EPA United States Environmental Protection Agency

Chemical Safety for Sustainability Rapid Exposure and Dosimetry Research

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Exposure Science in the 21st Century Grantee Kickoff Meeting
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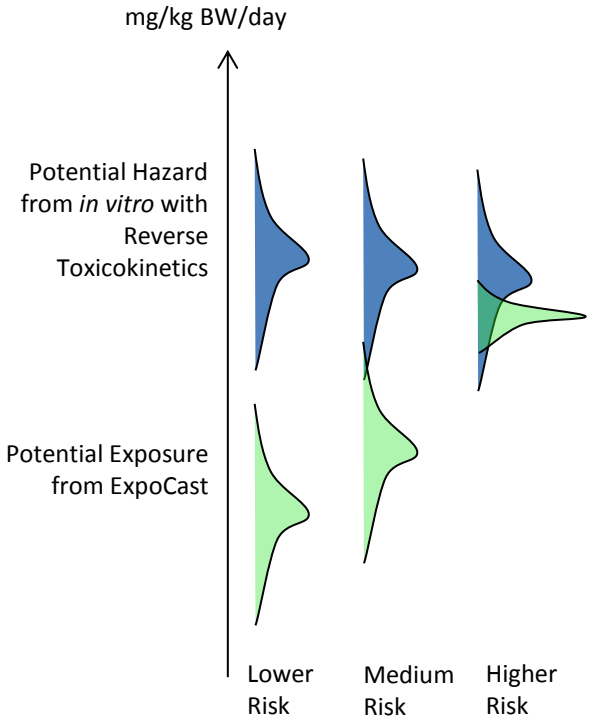
Rapid Exposure and Dosimetry Science Challenge

- The timely characterization of the human and ecological risk posed by thousands of existing and emerging commercial chemicals is a critical challenge facing EPA in its mission to protect public health and the environment

- **High throughput risk prioritization** relies on **three components** – high throughput **hazard** characterization, high throughput **exposure** forecasts, and high throughput **pharmacokinetics** (*i.e.*, dosimetry)

- While advances have been made in HT toxicity screening, evaluated exposure and dosimetry prediction methods applicable to 1000s of chemicals are needed

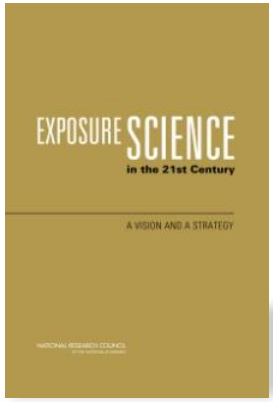


e.g. Judson *et al.,* (2011) Chemical Research in Toxicology

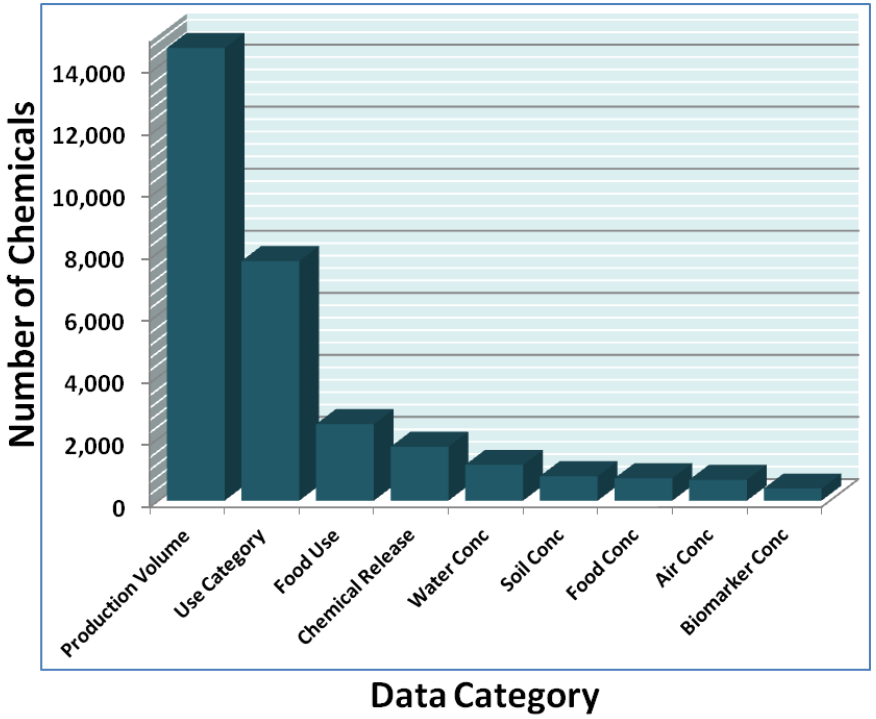
Exposure Science in the 21st Century

2012 NRC Report

Exposure Information Needed For:



- Screening and prioritization of chemicals for targeted toxicity testing, focused exposure assessments, or monitoring studies
- Quantification of aggregate or cumulative chemical exposures for integration with hazard data for human or ecological risk assessment
- Quantification of population vulnerability



Egeghy et al. (2012), "The exposure data landscape for manufactured chemicals"

Rapid Exposure and Dosimetry Project Research Approach

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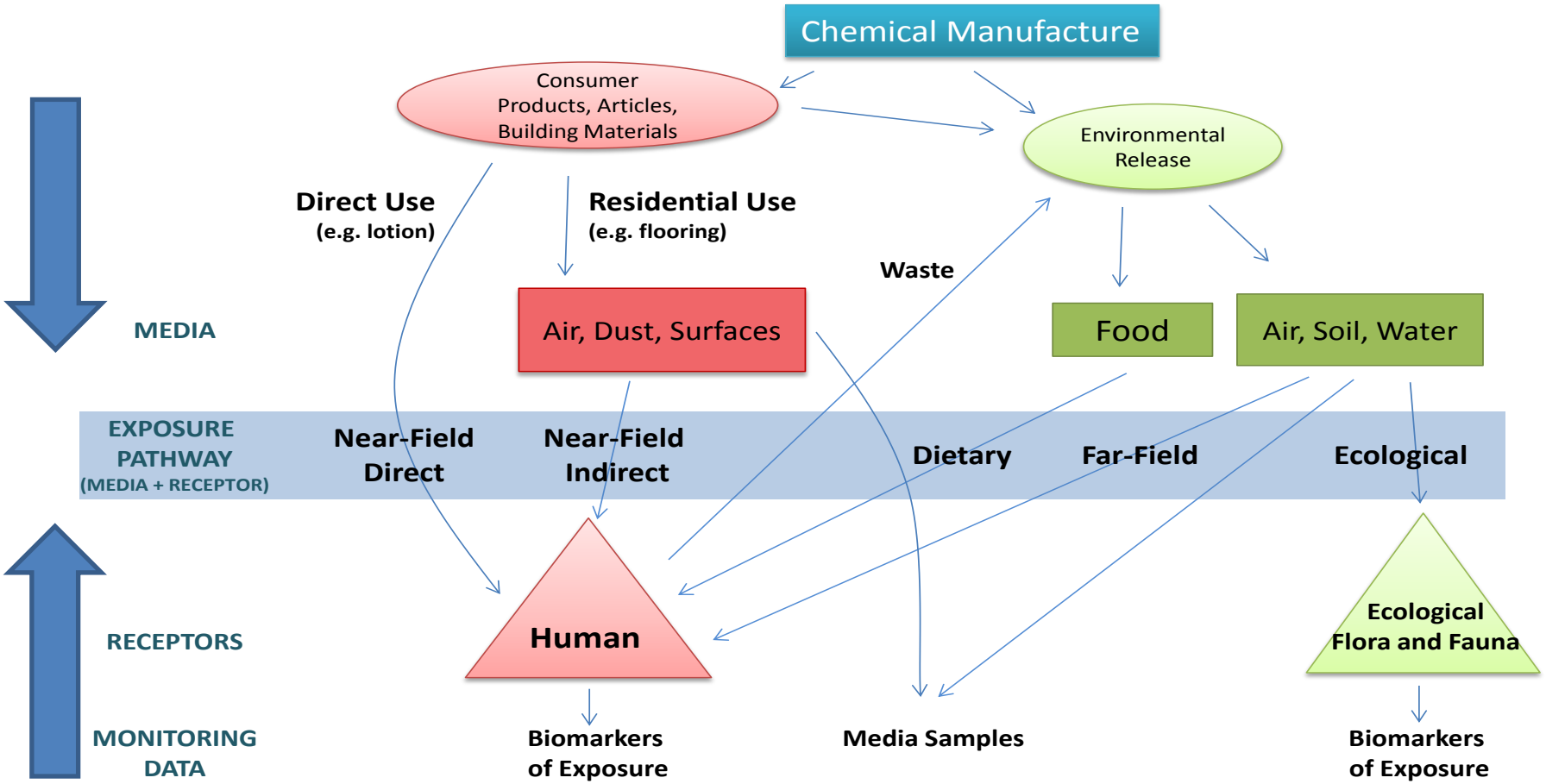
1. Develop the tools and data necessary to rapidly quantify human and ecological exposure potential of chemicals
    - Procurement and mining of exposure-related data for support of rapid exposure tools
    - Development and evaluation of high-throughput human and ecological exposure models
2. Generate the data and tools necessary to directly compare these rapid exposure forecasts to the bioactive concentrations identified by high-throughput toxicity testing
    - High throughput pharmacokinetics (HTPK) for rapid dosimetry
3. Ultimately apply high-throughput computational exposure and dosimetry prediction methods and data to support EPA decisions that protect human health and the environment
    - Statistical methods for model evaluation and calibration
    - Partner with CSS High Throughput Toxicology Project to develop risk-based metrics for prioritization

