RESEARCH BRIEF

Biomarkers of effect: What you need to know

HOW MANY TYPES OF BIOMARKERS DO WE KNOW?

Biomarkers are generally classified into three groups:

1. **Biomarkers of exposure**, which evaluate in biological samples taken from an organism the presence of an exogenous chemical, its metabolite, or the product of interaction between the xenobiotic and a target molecule or cell (e.g., urine levels of bisphenol A and phthalates metabolites or DNA abducts).

2. **Biomarkers of susceptibility**, which serve as indicators of the particular susceptibility of an individual organism to exposure to a xenobiotic (e.g., specific genetic polymorphisms).

3. **Biomarkers of effect**, which indicate the biochemical, physiological, or behavioral changes produced in the organism due to exposure to exogenous chemicals; they may be associated with an adverse health effect or disease (e.g., circulating hormone levels).

WHAT ARE BIOMARKERS OF EFFECT?

Biomarkers of effect, also called **biomarkers of biological response**, are observable and quantifiable biological changes in an organism that result from exposure to chemical contaminants. These biological changes can occur on biochemical, molecular, or cellular components or on processes, structures, or functions and may be associated with the development of diseases. These changes also provide information **in human biomonitoring (HBM)** studies on the magnitude of the body's response to chemical compounds, at a given time point during the process that connects exposure disease. Therefore, they can also be evaluated as indicators of a physiological or pathological biological process.

Biomarkers of effect can be objectively measured in different human biological samples, mostly in blood (serum) and urine.

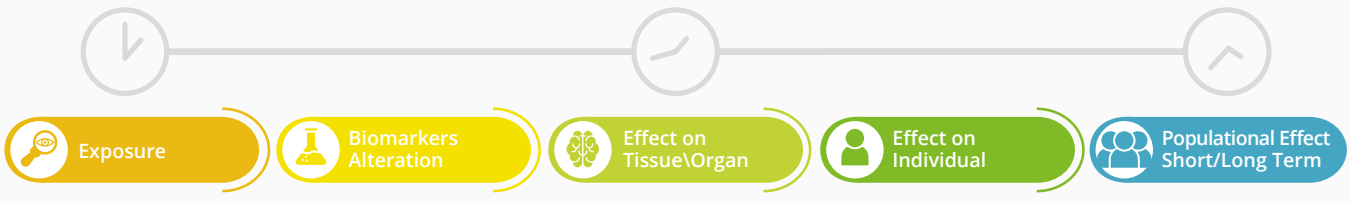
WHAT ARE BIOMARKERS OF EFFECT USED FOR?

There has been a marked increase in the use of effect biomarkers over the past few decades.

They are used to measure the interaction between a living organism and a xenobiotic (chemical, physical, or biological agent) and are particularly useful in assessments of the risk of developing a given disease.

Biomarkers of effect are important for establishing the relationship between exposure to contaminants and adverse health effects. These biomarkers provide information that allows the **minimization of adverse effects**, the **implementation of effective preventive interventions**, and the **identification of individuals who are more susceptible to particular chemical compounds.**

Figure 1: Effect biomarker timeline: From exposure to populational effect



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This research brief was produced by the University of Granada (Spain), School of Medicine, Environmental Medicine Group.

For more information please contact:
Prof. Mariana Fernández: marieta@ugr.es
HBM4EU coordinator: HBM4EU@uba.de
Knowledge Hub: HBM4EU@eea.europa.eu

UNDERSTANDING BIOMARKERS OF EFFECT

We are all familiar with effect biomarkers without knowing it.

Effect biomarkers are part of standard medical practice, allowing diagnoses to be established and permitting the evaluation of intervention programs, treatments and disease progression as well as the response to different therapies. They are also very important for risk assessment and for the development of new chemical compounds.
Many routine blood tests evaluate different effect biomarkers, including the determination of: creatinine, to assess renal function; bilirubin and transaminases, to assess liver function; and thyroid hormones, to analyze thyroid function.

