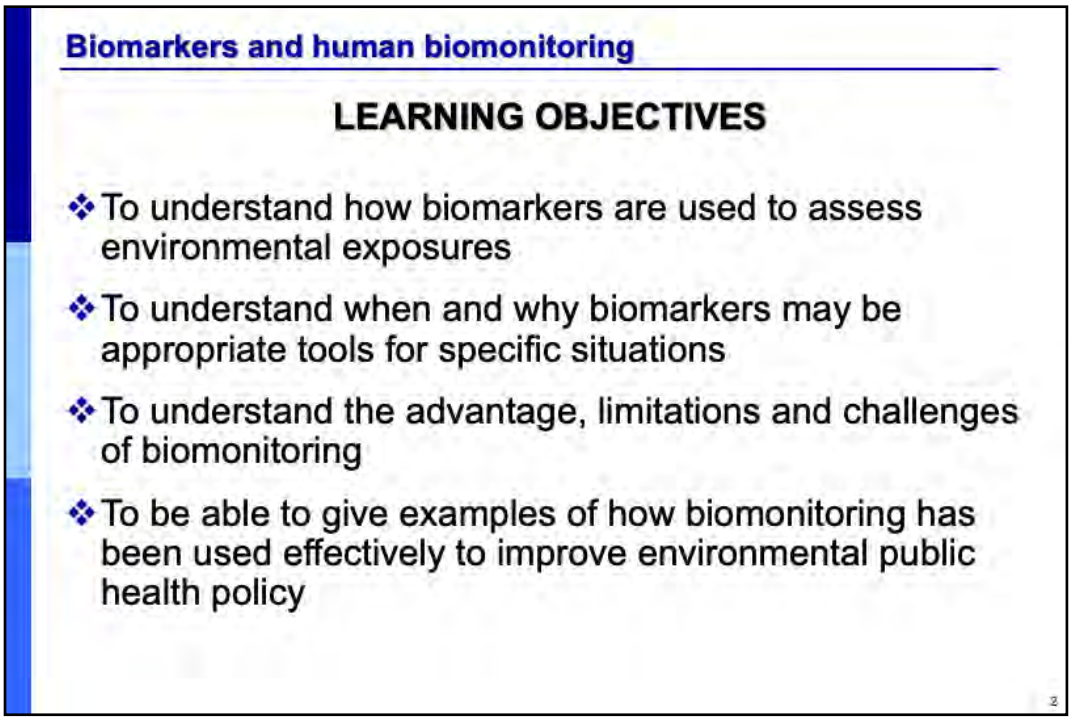
<<NOTE TO USER: Please add details of the date, time, place and sponsorship of the meeting for which you are using this presentation in the space indicated.>>

<<NOTE TO USER: This is a set of slides from which the presenter should select the most relevant ones to use in a specific presentation. These slides cover many facets of the problem. Present only those slides that apply most directly to the local situation in the region.>>


Biomarkers and human biomonitoring
LEARNING OBJECTIVES
To understand how biomarkers are used to assess environmental exposures
To understand when and why biomarkers may be appropriate tools for specific situations
To understand the advantage, limitations and challenges of biomonitoring
To be able to give examples of how biomonitoring has been used effectively to improve environmental public health policy
2

