



How has ORD Laid the Groundwork for Identifying and Linking Indicators of Exposure, Dose and Effect?

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Contributing Organizations: ORD--NCER



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RESEARCH & DEVELOPMENT

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Science Questions

- How has the HHRP used extramural grants to complement EPA's efforts to identify and link indicators of exposure, dose, and health effects?
- How have these efforts improved the scientific underpinnings of risk assessment?
- What scientific findings have contributed to a better understanding of the events involved in the exposure-dose-effects continuum?
- How does this research apply to "real-life" situations?
- How does this research provide the science to evaluate the effectiveness of environmental actions and policies?

Research Goals

Understanding Linkage: ORD is committed to understanding linkages in the source-to-exposure-to effects paradigm to develop indicators of health outcomes. The indicators can be used to evaluate the effectiveness of risk management decisions and actions.

The suite of grants described here fund:

- The identification of extant data to evaluate environmental health outcomes
- The development of biomarkers of:
 - Exposure
 - Effect
 - Susceptibility

Synthesis: ORD has sponsored internal EPA and international workshops to synthesize our understanding of how these biomarkers can be used to address uncertainties in the linkages between exposure, dose and effect. These workshops have focused on current knowledge and research needs to understand "real world" risk, e.g., the applications of biomonitoring to public health and research approaches for assessing public health impacts of risk management decisions.

Biomarkers of exposure and susceptibility:

Development of GO-Quant method to interpret gene expression data for thousands of genes. Data will be used with information on PON1 status, acetylcholinesterase measurements and urinary organophosphate pesticide (OP) metabolite concentrations to understand differences in individual responses to

environmental exposures for people in agricultural communities. Elaine Faustman U Washington, **Grant R832733.**

Children with the PON108 genotype, indicating lower paraoxonase levels and greater susceptibility to the effects of OP, have poorer mental development at age 2 than children with

Findings and Conclusions

the more protective wildtype (CC) genotype. Children whose mothers had the PON108 TT genotype also had significantly lower mental development at age 2. Brenda Eskenazi, U California, Berkeley, **Grant R832734.**

Linking emission levels to exposures to vulnerable communities:

Reducing ship diesel emissions by 1 ton/week decreases overall exposure minimally, but markedly decreases exposure distribution, yielding a greater environmental justice benefit. Reducing train diesel emissions by same amount decreases overall exposure, but has less effect on vulnerable communities. Julian Marshall, U of Minnesota, **Grant R833624**

Cumulative risk from heat stress:

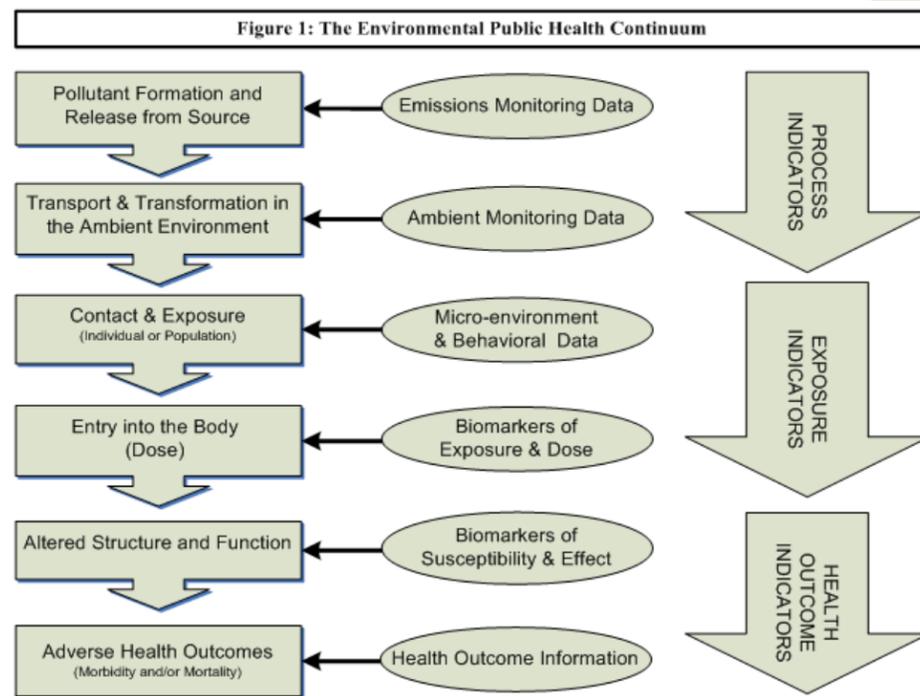
Fitted Heat Index (HI)/mortality relationship showed a non-linear relationship, with a steeper slope above 100 degrees HI. Impact of consecutive days of 95 degrees HI on mortality was approximately equivalent to a single day of 100 degrees HI. Kazuhiko Ito, NYUSOM, **Grant R833623**