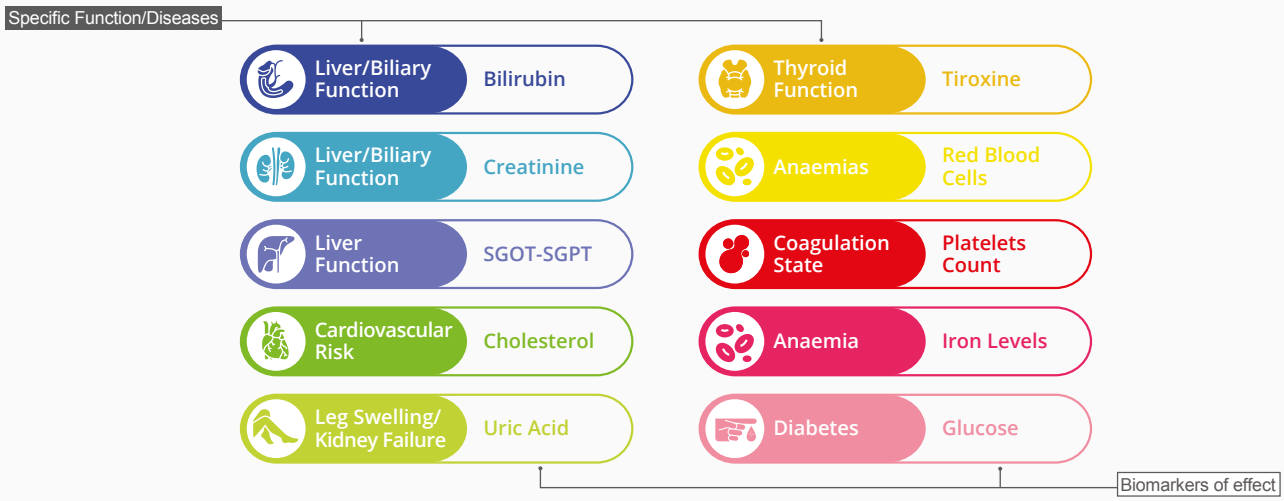
WHAT DOES A BIOMARKER OF EFFECT TELL US ABOUT OUR HEALTH?

An important advantage of effect biomarkers is that they can be used to determine how each person responds to exposure to a chemical compound. They therefore allow us to identify variations among individuals and also within the same individuals over time or as a function of particular physiological conditions.

Another important characteristic of an effect biomarker is the ability to detect changes in the organism before the development of a given adverse effect or disease. This early detection of alterations may help to implement more effective preventive actions.

EFFECT BIOMARKERS THEREFORE PROVIDE VALUABLE INFORMATION ON THE HEALTH STATUS OF INDIVIDUALS

Figure 2: Each biomarker of effect (e.g. iron, thyroxine, glucose or enzyme levels, and cell counts), easily quantified in a blood sample, allows for the identification of a specific cell or organ function.



BIOMARKERS OF EFFECT IN HUMAN BIOMONITORING PROGRAMS

Human biomonitoring involves the measurement of chemical concentrations in small samples of blood, urine, or hair in order to evaluate the total amount of a chemical in the body (internal dose), representing the input from all possible sources. Samples are preferably taken from large numbers of people to obtain a picture of the exposure of a population.

The identification of a chemical contaminant in a human sample implies a risk but does not demonstrate an adverse effect per se. However, if this exposure is associated with biological change, evaluated with an effect biomarker, it is possible to establish the relationship between the exposure and the biological alteration and between the dose and the observed response.

Effect biomarkers therefore offer an improvement in the information generated by human biomonitoring programs and help to evaluate the risk posed by these chemical compounds alone or in combination.

DOES HBM4EU INCLUDE BIOMARKERS OF EFFECT?

The Human Biomonitoring Initiative in Europe (HBM4EU) is looking at health effects from chemical exposure, and will use and combine data on biomarkers of exposure to chemical contaminants of particular interest (e.g., phthalates, bisphenols, heavy metals) and on biomarkers of effect, together with information on mechanisms of action from experimental studies.

