Key Environmental Health Data Streams: Exposure

Integrating Environmental Health Data to Advance Discovery
NAS Emerging Science for Environmental Health Decisions
January 10–11, 2013, Washington, DC

Elaine Cohen Hubal, US EPA Office of Research and Development

Disclaimer. Although this work was reviewed by EPA and approved for presentation, it may not necessarily reflect official Agency policy.
What Is Exposure Science?

- The bridge between the sources of chemical, physical and biological agents and human health
  - Provides crucial information to estimate real-life risks to health and to identify the most effective ways to prevent and reduce these risks.

www.isesweb.org
Exposure for Risk Assessment: Approaches

- Questionnaire based metrics (epidemiology)
- Surrogate exposure metrics (ambient measures)
- Exposure measurement (direct or point-of-contact)
- Biomonitoring (NHANES)
- Modeled estimates (indirect or scenario evaluation)
Exposure for Translation

Susceptibility
(Genetic Variants / Epigentic Modifications)

Biological Insight
(Toxicity Pathways)

Environmental Factors
(Exposure)

Improved Measures of Individual Etiological Processes and Individual Exposures

Key Perturbations
Key Targets

Biomarkers
Indicators Metrics

Extrapolation for Risk Assessment

Public Health Policy
Prevention

Personal Risk Profile

Information

Education

Personal Risk Management

Extrapolation for Translation

Systems Biology: Exposure at All Levels of Biological Organization

Environmental Source

Ambient Exposure → Population

Personal Exposure → Individual

Internal Exposure (Tissue Dose) → Tissue

Dose to Cell → Cell

Dose of Stressor Molecules → Biological Molecules

Perturbation

Stressor

Biological Receptor

Outcome

Disease Incidence/Prevalence

Disease State (Changes to Health Status)

Dynamic Tissue Changes (Tissue Injury)

Dynamic Cell Changes (Alteration in Cell Division, Cell Death)

Dynamic Changes in Intracellular Processes

Cohen Hubal, JESEE, 2008
Exposure Data Sources

Source/Stressor Formation

Production/Import Volumes
- EPA HPVIS
- EPA IUR
- EU ESIS

Environmental Releases
- DOE GHG

Chemicals in Consumer Products
- Household Products DB
- Cosmetic Voluntary Reg. DB

Exposure Limits
- NIOSH NOES
- AIHA WEEL
- OSHA PEL

Human Exposure Monitoring
- NHEXAS
- EUROPA Pest-Diet

Activity Patterns Information
- EPA NHAPS
- EPA CHAD

Human Biological Monitoring Data
- CDC NHANES
- NHEXAS
- CTEPP

Exposure

Transport/Fate

Indoor Air Monitoring Data
- DOE IndoorAir NHEXAS CTEPP

Outdoor Air Monitoring Data
- EPA NATA
- EPA AIRS/AFS
- UN IPCC GHG

Environmental Fate Simulator
- ECOTOX DB CESAR

Environmental Concentration

Product Usage Information
- EPA Pesticide Usage Data
- UK Pharmaceutical Usage

Production/Process Information
- EPA HPVIS ATSDR Tox Profiles DEA NFLIS

Human Biological Monitoring Data
- CDC NHANES
- NHEXAS
- CTEPP

Peter Egeghy, NERL
Network of exposure taxonomy used in ACToR; Egeghy et al, 2011
Exposure Data Landscape

Number of unique chemicals by data type in ACToR; Egeghy et al, 2011
Exposure Data Collection and Access: ACToR, Aggregated Computational Toxicology Resource

http://actor.epa.gov/
Exposure Data Collection and Access: ExpoCastDB Goals

- Consolidate observational human exposure data, improve access and provide links to health related data
  - House measurements from human exposure studies
  - Encourage standardized reporting of observational exposure information

- Provide separate interface with inner workings of ACToR
  - Facilitate linkages with toxicity data, environmental fate data, chemical manufacture information

- Provide basic user functions
  - Visualization (e.g., scatterplots, probability plots, goodness-of-fit)
  - Obtain summary statistics and estimate distributional parameters
  - Download customized datasets

http://actor.epa.gov/
Exposure Data Collection and Access: ExpoCastDB

- Four initial studies from National Exposure Research Laboratory
- Full raw data sets available for download
- Browse data capability
- Descriptive statistics capabilities
ExpoCastDB: Applications

• Investigate occurrence and co-occurrence of chemicals
  • How frequently was a particular pesticide (e.g., esfenvalerate) detected in nationwide AHHS study?

