Research Area: Exposure & Sources

Understanding and quantifying exposure is necessary to determine whether and under what conditions a chemical, product, or situation poses an unacceptable risk to human health or the environment. Questions have been raised regarding whether exposure to chemicals or chemical agents present in the environment might be related to, or directly contribute to, certain health conditions in the population, especially to potentially sensitive sub-populations. The question, "Is [insert name of chemical, substance, situation, or activity] safe?" refers to both hazard and exposure. Often, the simplicity of this question is met with less than a definitive answer because the exact nature of the exposure is inadequately assessed for most scenarios. Instead, regulators and the public, who lack high quality exposure information, often estimate exposures by applying surrogate exposure information such as the Toxic Release Inventory or production data and using conservative models and default assumptions.

In attempting to answer the question of safety, policy makers ask questions such as:

- What are the agents of concern?
- What are the levels of exposure found in the environment? What are the exposure trends for those agents?
- Do the current exposure data represent exposures to the general population or to a sensitive sub-population?
- What do these exposures mean for public health?

The need for more exposure information is increasing. For example, exposure estimates (both quantitative and qualitative) are increasingly being used to help prioritize chemicals for screening and testing programs involving children's health issues, and endocrine screening and testing programs. Increased attention is being focused on low dose exposures to individual chemicals and mixtures of chemicals found in the environment, raising even more complex exposure-related questions.

Exposure is usually determined by the time spent in contact with a particular chemical or mixture and the concentration in the air, water, soil, etc., in a specific situation. The amount of the chemical that is received or taken up by an organism through the skin, lungs, or gastrointestinal tract is referred to as the dermal, inhalation or oral dose, respectively. To some, exposure means there is an opportunity to receive a dose, not that a dose was actually received. Whether someone actually receives a dose, and whether the dose received is an effective dose, requires a more sophisticated biological analysis.

With advances in measurement technology and with the development of increasingly sophisticated pharmacokinetic models, scientists are now better able to measure and predict more relevant internal doses (e.g., dose to a target organ or tissue) of individual chemical substances and their metabolites. To measure and predict the internal doses of substances or mixtures, tools are being developed that will allow us to assess the formation of toxic metabolites, which will ultimately help to determine rates of detoxification and excretion. More research efforts are needed to develop these sophisticated tools to measure and model internal doses, body burdens, target tissue concentrations, detoxification, distribution and excretion. Of critical importance is the development of methods for obtaining biological measurements of exposure and for interpreting such data in a meaningful way. Equally critical is research to further determine if the data

are representative of the general population or of a defined sub-population.

Concerns about exposures to particular subpopulations, such as children, are increasing globally. For example, some claim that children may be exposed to higher levels of certain chemical substances (especially products used in and around the home and/or school and pesticides used on some food crops) and, at the same time, might be more sensitive to the potential effects of some chemicals than adults. These concerns have prompted requests for better exposure information for children, with an emphasis on *in utero* and neonatal exposures to certain chemical substances, particularly certain persistent chlorinated compounds found in the environment. In addition to the need to test the hypothesis that infants and children are more sensitive than adults to chemical exposures, data on childhood exposure must be generated for various age groups of children.

Concerns are likely to extend beyond children as reports of increased sensitivity (related to either toxicity or exposure) are made for other sub-populations.

The March 2001 release by the Centers for Disease Control [CDC] of its *National Report on Human Exposure to Environmental Chemicals* attests to the critical importance of understanding the possible impact and interpretation of chemicals in human tissues. CDC reported measurable levels of the 27 chemicals in this first report and indicated its intention to expand the list to 100 chemicals, which includes chlorinated chemicals. The challenge, both from an exposure perspective, as well as from a toxicology perspective is to be able to place into perspective the meaning of these kinds of results. As noted by Dr. James Pirkle, deputy director of the CDC Environmental Health Laboratory, *"Just because it's measured in a person doesn't mean that it causes a disease."*[1] This statement highlights the importance of conducting research necessary to determine whether the levels reported by CDC are representative of exposures to the general population or to a sensitive sub-population as well as to characterize the overall meaning about whether these exposures have direct relevance to public health, policymakers, and the public.

Another important aspect of predicting exposures to humans and wildlife is collecting, interpreting, and modeling data related to releases of substances and mixtures found in the environment. To predict such potential exposures, data concerning sources, releases, and environmental fate, including transport and deposition, must be obtained and analyzed. Over the last decade, worldwide attention has focused on the production, sources, releases, environmental transport, deposition, and fate of persistent, bioaccumulative toxins (PBTs). However, there is a need to better understand the storage, depuration, and re-suspension of PBTs in the environment, the amount of these substances existing in soils and sediments, and the environmental trends in concentrations. Public and scientific interest has expanded to include short-lived substances, such as those that might affect ozone formation in the troposphere. Industry will likely be urged to develop exposure information for these substances. Similarly, dietary and indoor air exposures are expected to drive exposure estimates for many chlorinated substances.

As a result of the intense interest in the consequences of exposure of infants, children, and adults to various chemical substances, including chlorinated

[1] CDC, National Report on Human Exposure to Environmental Chemicals, Frequently Asked Question, in the Press Release package, March 21, 2001,

compounds, obtaining more complete and accurate exposure data is critical. This will permit the application of more realistic models and exposure assessment procedures, as well as more accurate (and in many instances, less conservative) estimates of ranges of potential risks.

RESEARCH THEMES:

RFHEE intends to partner with others, including governmental agencies and other organizations, to examine and understand the potential exposures for key chlorinated compounds, which might include TCDD and dioxin-like compounds, other PBTs, disinfection byproducts, and certain short-lived compounds. Of particular interest to RFHEE is to focus its support on projects that:

- Contribute to the quantification of exposures to key chlorinated substances so that real data, rather than cautious default assumptions, are used when estimating exposures. In particular, research should contribute to answering questions about levels in the environment, trends, pathways of exposure, sources, and ability of available samples to represent actual exposures. These questions are part of the larger quest to determine the relationship, if any, between exposures to chlorinated compounds found in the environment and public health.

CANDIDATE PROJECT AREAS:

See separate list.