Environmental Chemical Exposure Pathways



Developing Models and Supporting Data to Rapidly Predict Near-Field Exposure to Chemicals

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Data

Chemical molecular structures and chemical function

Chemical end-use including presence in consumer products

Population patterns of consumer product purchasing

Patterns of consumer product use

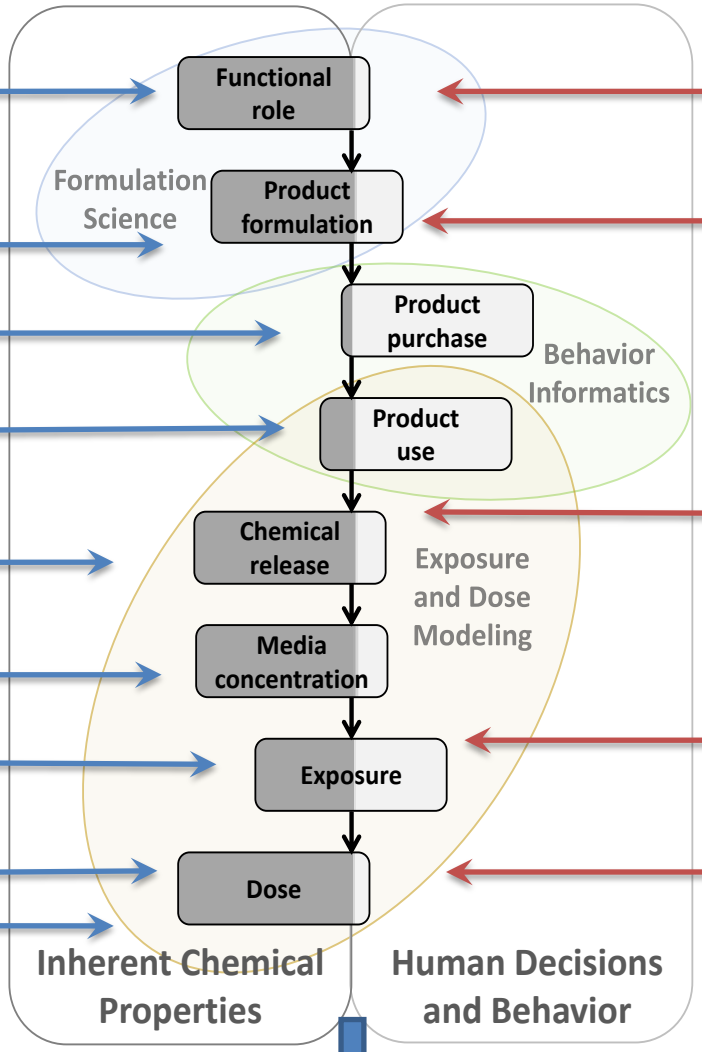
Data describing emission of chemical from articles