Impact and Outcomes

This research portfolio is providing tools for risk managers at the federal and local level to determine the effects of environmental policies and actions in the real world. Examples include:

- **Biomarkers of pesticide exposure and susceptibility:** Development of tools for predicting who in an agricultural community will be most susceptible to the effects of exposure to pesticides. Application: Focused educational outreach to protect the most vulnerable members of the population. **Grants R832733, R832734**
- **Linking emission levels to exposures to vulnerable communities:** Targeted diesel emission reduction can result in greater impact to vulnerable communities. These results can inform local and state policymakers in targeting environmental policies. **Grant R833624**
- **Risk from heat stress:** The New York City Department of Health and Mental Hygiene formally recommended that the Office of Emergency Management and National Weather Service should modify the threshold for heat advisories and activating a response. **Grant R833623**
- **New RfA on "Understanding the Role of Nonchemical Stressors and Developing Analytic Methods"** will be issued in early 2009 as a result of the Workshop on Community-Based Risk Assessment.
- **NCCT-hosted Exposure Prioritization Community of Practice:** Discussions begun in workshops on Biomonitoring and Community continue in this broad inter-Agency and stakeholder group.

Methods/Approach



Science to Achieve Results: Source to Outcomes Indicators

Issues in Tribal Environmental Research and Health Promotion: Novel Approaches for Assessing and Managing Cumulative Risks and Impacts of Global Climate Change (September 2006). 2 grants. Goal: To identify subsistence resources, sensitive subpopulations, exposure sources/routes, and relation between stressors and health.

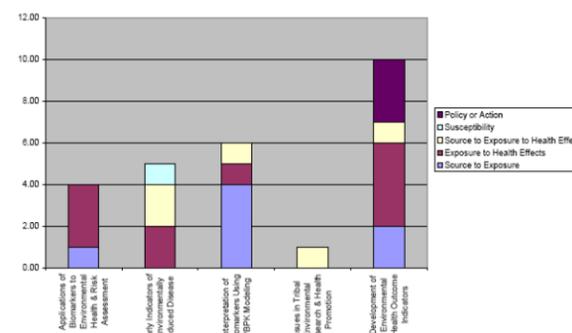
Application of Biomarkers to Environmental Health and Risk Assessment (November 2003). 4 grants. Goal: To validate, interpret and/or apply currently known biomarkers.

Interpretation of Biomarkers Using Physiologically Based Pharmacokinetic Models (June 2006). 6 grants. Goal: To develop modeling techniques to be used to understand and characterize target tissue dose and exposures that are consistent with biomarker data.

Early Indicators of Environmentally Induced Disease (October 2004). 5 grants. Goal: To develop methods and tools for identifying early indicators or predictors of environmentally induced disease.

Development of Environmental Health Outcome Indicators (August 2006 and June 2007). 10 grants. Goal: To develop outcome-based indicators that reliably signal trends in source to exposure, exposure to outcome, and ultimately, source to exposure to outcome relationships.

Development of Indicator Type by RfA



EPA and ORD have set assessing the impact of risk management decisions as a strategic goal. This is seen as an integral part of the risk assessment and risk management paradigm.

ORD's grants program has developed six RfA's to identify and link indicators of exposure, dose, and health effects, with the ultimate goal of establishing indicators of "real life" exposures and health outcomes. This research serves the public through the generation of data and models that inform critical needs in environmental health and is aligned with research in ORD's Laboratories.

Future Directions

Many of the grants made as a result of these Request for Applications (RfAs) were recently awarded. Several useful tools should be developed in the next 2 or 3 years. Research results from the RfA "Issues in Tribal Environmental Research and Health Promotion" will be used to examine health outcomes in tribal populations resulting from current trends in chemical exposure or climate change. Research results from the RfA "Development of Environmental Health Outcome Indicators" will be used to determine if environmental actions or policies have resulted in "real world" improvements to environmental conditions and human health. A new RfA will be issued in 2009 to fund a third set of grants in this area.

Researchers Involved

Elaine Faustman, University of Washington
 Brenda Eskenazi, University of California, Berkeley
 Julian Marshall, University of Minnesota
 Kazuhiko Ito, NYUSOM

Evaluation of Risk Management Decisions