

- a. Symposium topic.

**The Exposure Dimension of Environmental Epidemiology: A Critical but Under-Explored Study Quality Issue in Environmental Health**

- b. Symposium organizer name, affiliation, and contact information.

Judy S. LaKind, Ph.D.  
President, LaKind Associates, LLC  
Adjunct Associate Professor, Department of Epidemiology and Public Health  
University of Maryland School of Medicine  
Adjunct Associate Professor, Department of Pediatrics  
Pennsylvania State University College of Medicine,  
Milton S. Hershey Medical Center  
106 Oakdale Avenue  
Catonsville, MD 21228  
PH 410 788 8639  
Email: lakindassoc@comcast.net

Timothy J. Buckley, Ph.D.  
Director, Human Exposure & Atmospheric Sciences Division  
National Exposure Research Laboratory  
US EPA Office of Research and Development  
109 TW Alexander Drive  
Research Triangle Park, NC 27709  
PH: 919-541-2454  
Email: [buckley.timothy@epa.gov](mailto:buckley.timothy@epa.gov)

- c. Symposium overall abstract

Epidemiological research plays a critical role in assessing the effects of various chemical, physical, biological, and social exposures on human health both in the general population and the workplace. However, even epidemiological studies that are specifically designed to test causal hypotheses in humans often report conflicting results. For example, this has been the case for the rapidly growing number of studies utilizing observational cross-sectional databases such as NHANES. In the presence of substantial disagreement across study findings, regulatory bodies and consensus panels charged with setting policy to protect public health typically rely on weight-of-evidence (WOE) assessments. Study quality is an important consideration in a WOE assessment, and as part of that assessment, the exposure data quality must be evaluated. While determination of study quality will always to some extent involve professional judgment, there appears to be an emerging consensus that any evaluation of study quality should rely on agreed-upon criteria that are applied systematically. Currently, there is a paucity of instruments for evaluating quality of environmental epidemiology studies and more specifically for the exposure data generated in these studies; scant attention has been paid to the quality of exposure assessments in studies used in WOE assessments. This underscores a need for methodological quality assessment tools that are designed specifically for human population studies evaluating



health outcomes associated with environmental exposures. In this symposium, we will describe various aspects of quality of exposure assessment in environmental epidemiology research – including those occurring in occupational settings - and the need for exposure quality assessments in peer review of manuscripts and grant proposals, as well as in studies used as the underpinnings for WOE assessments. We will also discuss opportunities for improving our ability to evaluate exposure data in environmental epidemiology research.

d. Symposium speakers, including affiliation, and presentation title, and short description of the presentation. Session lengths will permit 3 (in 60 minutes) or 5 (in 90 minutes) talks.

**1. Dr. Michael Goodman, Rollins School of Public Health, Emory University: Systematic assessment of study quality: experience to date.**

While determination of study quality will always to some extent involve professional judgment, there appears to be an emerging consensus that any evaluation of the strength of evidence should rely on agreed-upon criteria that are applied systematically. These considerations motivated the development and refinement of several study quality assessment tools that are used in clinical and other related research. Some of these tools (e.g., STROBE for observational studies and CONSORT for clinical trials) address general issues that apply across disciplines. Other tools were developed specifically for various areas of medicine or life sciences (e.g., STREGA for genetic studies, GRADE for comparative treatment effectiveness research, and STARD for studies of diagnostic accuracy.) In view of the current tendency towards standardization of weight-of-evidence assessment that incorporates study quality, the relative paucity of instruments for evaluating environmental epidemiology studies is notable, but recent years have seen some progress in this area as well. Commonly evaluated study components include: 1) relative merits of different observational and experimental designs, 2) methods of minimizing selection bias, 3) strength and weaknesses of various exposure assessment approaches, 4) accuracy of outcome ascertainment; 5) data analysis methods, 6) adjustment for confounders, and 7) reporting and interpretation of findings. Much of the accumulated experience from other fields of science can readily be adapted to assessment of environmental health studies. Certain aspects of study quality that are specific to environmental health research will also be discussed.

**2. Dr. Judy LaKind, LaKind Associates, LLC, University of Maryland School of Medicine: Exposure uncertainties in epidemiology: BPA and phthalates as case studies**

Systematic reviews of the epidemiology literature for BPA and phthalates reveal inconsistencies in results that are likely due to study design issues. An important methodological issue, which pertains specifically to studies of chemicals with short (e.g. hours, days) physiologic half-lives such as BPA and phthalates, is whether single measures of these compounds and/or their metabolites provide robust representations of long-term exposure status. Relatively few papers have followed study participants over time to examine temporal variability for these types of chemicals. The need for better exposure assessments for these types of chemicals will be reviewed and case studies discussed.

**3. Dr. Jon Sobus, National Exposure Research Laboratory, US EPA Office of Research and Development: A proposal for assessing study quality: Biomonitoring, Environmental Epidemiology, and Short-Lived Chemicals (BEES-C) Instrument**



Environmental epidemiology studies can be an effective means to assess impacts on human health from exposure to environmental stressors. Exposure scenarios are often extremely complex, and proper assessment is critical for understanding exposure-health effect linkages. Biomarkers are now regularly utilized as exposure surrogates in environmental epidemiology studies. This strategy has proven effective for a small number of biomarkers that persist in the environment and the human body. However, environmental epidemiology studies that utilize biomarkers of short-lived chemicals are considerably more challenging. For these studies, it can be difficult to select and measure biomarkers that accurately reflect biologically-relevant exposure to a specific chemical during a critical time window. There is currently limited guidance for the design, implementation, and interpretation of environmental epidemiology studies that utilize biomarkers of short-lived chemicals as quantitative exposure surrogates. To address this need, we developed the Biomonitoring, Environmental Epidemiology, and Short-Lived Chemicals (BEES-C) instrument. This instrument is intended to guide research proposals, technical manuscripts, and weight-of-evidence assessments based on quality criteria for: 1) biomarker selection and measurement, 2) study design and execution, and 3) general epidemiological considerations. This presentation will discuss key challenges in using biomarkers of short-lived chemicals in environmental epidemiology studies, highlight the key components of the BEES-C instrument, and offer examples for evaluating proposals/studies based on the BEES-C criteria. While the BEES-C instrument is specifically designed to support environmental epidemiology research, it can also aid exposure studies seeking to identify and evaluate exposure factors.