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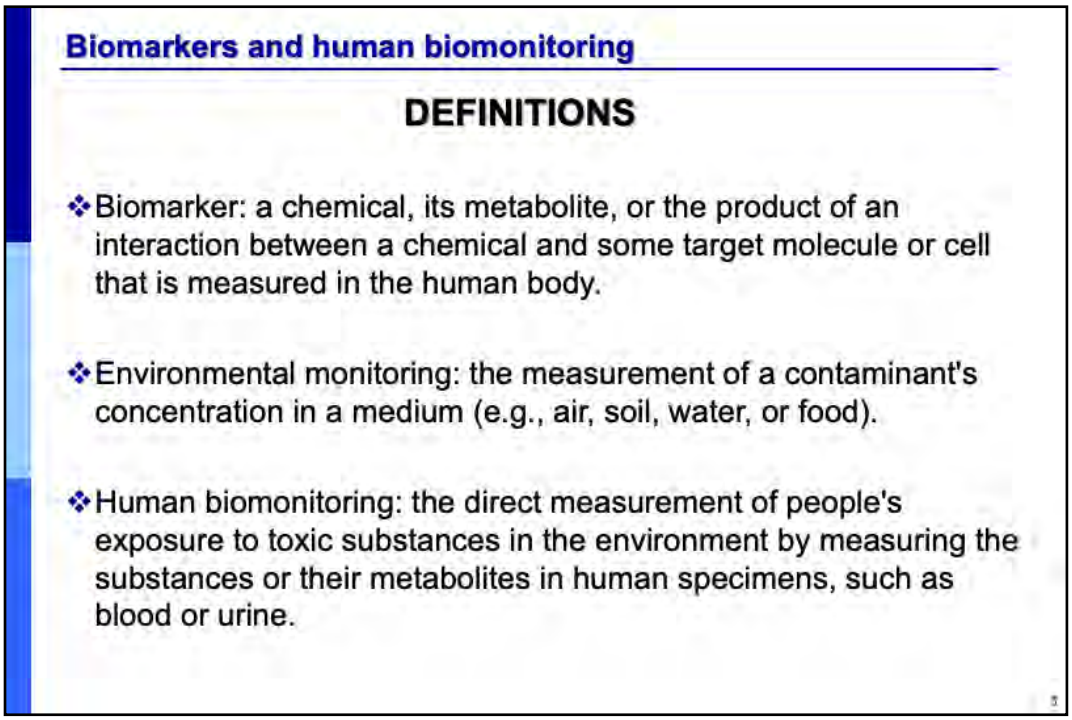

For clarity here are the definitions of three major concepts.

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While this talk concentrates on biomarkers and human biomonitoring, it is notable that it is also common to biomonitor other species – for example measuring methylmercury in fish is also biomonitoring as is measuring atrazine in frogs. Measuring contamination in other species can assist in developing both exposure risks for humans and information on toxicities.

Refs:

Definition for biomarker:

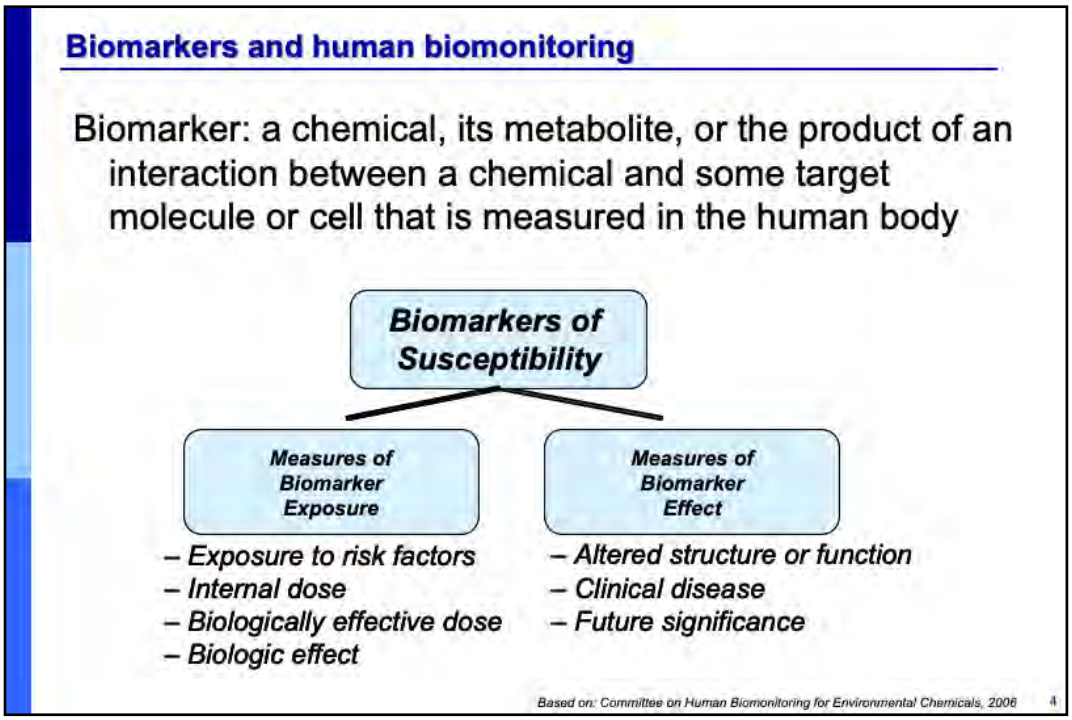
•WHO. Environmental Health Criteria 237. Principles for evaluating health risks in children associated with exposure to chemicals. *WHO*, 2006.

