throughout the process to ensure that public concerns and aspirations are consistently understood and considered.	To partner with the public in each aspect of the decision including the development of alternatives and the identification of the preferred solution.	To place final decision-making in the hands of the public.
Promise to the Public:	Promise to the Public:	Promise to the Public:	Promise to the Public:	Promise to the Public:
We will keep You informed.	We will keep you informed, listen to and acknowledge concerns and provide feedback on how public input influenced the decision.	We will work with you to ensure that your concerns and aspirations are directly reflected in the alternatives developed and provide feedback on how public input influenced the decision.	We will look to you for direct advice and innovation in formulating solutions and incorporate your advice and recommendations into the decisions to the maximum extent possible.	We will implement what you decide.
Example Techniques to Consider:	Example Techniques to Consider:	Example Techniques to Consider:	Example Techniques to Consider:	Example Techniques to Consider:
• Fact sheets • Web Sites • Open houses	• Public comment • Focus groups • Surveys • Public meetings	• Workshops • Deliberate polling	• Citizen Advisory Committees • Consensus building • Participatory decision-making	• Citizen juries • Ballots • Delegated decisions

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APPENDIX III

Biomonitoring Program/Project Checklist

PHASE	TASK
PLANNING	Establish goals to guide planning decisions
	☐ Conduct a needs assessment, define goals and objectives for the program, and draft a timeline
	☐ Develop administrative rules by using existing rules as templates
	☐ Secure funding through legislation or competitive grant applications
	Selection of target population
	☐ Identify populations at risk, potential adverse health effects, and/or opportunities for using for surveillance or evaluation of efforts to reduce exposure
	☐ Consider ethical factors, e.g., age and ability to consent
	☐ Develop sampling plan, e.g., convenience sample, stratified random sample
	☐ Identify resources required to access target population
	☐ Identify a comparison population for appropriate biological reference values if they do not exist
	Identify stakeholders and partners
	☐ On the basis of a thorough needs assessment, identify potential partners
	☐ Define the roles and responsibilities of relevant stakeholders and partners
	☐ Determine levels of communication and involvement with partners and stakeholders
	Engage the community
	☐ Determine goals of community engagement as influenced by overall program goals
	☐ Assess physical and informational needs of staff who will conduct community engagement
	Selection of chemical analytes
	☐ Identify appropriate analytes in collaboration with all partners
	☐ Consider sensitivity and LOD/MDL for comparing background exposure vs. exposure of interest
	☐ Consider specificity especially if metabolites share common parent compounds
	☐ Consider practicality and feasibility; consult with laboratory experts
	☐ Consider availability of reference ranges for results interpretation
	☐ Consider pharmacokinetics, which will dictate matrix used and sample management
	☐ Consider health relevance; analytes should be pertinent to exposure of interest and health outcome of concern

APPENDIX III

Biomonitoring Program/Project Checklist

PHASE	TASK
PLANNING (continued)	Plan for biospecimen collection
	☐ Develop protocols, quality assurance, and control measures
	☐ Determine chemical analyte and relevant biomatrix
	☐ Confer with laboratory colleagues to determine biospecimen volume, collection materials, procedures, handling, storage, and transport
	☐ Determine relative ranking of chemical analyses in case of low specimen volume
	☐ Generate specimen collection diagram
	Plan for other data collection activities and instruments
	☐ Consider conducting surveys for participants who provide biospecimens
	☐ Consider collecting demographic information that may affect exposure conditions
	☐ Consider collecting diet information to account for dietary intake of chemical of interest
	☐ Consider collecting data from administrative records, e.g., medical or employment
	☐ Consider collecting geographic information, e.g., residential address or census block
	☐ Consider collecting environmental and non-human biological samples for contaminants
	☐ When possible, conduct usability testing or focus groups to get feedback on materials before they are used
	Develop a written protocol
	☐ Refer to the protocol development section of the CSTE biomonitoring guidelines document entitled <i>"Biomonitoring in Public Health: Epidemiologic guidance for state, local, and tribal public health agencies"</i> for a detailed list of elements that belong in a biomonitoring protocol (including IRB submission/approval)
	☐ Determine eligibility criteria
	☐ Ensure the protocol developed is specific to the study population
	☐ Identify ethical considerations and develop informed consent forms
	☐ Consider specimen banking concerns, and if needed, include in informed consent
	☐ Consider concerns about communicating individual results to participants

APPENDIX III

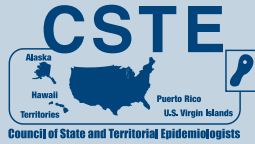
Biomonitoring Program/Project Checklist

PHASE	TASK
IMPLEMENTATION	Develop process for data management
	☐ Develop ID or barcode system to preserve confidentiality and private data on individuals
	Collect biospecimens
	☐ Ensure documentation of biospecimen collection and transport
	☐ Determine system for labeling, receiving, and tracking biospecimens at the laboratory
	☐ Consider biorepository and long-term storage issues
	Conduct laboratory analysis of biospecimens
	☐ Work with partners to identify standard laboratory analytical methods
	☐ Consult with CDC laboratories and/or APHL, as needed
	Conduct statistical analysis of biospecimens
	☐ Conduct descriptive and exploratory analyses to determine distributions and outliers
	☐ Consider how non-detects will be managed, e.g., LOD/ $\sqrt{2}$
	Interpret results
	☐ Consider limitations and difficulty attributing exposure to a particular source
COMMUNICATING RESULTS	☐ Consider chemical's half-life and pharmacokinetics
	☐ Determine the relevance to health, i.e., how these chemical levels are linked to previous or existing health conditions and future risk
	☐ Compare results to a reference population
	Communicate results of analyses with participants
	☐ Define levels of concern, comparison populations, and communication methods
	☐ Consider triggers for communicating results to individual participants
	☐ Consider timing of results communication, especially if medical follow-up is indicated
	☐ Where possible, conduct usability testing or focus groups to get feedback on materials before implementing them

APPENDIX III

Biomonitoring Program/Project Checklist

PHASE	TASK
COMMUNICATING RESULTS (continued)	Communicate results of analyses with affected communities and other stakeholders
	☐ Describe study objectives
	☐ Explain study methods
	☐ Interpret findings by referencing studies of comparable populations; communicating impact of results; and identifying actions individuals, communities, and public health agencies can take to reduce exposure
	☐ Define clear, concise message about the findings
PUBLIC HEALTH ACTION	☐ Report findings, e.g., what we found, what we learned
	Use biomonitoring to inform public health action
	☐ Use biomonitoring results to inform new policies and preventive actions
	☐ Use biomonitoring results to evaluate exposure reduction actions



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