Chemicals measured in residential media

Human activity patterns and exposure factors

Human physiology and pharmacokinetic properties of chemicals

Human biomonitoring data



Models

Models predicting chemical function from chemical properties or structures

Models predicting product formulations

Models describing fate and transport of chemicals within a residence

Mechanistic and heuristic-based human exposure models

Dosimetry/pharmacokinetic /PBPK models

High-throughput Predictions of Chemical Exposures and Internal Doses

Development and Analysis of New Exposure-Related Data

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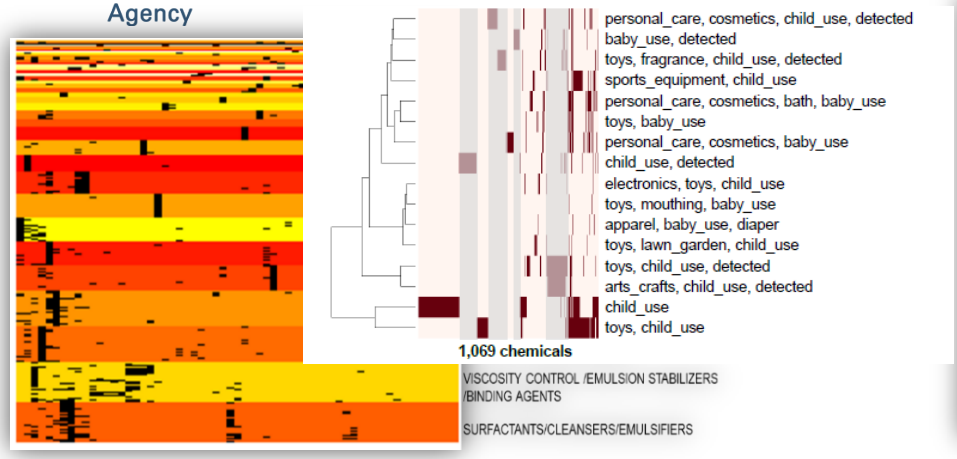

New Chemical Use Information

New Monitoring Data

New data on chemicals within and emission from consumer products

nielsen

Consumer Product Use Information

New data on physico-chemical properties

Chemical Ingredients in Consumer Products

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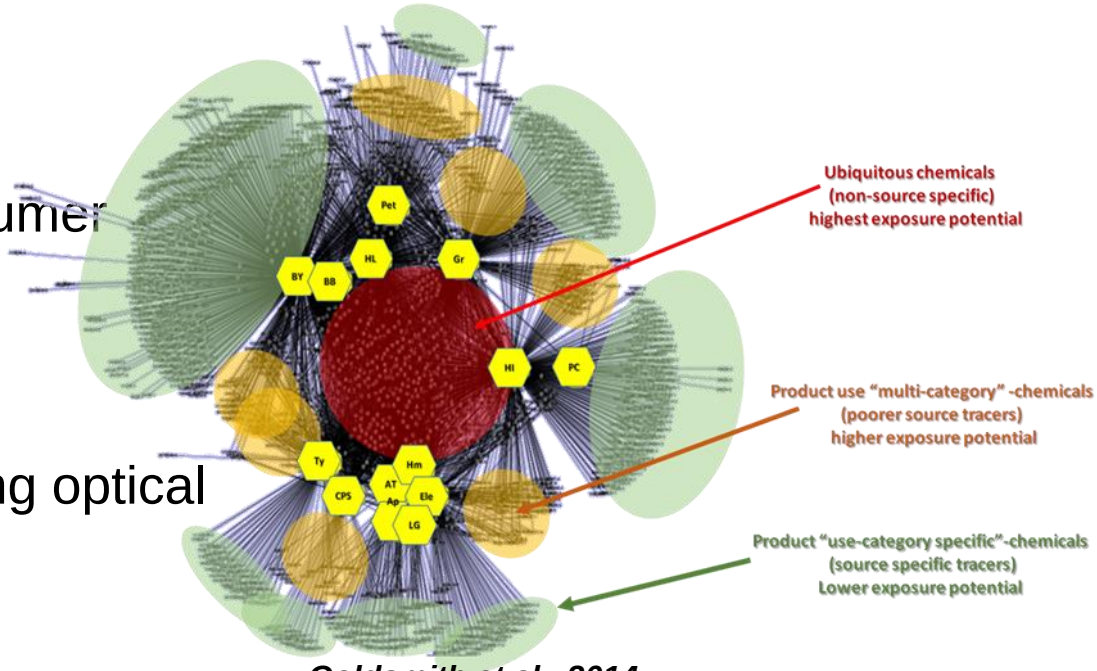
- What chemicals are in consumer products and in what concentrations?
- Data curated from publically available MSDS Sheets using optical character recognition
- Workflows for crowdsourced curation and quality assurance
- Quantitative information >1800 chemicals in >9000 consumer products by consumer product category