Definition for environmental monitoring:

•Agency for Toxic Substances & Disease Registry. Case studies in environmental medicine. *Pediatric Environmental Health*, 2002, appendix F: 83. Available at *www.atsdr.cdc.gov/csem/pediatric/appendixf.html#env* – accessed March 2011

Definition for human biomonitoring:

•Centers for Disease Control and Prevention. National Biomonitoring Program. CDC. Available at *www.cdc.gov/biomonitoring/* - accessed March 2011.



The advantage of biomonitoring – the measurement of a chemical or its metabolite in the body – is that it represents an actual measure of integrated exposures via all routes of exposure which is not susceptible to assumptions or models.

Biomarkers are useful because they have the potential to measure the actual, integrated internal dose from all routes of exposure.

<<READ DEFINITION>>

There are several different categories of biomarkers, that measure exposure, effect and susceptibility (definitions below). Each is useful for answering different questions. In this presentation we are most concerned with biomarkers of exposure. In fact, there can overlap as the chemical makes its way down the metabolic cascade and into the body systems.

<<REVIEW CONTINUUM IN GRAPHIC>>

A biomarker of exposure: a chemical, its metabolite, or the product of an interaction between a chemical and some target molecule or cell that is measured in the human body (e.g. cotinine in blood or urine for second-hand tobacco smoke, benzene metabolites in urine for traffic-related pollution).

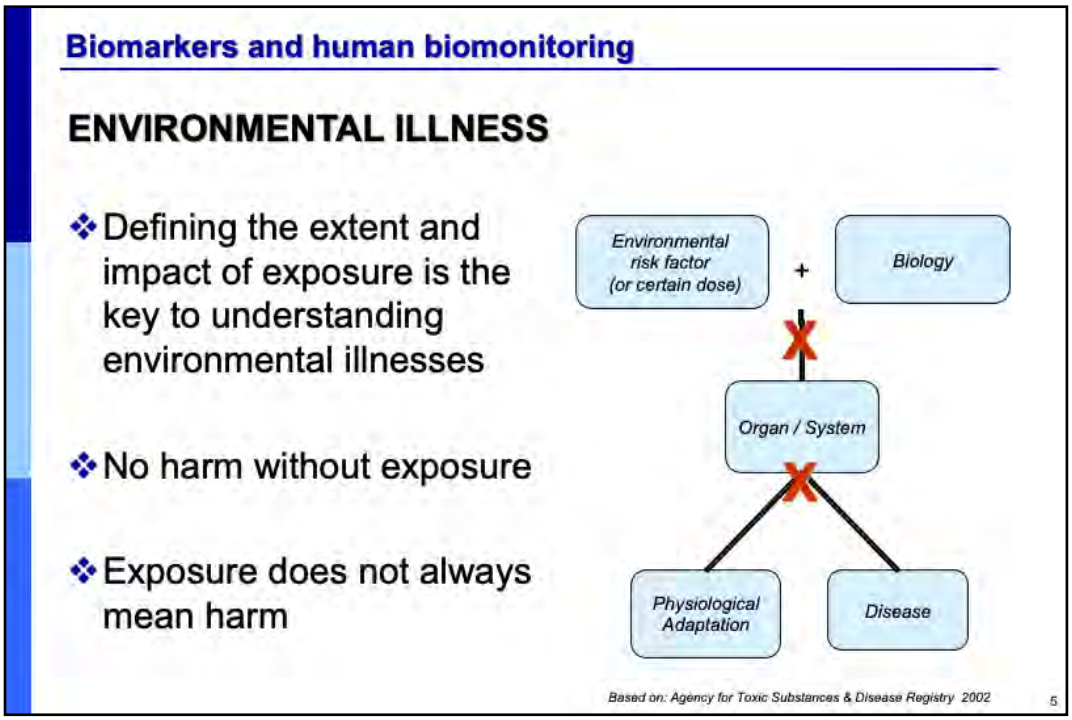
A biomarker of effect: A measurable biochemical, physiologic, behavioral, or other alteration in an organism that, depending on the magnitude, can be recognized as associated with an established or possible health impairment or disease (e.g. DNA adducts).

