Uses of human biomonitoring data in risk assessment

Fact sheet series: Topics in risk assessment of substances under the *Canadian Environmental Protection Act, 1999* (CEPA 1999)

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Human biomonitoring surveys

Biomonitoring is the measurement of substances as parent compounds, their metabolites or their reaction products in human tissues and fluids. These measurements are usually taken from blood and urine and sometimes in other tissues and fluids such as breast milk. These measurements are often referred to as biomarkers of exposure. Biomonitoring data represents exposure from multiple sources. This includes indoor and outdoor air, soil, dust, water, food and/or potential exposures from products used frequently by consumers, such as cosmetics and health products. Biomonitoring data also incorporates exposures from all routes (oral, dermal and inhalation). These measurements may allow for direct and more precise assessment of the distribution of risk in a given population. The measurements incorporate individual variability in exposure and the movement of a substance in the body (absorption, distribution, metabolism and excretion) compared to estimating each separate exposure scenario (for example, environmental media, food, cosmetics) through modelling. Although biomonitoring data may provide an estimate of overall exposure to a substance, its presence in the body does not necessarily mean that it is causing harm. Similarly, absence of a substance measured in blood or urine, does not necessarily mean the individual was not exposed to a given substance.

Biomonitoring data does not identify the sources of exposure (source attribution) or how long a substance has been in the body. There are also limitations in identifying the duration of exposure, especially for substances with longer half-

lives. Careful consideration of the study design, biomarker selection, toxicokinetics, toxicology, and populations examined are critical when interpreting and communicating biomonitoring data. When interpreting biomonitoring results it is important to take into consideration background levels, complex metabolic interactions and/or difficulty correlating measured concentrations of multiple metabolites to exposures from a single substance.

In Canada, biomonitoring data in the general population is being collected on an ongoing basis since 2007 as part of Statistics Canada's Canadian Health Measures Survey (CHMS). Canadian biomonitoring data are also available in various subpopulation studies, such as the Maternal-Infant Research on Environmental Chemicals (MIREC) study, the Alberta Biomonitoring Program, the First Nations Biomonitoring Initiative (FNBI) and the Northern Contaminants Program (NCP). Other population studies such as the United States National Health and Nutrition Examination Survey (NHANES) are also available.

Biomonitoring and risk assessment

Human health risk assessments often use predictive models or algorithms to estimate potential exposure of Canadians to substances. Measurements such as the levels of a substance in the environment (air, water, dust) and the concentration of a substance found in products are used to feed into the models and algorithms. Various assumptions are applied when estimating substance exposure to the general or susceptible populations. These include assumptions about the route of exposure, intake rate, fraction that is absorbed or metabolised, and the potential sources of exposure. These assumptions may add uncertainty to the risk characterization, especially for substances that are used in many different ways. In some circumstances, the use of human biomonitoring data may provide a more accurate estimate of exposure for risk characterisation relative to use of predictive models. Further, biomonitoring data incorporate individual variability in exposure and the movement of substances in the body (kinetics) through absorption, distribution and excretion.

Human biomonitoring data can be used in human health risk assessments in a number of ways, including:

- for quantitative and/or qualitative exposure and risk characterization
- for tracking trends in how levels of substances are changing in the general population over time
- for identifying subpopulations with higher exposure levels, such as by sex or age

- for comparing estimates of exposure derived from predictive models (for example, dietary intakes derived using monitoring data in foods and dietary consumption rates)

The use of human biomonitoring data in a risk assessment is feasible if it is determined that a biomarker of exposure is specific and sensitive, such that concentrations measured reflect exposure to the substance of interest. In addition, biomonitoring data generated from outside Canada may also be used. These data would be evaluated on a case-by-case basis.

Methods for using biomonitoring data

Human biomonitoring data can be interpreted using several different methods, including comparison of animals/humans data and more recently through the use of reverse or forward dosimetry.

Qualitative approaches may be considered for using biomonitoring data in risk assessment in various ways. Such approaches have been used in the existing substances risk assessment program for substances which are detected in the general population at very low frequencies and are, accordingly, considered to be of low concern to human health. This approach was published in the biomonitoring-based approach 1 science approach document. When biomonitoring data indicates that the general population has limited potential exposure or exposure potential is below levels which could result in health effects, the substances are considered to be of low concern. An example of this is found in the biomonitoring-based approach 2 science approach document.

If the concentration found in a specific medium (for example, blood or urine) associated with a critical health effect is known, then concentrations reported in human biomonitoring studies can be compared directly to levels associated with that critical health effect. For example, the risk characterization for perfluorooctanoic acid (PFOA) was based on a comparison of levels of PFOA measured in the whole blood of adults, infants and children with serum levels associated with the development of adverse effects in laboratory animals.

Reverse dosimetry (or exposure reconstruction) has been used in some risk assessments. In reverse dosimetry, internal body measurements (for example, mg/L of a substance or mg/g creatinine) of a given substance from biomonitoring studies are converted to external measurements, in general using kinetic data to estimate daily intake levels (mg/kg/day). For example, the health risk assessment

of triclosan provides details of the application of reverse dosimetry with the use of biomonitoring data.

In forward dosimetry, an external exposure associated with a critical health effect or exposure guidance values (for example, presented in mg/kg bw/day) is converted to an internal dose. For example, forward dosimetry is applied in the derivation of biomonitoring equivalents (BEs). BEs are defined as the concentration (or range of concentrations) of a substance or its metabolites in a biological medium (blood, urine, or other medium) that is consistent, or directly related, with an existing health-based exposure guidance value, such as a reference dose (RfD) or tolerable daily intake (TDI)[Footnote 1]. This quantitative approach may be applicable when there is widespread presence of the substance in the general population and allows a comparison of the biomonitoring data against health-based guidance values or biomonitoring equivalents. For example, a BE approach was used with the Selenium-containing Substance Grouping risk assessment. Forward dosimetry can also be derived using other approaches, such as biokinetic models (models that simulate substance behaviour after it is incorporated into the human body) and simple mass balance approaches. For example, the Government of Canada's risk assessment of cobalt and cobalt-containing substances applied an existing biokinetic model to derive blood equivalent concentrations for comparison with the critical health effects.
In addition to use in risk assessment, biomonitoring data can also be an important tool in substance-based performance measurement. Risk management measures that decrease the levels of substances in the general population would be seen as highly effective. For example, through risk management actions already in place, the levels of lead in the blood of Canadians have declined over 70% since the 1970s.

Advances in the field of analytical chemistry have improved the availability of human biomonitoring data with over 500 substances being monitored in various human biological matrices.

Footnotes

Footnote 1

Hayes et al., 2007