Goldsmith et al., 2014

Chemical Use Information for >30,000 Chemicals

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- Chemical-Product Categories (CPcat) database maps many different types of use information and ontologies onto each other
- Includes CPCPdb with information on >2000 products from major retailers

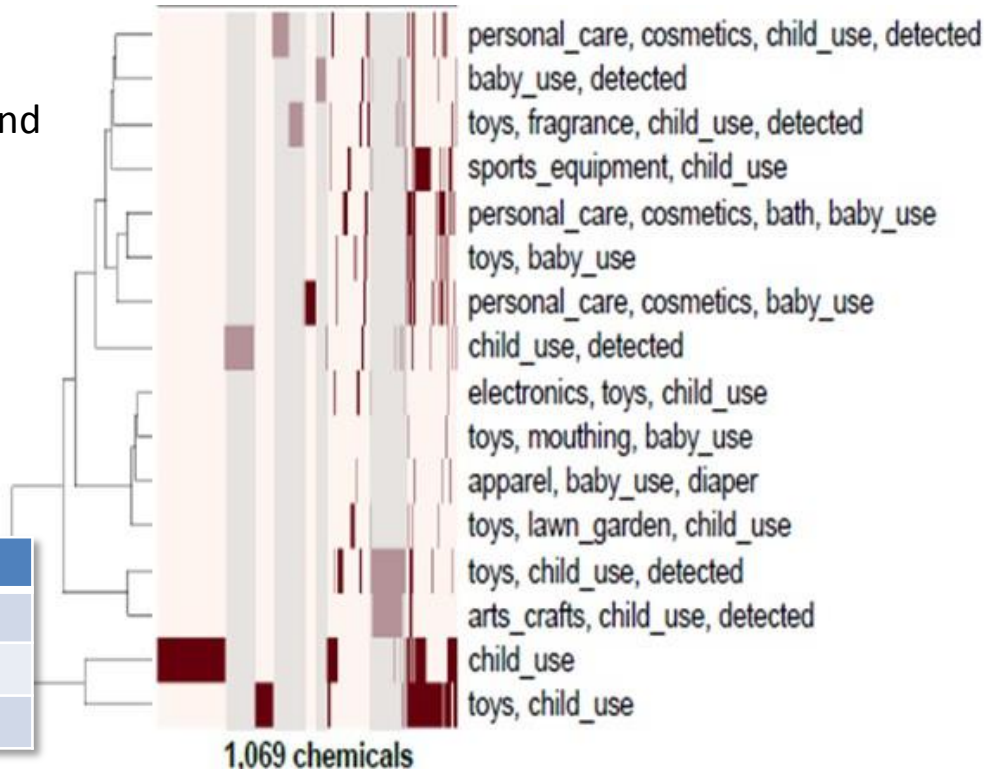

Table: Hits per use category for a given chemical

CASRN	Category 1	Category 2	…	Category 12
65277-42-1	0	10	…	1
50-41-9	31	7	…	3
…	…	…	…	…

Binary matrix

CASRN	Category 1	Category 2	…	Category 12
65277-42-1	0	1	…	0
50-41-9	1	1	…	0
…	…	…	…	…