A biomarker of susceptibility: An indicator of an inherent or acquired ability of an organism to respond to the challenge of exposure to a specific chemical substance. (e.g. G6PD deficiency)

Ref:

•Committee on Human Biomonitoring for Environmental Toxicants, National Research Council. Human biomonitoring for environmental chemicals. *National Academies Press*, 2006.

Image based on: Committee on Human Biomonitoring for Environmental Toxicants, National Research Council. Human biomonitoring for environmental chemicals. National Academies Press, 2006.



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Understanding environmental illness requires knowledge of the entire cascade of events from the release of an environmental contaminant through absorption, actions and damage within the body and the development of disease. Defining the extent and impact of exposure is a central element of understanding environmental disease.

Diagram: Environmental contamination and biological exposure will lead to absorption of an internal dose, followed by distribution, metabolism and excretion. Upon organ contact, either physiological adaptation will take place or a disease will develop.

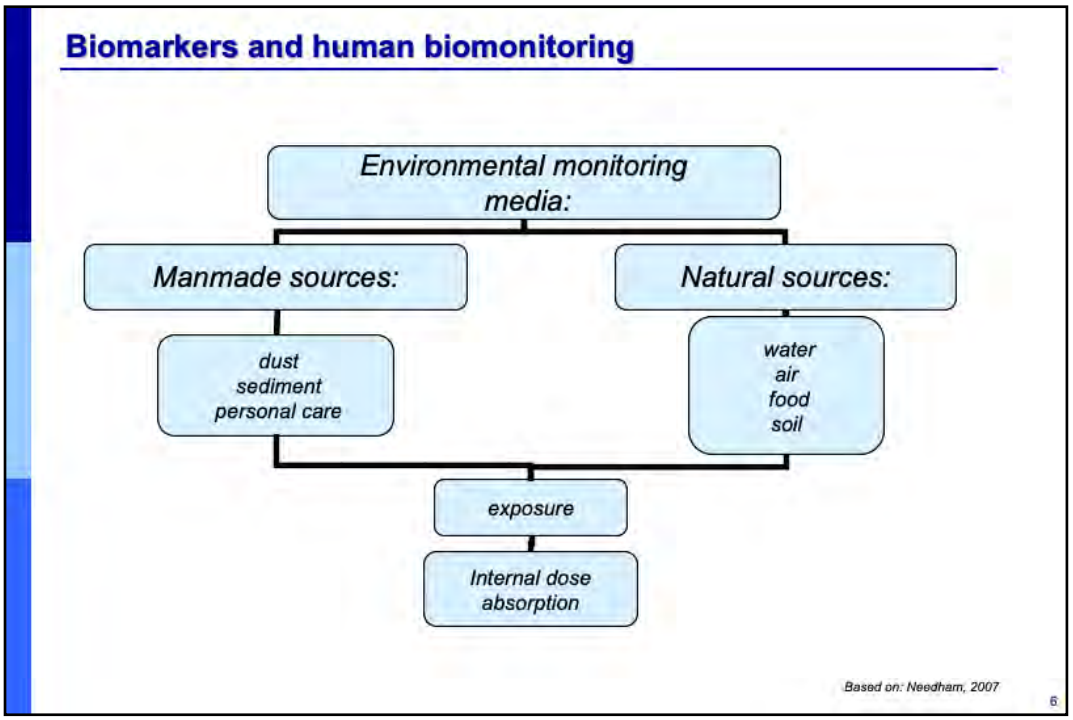
<<CLICK FOR ANIMATION>>

In simple terms, there can be no harm without exposure, but

<CLICK FOR ANIMATION>>

Exposure alone is not enough to prove or ensure harm.

