

Exposure Evaluations Through Biomonitoring

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ABSTRACT: *Testing and screening are conducted, in most cases, to support risk assessment. Therefore, any discussion of testing methodologies should take into account not only testing or hazard evaluation, but also exposure evaluation. Although the workshop exposure assessment discussion focused on a biomonitoring approach, an environmental factors approach to exposure assessment is much more broadly used for Toxic Substances Control Act (TSCA) decision-making. The level of detail needed for exposure assessment depends on the type of decisions involved. Exposure assessment may be at a screening level or may involve detailed data collection and analysis, including biomonitoring when the costs are warranted.*

Humans are exposed to chemicals via breathing air, drinking water or bathing, coming in contact with soil, eating food, using consumer products, etc. Exposure assessment is the determination or estimation (qualitative or quantitative) of the magnitude, frequency, duration, and route of exposure, either for a particular exposure scenario, or for up to all known potential exposures to a given chemical. These comments provide an overview of the status of human exposure assessment, how improving exposure screening and assessment and helping to ensure quality and consistency among exposure assessors are key to improving how human risk assessments are performed, other ways to improve the science of exposure assessment, a description of the tiered approach and the use of monitoring to validate modeling.

■ OVERVIEW OF HUMAN EXPOSURE ASSESSMENT

A 1991 National Academy of Sciences, National Research Council report (10) stated that "Exposure assessment is an integral and essential component of . . . risk assessment.... Exposure assessment is an equal partner with toxicology."

Other documents and scientists have noted that exposure assessment is still perhaps the overall weakest link in risk assessment, and has the greatest opportunities for improvement. Therefore, it is important to incorporate its status into any testing and screening review.

Humans are exposed to chemicals via breathing air, drinking water or bathing, coming in contact with soil, eating food, using consumer products, etc. Exposure assessments attempt to assess the degree or magnitude of contact a person has with a chemical, either from a particular route of exposure or exposure scenario, or as a summation of up to all known potential exposures. Qualitative exposure screening tools estimate the likelihood and magnitude of exposure and the nature of potentially exposed populations.

Factors affecting the degree of exposure include the duration and frequency of exposure, the route of exposure (e.g., oral, skin, and inhalation), and the degree of uptake of the chemical from a given route and location on the body (i.e., there can be large differences in body area (e.g., hands versus forehead) skin permeability). Other factors affecting the degree of exposure include human characteristics such as differences in metabolic activation and deactivation of a chemical, differences in age (e.g., adults and children have large differences in the amount of air breathed per minute, the amount of food or liquid consumed per day, body weights, and body surface areas). Even among adults or children as individual

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groups, there can be large differences in physiological parameters such as body weight and consumption of food.

The degree of contact with a chemical is driven by the known (i.e., measured) or suspected concentration(s) of a chemical in the media being assessed. Analytical measurements of the medium of interest yield direct values for use in exposure assessments. Biomonitoring of body fluids (e.g., urine, blood, or exhaled air) or body parts (e.g., hair or fingernails) can be used in the exposure assessment (see below for further discussion). Various modeling approaches can be used to factor-in a chemical's stability, home air changeover rates, weather conditions, the distance from the source of exposure to the potentially exposed subject, or other information.

Improving exposure screening and assessment, and helping to ensure quality and consistency among exposure assessors, are key to improving how human risk assessments are performed:

In recent years, great strides have been made toward improving the science of exposure screening and assessment, both in the values and approaches used, and in helping to ensure consistency and quality among exposure assessors (13, 14, 15). Current US Environmental Protection Agency (EPA) efforts include revising the Exposure Factors Handbook, development of additional resource and guidance documents such as the "Residential Exposure: A Source Book" cooperative effort between EPA, the Society for Risk Analysis, and the International Society of Exposure Analysis, and the "THERdbASE" (Total Human Exposure Risk Database and Advanced Simulation Environment) cooperative agreement between EPA and the University of Nevada, Las Vegas. The latest version of THERdbASE is available to exposure assessors around the world via the Internet's World Wide Web (<http://eeyore.lv-hrc.nevada.edu>) as a downloadable set of files. Once the files are downloaded, exposure assessors are able to model a wide variety of possible exposures using data they can input and data available from several THERdbASE databases (e.g., food consumption patterns,

physiological parameters, human activity patterns, and chemical properties).