Dionisio* et al. *(2015)

http://actor.epa.gov/cpcat/

Innovative Environmental Monitoring Data

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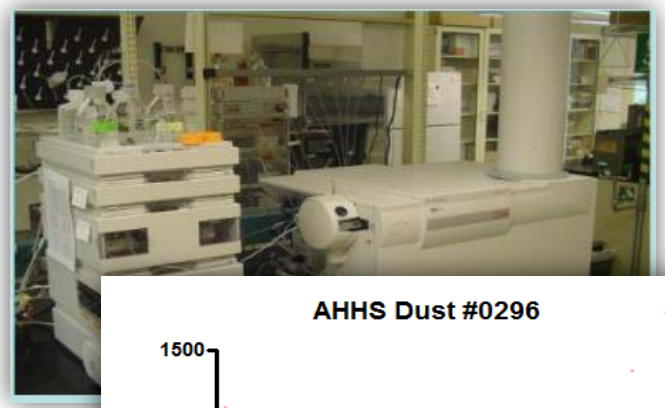
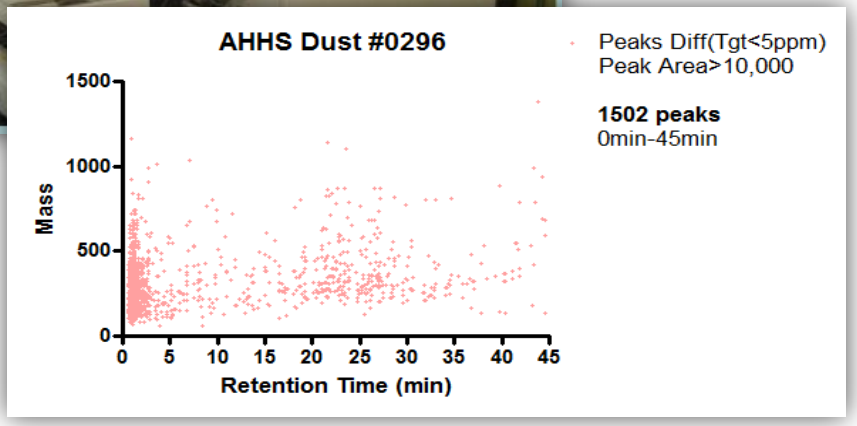
- What chemicals are found in dust in homes and where did they come from?
- Time of Flight (ToF) Mass Spectrometry of house dust and supporting chemoinformatics
- 56 samples from American Healthy Homes Study resulted in potentially 300,000 mass features
- How do the compounds found in dust compare with those we predict to find there using our chemical use and fate and transport models?
- Apply methodology to other media



Courtesy of Mark Strynar and Shuang Liang, NERL



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Contracts Awarded in December 2014 to Collect Exposure Data

Exposure Screening Tools for Accelerated Chemical Prioritization (ExpoCast)

- Solicitation posted May 22, 2013

- Two awardees:

  Battelle Memorial Institute (Columbus, OH) and

  Southwest Research Institute (San Antonio, TX)

- Contract will be used to obtain data on:
  (1) Key physical-chemical properties
  (2) Chemical emissions from consumer products used indoors
  (3) Chemical occurrence in consumer products
  (4) Chemical occurrence in environmental and biological media

Development of Models of Chemical Use and Product Composition

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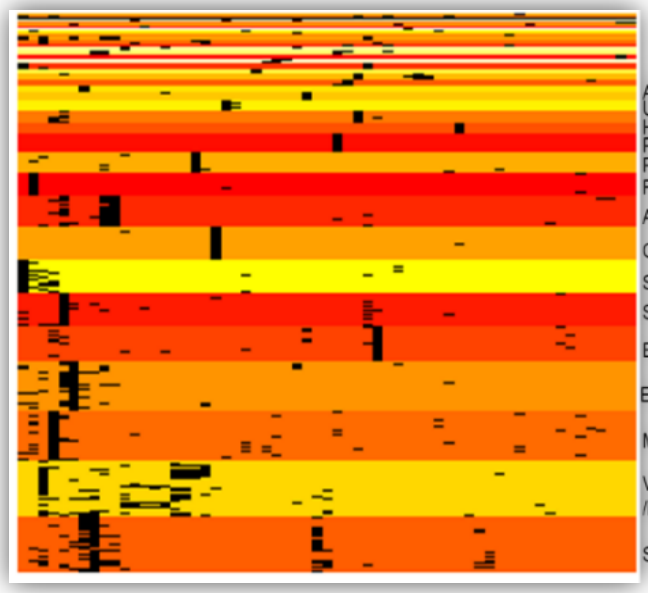