Image based on: Agency for Toxic Substances & Disease Registry. Exposure-disease model. Case studies in environmental medicine. Pediatric Environmental Health, 2002, appendix A. Available at www.atsdr.cdc.gov/csem/pediatric/appendixa.html – accessed March 2011



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The top portion is the realm of environmental monitoring – the measurement of pollutants and their breakdown products in various environmental media such as air, water, food, soil, and manmade objects.

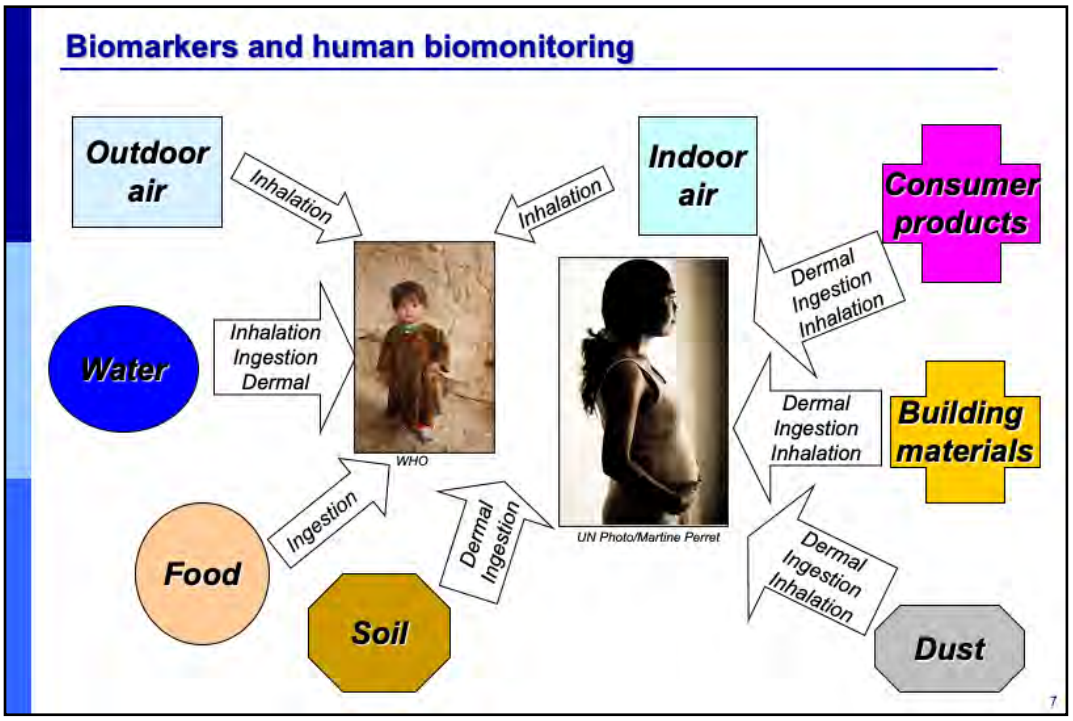
The lower portion is the realm of biomonitoring – the direct measurement of contaminants in the body.

In the middle, bioavailability modifies exposure routes or pathways – that is some contaminants are so tightly bound to their environmental medium that they are not available to be absorbed into the system by specific routes of exposure, which brings us finally to

EXPOSURE leading to absorption which is the key step which is often one of the most difficult to characterize.

This presentation will briefly describe biomarkers and environmental monitoring and exposure modeling, but is mostly concerned with the increasingly important tool of biomonitoring for understanding exposures.

Image based on: Needham LL et al. Uses and issues of biomonitoring. International Journal of Hygiene and Environmental Health, 2007, 210:229-238.