**4. Dr. Jane C. Schroeder, Environmental Health Perspectives, National Institutes of Environmental Health Sciences: Evaluating and improving the quality of exposure assessment in environmental epidemiology: the role of peer review and journal standards**

Peer reviewers and journal editors can improve the quality of environmental epidemiology by critically evaluating methods and demanding clear and complete reporting, but may lack the specific expertise needed to critique exposure assessment. Use of standardized instruments to evaluate the quality of exposure assessment could improve the quality of peer review, but strict adherence to generic standards that may not be valid or appropriate for all study designs, exposures, and outcomes could have a negative impact by preventing the publication of informative research. I will discuss approaches that might be used by reviewers and editors to improve the quality of exposure assessment in environmental epidemiology, and potential limitations and barriers that would need to be addressed to implement them successfully.

**5. Dr. Junfeng (Jim) Zhang, Nicholas School of the Environment & Duke Global Health Institute: Improving Exposure Assessments in NIH Grant Proposals**

Research grants submitted to National Institutes of Health (NIH) are peer reviewed at Study Sections. Up to now, no study sections have been organized around the theme of exposure science, making it difficult to review proposals focusing on exposure analysis. Although exposure assessment is a significant component of environmental and occupational health studies, reviewer expertise on exposure assessment is often underrepresented in study sections



that are normally organized by health outcome. Because of the imbalance of reviewers' expertise, emphases have been often placed heavily on outcome assessment and inadequately on exposure assessment. This review paradigm, in turn, does not provide incentives for investigators to spend more effort on improving exposure assessment and thereby negatively affects the overall quality of the study. This is particularly troubling when it is well recognized that the uncertainty in exposure estimates is larger than the uncertainty in outcome assessments but is justified by the notion that "there is nothing we can do about it [improving exposure estimates]". Despite the rapid advancement in exposure science, cutting-edge exposure assessment technologies have rarely been applied in epidemiological studies. This is largely due to the fear that novel methodologies will be reviewed as too risky. Moving forward, the role of exposure science in environmental health shall be enhanced, starting with improved two-way communications. On one hand, the advancement in exposure assessment methodology needs input from health scientists, which will improve the relevance and usefulness of the methods. On the other hand, health scientists need to welcome advices from exposure scientists. The NIH grant review system needs more active participation of exposure scientists and needs to encourage health studies using novel exposure assessment methods. Special funding programs should be made available to encourage collaborations between exposure scientists and epidemiologists in the development or application of high-risk and high-impact exposure analysis methods.

#### **6. Dr. Carol Burns, The Dow Chemical Company: Challenges of exposure assessment quality on occupational epidemiology risk estimates**

High quality exposure assessments are essential to the validity of occupational epidemiology studies. However, changes occurring in the manufacturing work force and work environment over the past two decades have led to significant challenges in conducting exposure assessments in occupational epidemiological studies. Key changes include fewer workers required to run operations, less discriminating job titles, worker cross-training, frequent use of rotating work shift schedules, outsourcing, and acquisition and merger of companies. Concurrent with these are the availability of advanced analytical methods to detect concentrations of specific chemicals and/or their metabolites in blood and urine at increasing smaller levels. Biomonitoring can be incorporated in industrial hygiene surveys to augment the quantification of current exposures. Further, biomonitoring can enhance and validate job exposure matrices that estimate exposures in the past. However, the pharmacokinetics of each chemical must be considered in the design of collection and subsequent interpretation of the worker exposure. These changes present unique challenges in estimating and validating exposure in epidemiology studies. Examples of biomonitoring data and their use (and misuse) in epidemiology studies will be presented.

#### **7. Dr. Patrick Breyse, Johns Hopkins University Bloomberg School of Public Health: Improving Exposure Assessment Technology**

Exposure assessment is an integral component of occupational and environmental epidemiology, risk assessment and management, as well as regulatory compliance. For the most part, air sampling and analysis tools used in occupational and environmental exposure assessments are

based on technologies that have changed little since the 1970s. In many cases the lack of simple, inexpensive, exposure assessment technologies has limited epidemiologists' and risk assessors' ability to evaluate the environmental and occupational causes of disease. While there have been tremendous investments and advances in medical diagnostic and biomonitoring technologies (e.g., glucose testing, human genetics), there has been less effort invested in advancing the science of exposure assessment. Developing and applying new sensing technology for personal sampling can improve the way epidemiologic studies are conducted. Time-series panel studies that investigate short-term (hours to days) changes in personal exposure that are linked to changes in health care encounters, symptoms, and biological markers of preclinical disease and/or susceptibility are needed to more fully evaluate the impact of chemicals and other agents on health. Current sampling technology limits our ability to assess time-varying concentrations. The purpose of this paper is to discuss the current state of air sampling and health assessment and the need for improved assessment technology for use in health effects studies.

#### **8. Panel Discussion**

The panel will discuss audience questions related to improving exposure science in environmental and occupational epidemiology research. In addition, methods for incorporating evaluation of exposure science components in reviews of publications and grant proposals will be explored.