ADVANCED EXPOSURE METRICS FOR CHEMICAL RISK ANALYSIS

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Direct measurement of human exposure to environmental contaminants in real time (when the exposure is actually occurring) is rare and difficult to obtain. This frustrates both exposure assessments and investigations into the linkage between chemical exposure and human disease. However, it is feasible to obtain information on the levels of environmental contaminants (and their metabolites and adducts) in the biofluids of individuals that may have been exposed. Furthermore, it is feasible to obtain information on the occurrence of specific diseases and other adverse conditions in various human demographics. The Agency's exposure and risk assessments could be greatly improved if these chemical biomarkers could be used to both reconstruct previous exposure scenarios, and to predict the future likelihood of adverse effects. While progress has, indeed, been made along these paths, biomarker methods based solely on xenobiotics and their metabolites/adducts are inherently limited. This new research program (still in the planning stages) is based on the belief that systems biology approaches and 'omic-based biomarkers, when used in conjunction with tradition biomarkers, offer great promise for both exposure reconstruction and for elucidating the linkages between exposures and adverse outcomes.

A significant amount of research has already been devoted to the use of systems biology approaches and 'omic techniques (transcriptomics, proteomics, and metabolomics) to screen chemicals for hazardous effects. However, changes in transcripts, proteins, and endogenous metabolites may, in some cases, be more-certain indicators of chemical exposures than of apical chemical effects. Nonetheless, these powerful new techniques have rarely been applied as biomarkers of exposure. In comparison to (or in combination with) conventional biomarkers, 'omic markers of exposure offer considerable promise for exposure assessment. Note that 'omic markers are a unique pattern of a large number and wide variety of transcript, protein, or endogenous metabolite changes. These signatures may be more informative and more chemical-specific than a conventional biomarker. Also, taking advantage of the earlier research in 'omic markers for effects, these markers of exposure may, in some cases, be able to identify exposure to a specific mode-of-action-active chemical. Indeed, 'omic markers can sometimes serve as a linkage across the source-to-outcome continuum, functioning concomitantly as markers of exposure, dose characterization, and effects.

This abstract has been reviewed in accordance with the U.S. Environmental Protection Agency's peer and administrative review policies and approved for presentation and publication.