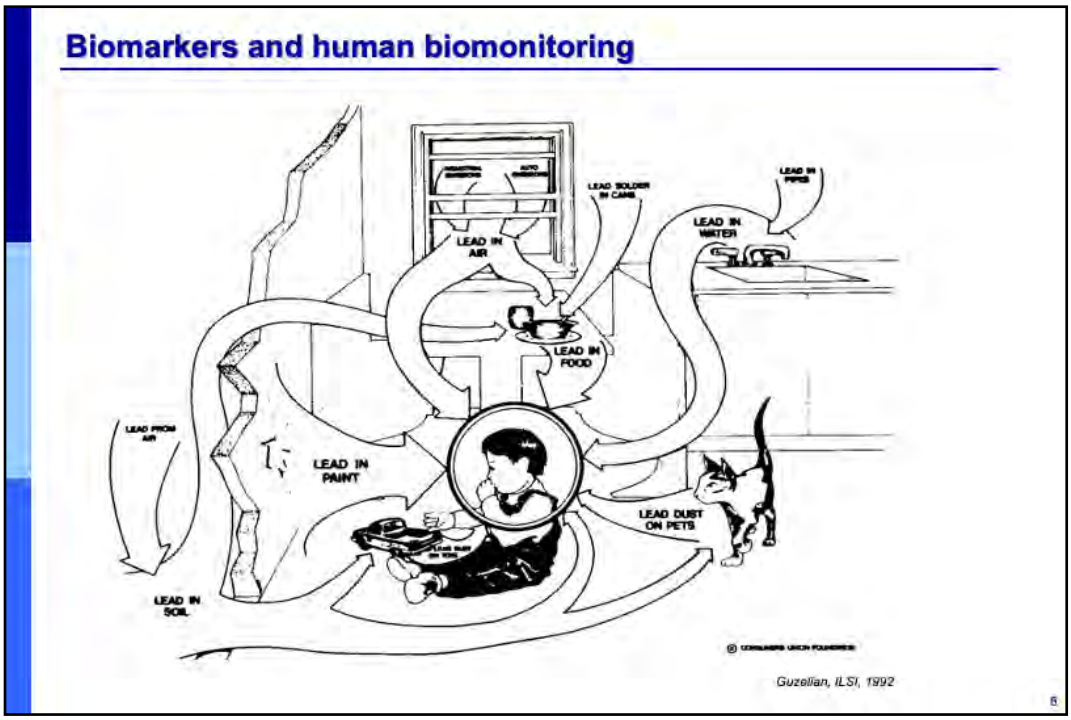
Environmental monitoring, also known as ambient monitoring, is the measurement of chemical substances in media (or matrices) like indoor and outdoor air, water, food, soil, dust, consumer products, building materials, etc. This is critical to understanding the sources of exposure, but is incomplete without information about

exposure pathways. In order to predict internal dose, complex exposure models are constructed which involve applying sets of standardized assumptions about activity levels, dietary choices, behavior, etc.

<<NOTE TO USER: The image of the pregnant woman is intentional. When considering exposures in children, it is always important to consider the "parenteral" exposure from mother to fetus. Mothers absorb environmental toxicants via the standard routes of inhalation, ingestion and dermal absorption, then the chemicals are transformed and many reach the fetus via the blood stream (some by diffusion across the placenta). These are qualitatively unique exposures which may pose serious risks to the developing fetus depending upon internal dose and timing.>>

Right image: United Nations. Martine Perret.

Left image: WHO. Afghanistan, 2010.



This picture shows the many different pathways by which a child can be exposed to environmental chemicals, in this case lead. Building exposure models based upon ambient monitoring requires making many assumptions about routes of exposure including quantitative importance of each route of exposure and rates of absorption into the body from each route. This is difficult for adults, but even more complex for children who are constantly growing and changing, have changing behavior patterns and live in changing living zones based upon size and activity. Exposure modeling for children requires utilization of a multi-lifestage approach and has multiple sources of potential error and uncertainty. Regulatory agencies and researchers are continuously revising and improving upon complex and extensive exposure models but there is always both uncertainty and error attached to exposure estimates generated with models.

Ref:

•WHO. Environmental Health Criteria 237. Principles for evaluating health risks in children