• Comparisons across studies
  • How does avg. permethrin loading differ between homes in AHHS and daycares in CCC?

• Download individual sample-level structured data
  • Derive input distributions for probabilistic exposure models (such as SHEDS)
  • Use with readily available algorithms (U.S. EPA, 1992) and exposure factors (U.S. EPA, 1997) to produce quick deterministic estimates of uptake resulting from exposure to specific chemicals
Heatmap of CTEPP NC & OH chemical detection frequencies in different media

Sumit Gangwal, et al. NCCT
Background:
- Significant progress has been made in collecting and improving access to genomic, toxicology, and health data
- These information resources lack exposure data required to:
  - translate molecular insights
  - elucidate environmental contributions to diseases
  - assess human health risks at the individual and population levels

Aim:
- Facilitate centralization and integration of exposure data to inform understanding of environmental health
- Bridge gap between exposure science and other environmental health disciplines

Vehicle:
- Carolyn Mattingly, Mount Desert Island Biological Laboratory
- LRI seed funding, followed by NIEHS RO1
Design and Evaluation of the Exposure Ontology: ExO

• Develop an exposure ontology consistent with those being used in toxicology and other health sciences
• Facilitate centralization and integration of exposure data to inform understanding of environmental health
• Bridge gap between exposure science and other environmental health disciplines
  – Initially focus development on human exposure to chemicals
  – Ultimately, provide domains that can be extended to encompass exposure data for the full range of receptors and stressors
Definitions of Central Concepts

- **Exposure Stressor** - An agent, stimulus, activity, or event that causes stress or tension on an organism and interacts with an exposure receptor during an exposure event.

- **Exposure Receptor** - An entity (e.g., a human, human population, or a human organ) that interacts with an exposure stressor during an exposure event.

- **Exposure Event** - An interaction between an exposure stressor and an exposure receptor.

- **Exposure Outcome** - Entity that results from the interaction between an exposure receptor and an exposure stressor during an exposure event.

Mattingly et al, ES&T 2012
High-level schematic of Exposure Ontology (ExO) integration within a broader biological context.

Mattingly et al, ES&T 2012
Exposure Data Collection and Access: Pilot Curation of Exposure Data into CTD

- Chemicals
  - chemical-gene interactions
  - chemical-disease relationships
- Genes
  - gene-disease relationships
- Diseases
  - Exposure Data (curated and public sources)

The Gene Ontology: functional annotations
Pathway data

Carolyn Mattingly

Office of Research and Development
National Center for Computational Toxicology
Example: High Throughput Exposure Prioritization

There are thousands of chemicals, many without enough data for evaluation.

High throughput in vitro methods beginning to bear fruit on hazard for many of these chemicals.

Methods exist for approximately converting these in vitro results to daily doses needed to produce similar levels in a human.

Without a similar capacity for exposure cannot place risk early into prioritizations.

Framework for High Throughput Exposure Screening

*Wambaugh et al. Submitted*

Space of Chemicals (e.g. ToxCast, EDSP21)

(Bio) Monitoring

Dataset 1

Dataset 2

Exposure Inference

Inferred Exposure

Joint Regression on Models

Evaluate Model Performance

Calibrate models

Estimate Uncertainty

Apply calibration and uncertainty to other chemicals
Data Availability for Model Predictions and Ground-truthing

Ground—truth with CDC NHANES urine data

Focusing on U.S. median initially

Capable of adding population variability, but will need consumer use models

“Ground-truthing” Chemicals

NHANES volatile, insoluble

IUR (6759 compounds with production of >25,000 lbs a year)
CPRI (242 pesticides with total lbs applied)
ExpoCast + ToxCast

Wambaugh et al. In prep

~93% Phase I and ~89% Phase II coverage by ExpoCast

Chemicals with indoor/consumer use in red

Chemicals with far field (industrial/agricultural) release in blue
Acknowledgements

• US EPA ORD – Richard Judson, Peter Egeghy, John Wambaugh, Woody Setzer, plus

• ExO– Carolyn Mattingly, Tom McKone, Judy Blake