Other recent noteworthy efforts helping to ensure quality and consistency include those of the European Centre for Ecotoxicology and Toxicology of Chemicals (1, 3, 4, 7, 8, 11)

■ WAYS TO IMPROVE EXPOSURE SCREENING AND ASSESSMENT

Two recent publications in particular have discussed improvements to exposure screening and assessment techniques. Whitmyre et al. (16) noted the following potential improvements:

- use of more appropriate exposure default values;
- incorporation of time-activity data;
- the use of reasonable exposure scenarios;
- the use of stochastic or probabilistic approaches;
- use of bivariate analysis;
- use of less than lifetime exposure; and
- incorporation of physiological considerations relevant to absorbed dose estimation.

Whitmyre et al (16) also discussed other ways to improve the exposure assessment process, and identified key research needs.

Paustenbach (12) presented several "lessons learned" in the United States about how to improve exposure assessments. They include:

- avoid too much emphasis on risk estimates for the maximally exposed individual (MEI);
- evaluate the uptake (absorbed dose) for both the 50% and 95% persons;
- avoid repeated use of conservative or worst-case assumptions. Incorporate Monte Carlo techniques whenever possible;
- ensure a proper statistical analysis of environmental data;
- conduct sensitivity analysis to understand fragility of dose estimates;
- understand the role of environmental fate when estimating exposure;
- validate the reasonableness of the exposure estimates;

- consider using biological monitoring to confirm exposure estimates; and
- consider all indirect pathways of exposure.

■ A TIERED APPROACH: ESSENTIAL FOR SOUND RESOURCE ALLOCATION

Many companies, regulatory agencies, and others use a tiered approach to risk assessment and its components, such as exposure assessment. Iterations proceed from low effort, inexpensive first-cut evaluations to increasingly complex, costly and data intensive assessments. The appropriate level of exposure assessment, whether preliminary, qualitative, or quantitative, is determined by the nature of the decisions to be made. Iterations would be increasingly detailed with the specific approach selected at each iteration or tier being determined by considering the decision-making needs, available resources, existing data, and other factors.

A preliminary exposure screening is frequently used to set priorities for testing, product development or regulation. This may be simply a volume cut as an exposure surrogate, or it may involve very rough exposure scenarios quantifying the likelihood, of some exposure, but not the magnitude. Although still a preliminary screen, consideration of factors such as likelihood, magnitude, and nature of exposed population can assist in obtaining the most benefit from decisions for testing, regulatory consideration, or other expenditures. Such an initial exposure assessment may be designed to determine whether potential for exposure exists. It may be based on available public, government, or company data to support initial development or risk assessment activity, and to identify key data needs and areas of uncertainty to be addressed later.

Later iterations, i.e., detailed exposure assessments, are generally conducted by one of three approaches: predictive, direct, and reconstructive. The predictive approach estimates exposures based on modeling of a chemical's transport to the receptor and transformations resulting from environmental fate processes, as well as on knowledge of activities that bring the receptor

organism into contact with the chemical. The direct approach attempts to quantify exposure while it is taking place by measuring concentration of the agent in the media of contact, e.g., air in the breathing zone. The reconstructive approach back-calculates exposure based on concentrations of a chemical or a chemical's metabolite in biological tissues, fluids, or exhaled breath.

Use of the reconstructive method concurrently with model development for the predictive method enhances future optimization and improves confidence in modeling results. It is useful to compare biomonitoring results to modeling results to validate or confirm the modeling approach, assumptions, and parameter values. Publications discussing biomonitoring and model validation are National Academy of Sciences (9) and US EPA (14). As predictive modeling is less costly and time-consuming than biomonitoring, validation studies increase assurance of effective resource deployment.

These later iterations involve an increase in sophistication in exposure assessment techniques as required to support a particular level of decision-making. Key in this activity is the judgment of the risk assessment experts about how much information is needed at any given time in the product development or risk assessment cycle, along with expert judgment about when enough risk assessment-related work has been done to support, for example, commercialization of the chemical and the resulting potential for human and environmental exposures. References discussing the tiered approach to human risk assessment for chemical exposures include Hakkinen and Leep (6), Jayjock and Hawkins (8), European Centre for Ecotoxicology and Toxicology of Chemicals (3), European Commission (4), and Organization for Economic Cooperation and Development (11). From a resource allocation standpoint, it is important to recognize that monitoring, and even modeling techniques for exposure assessment are quite costly and would not be economically supportable, even at an early tier, for more than a small number of chemicals or chemical applications.

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