Before the implementation of effect biomarkers in human biomonitoring programs, it is necessary to carry out a careful selection and validation process. The biomarkers should allow for the reliable and simple identification and measurement of specific biological changes produced by the chemical compound of interest, and the measurements must be accurate, precise, reproducible, and easy to understand.

Biomarkers of effect will be investigated in human observational studies. HBM4EU will first focus on specific health problems in relation to reproduction, neurodevelopment, and behavior.

HOW CAN THE INFORMATION OBTAINED IN THE HBM4EU INITIATIVE BE USED?

Biomarkers of effect investigated under HBM4EU may help to understand the mechanisms underlying the effects of environmental contaminants on human health.
Recent investigations appear to demonstrate that the correct measurement of both the exposure and its early as well as clinical effects is crucial to establish a causal relationship between exposure and disease.

Information on biomarkers of effect in population studies will be combined with mechanistic toxicological information reported in experimental studies and with information from published Adverse Outcome Pathways (AOPs), an advanced framework supported by the Organisation for Economic Co-operation and Development (OECD), the European Commission (EC) and United Stated Environment Protection Agency (US EPA), linking biomarkers of exposure with health outcomes.

In addition, interesting new research possibilities have been opened up by the development of new biomarkers of effect using genomic, epigenomic, transcriptomic, lipidomic, proteomic, and metabolomic information (-omic biomarkers).

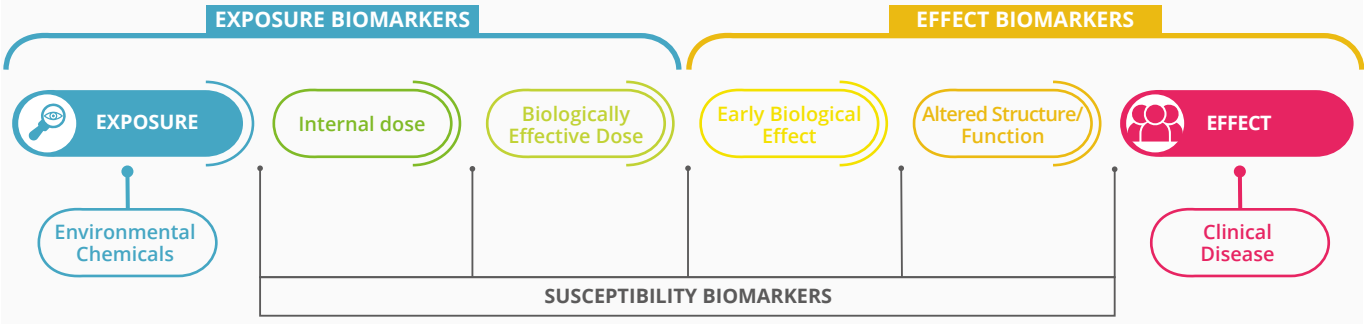
HOW IS THE EUROPEAN UNION PROTECTING THE CITIZENS?

The HBM4EU initiative is evaluating the concentrations of environmental chemical compounds and their metabolites (biomarkers of exposure) in biological samples in different European populations. These biomarkers will be complemented with information on biomarkers of effect in order to improve our understanding of the relationship between exposure to chemical contaminants and their adverse effects on human health.

Increased knowledge of possible risks to human health will result in more effective preventive policies to reduce exposure to the contaminants of greatest concern.

Internal dose: The amount of chemical absorbed by the body (measured in a biological sample).
Biological effective dose: The amount of chemical that produces a biological change in the organism.
Early biological effect: The first biological change after exposure to the chemical.
Late biological effect: Alteration in structure/function of the organism that ultimately triggers an adverse health effect or clinical disease.

Figure 3: Link between chemical exposure, internal dose, biomarkers (exposure and effect) and the effect leading to a clinical disease



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