700+chemicals in Personal Care Products Clustered by their Functional Uses

Data-based Generic Product Formulations, e.g. Shampoo

Function(s)	Percent of Formulations	Mean %	SD	Number of Unique Chemicals	Most Common Chemical
Solvents	39.88	32.9	35.4	7	AQUA (7732-18-5)
Surfactants/ Cleansers/Emulsifiers	30.06	5.4	3.7	22	SODIUM LAURYL SULFATE (151-21-3)
Viscosity-Controlling /Emulsion Stabilizers/Binding Agents	45.66	1.4	1.5	7	CETYL ALCOHOL (36653-82-4)
Antidandruff Agents	24.86	1.1	0.6	1	ZINC PYRITHIONE (13463-41-7)
Buffering Agents	24.86	1.1	1	7	AMMONIUM CHLORIDE (12125-02-9)
Preservatives	14.45	1	2.5	12	IMIDAZOLIDINYL UREA (39236-46-9)

- Classification models for chemical functions based on properties; application to existing chemical lists
- Models for likely concentrations in consumer products based on function

Development of Models of Emission of Chemicals from Articles of Commerce

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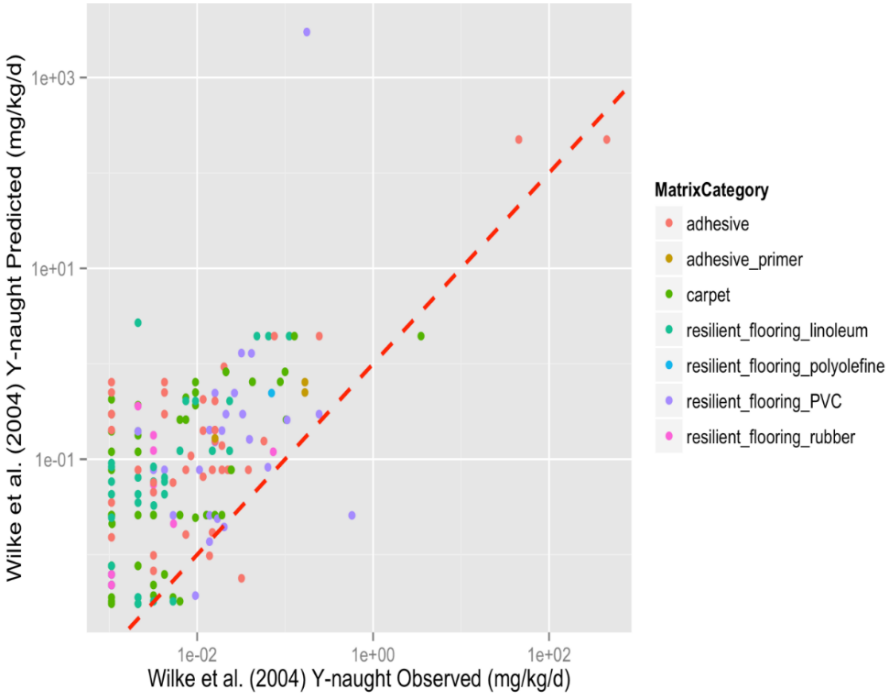

Courtesy of Chantel Nicolas

Indoor Fate and Transport and Resulting Exposures

Heuristic-Based Models of Exposure

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Heuristic	Description
ACToR "Consumer use & Chemical/Industrial Process use"	Chemical substances in consumer products (*e.g.*, toys, personal care products, clothes, furniture, and home-care products) that are also used in industrial manufacturing processes. Does not include food or pharmaceuticals.
ACToR "Chemical/Industrial Process use with no Consumer use"	Chemical substances and products in industrial manufacturing processes that are not used in consumer products. Does not include food or pharmaceuticals
ACToR UseDB "Pesticide Inert use"	Secondary (*i.e.*, non-active) ingredients in a pesticide which serve a purpose other than repelling pests. Pesticide use of these ingredients is known due to more stringent reporting standards for pesticide ingredients, but many of these chemicals appear to be also used in consumer products
ACToR "Pesticide Active use"	Active ingredients in products designed to prevent, destroy, repel, or reduce pests (*e.g.*, insect repellants, weed killers, and disinfectants).
TSCA IUR 2006 Total Production Volume	Sum total (kg/year) of production of the chemical from all sites that produced the chemical in quantities of 25,000 pounds or more per year. If information for a chemical is not available, it is assumed to be produced at <25,000 pounds per year.

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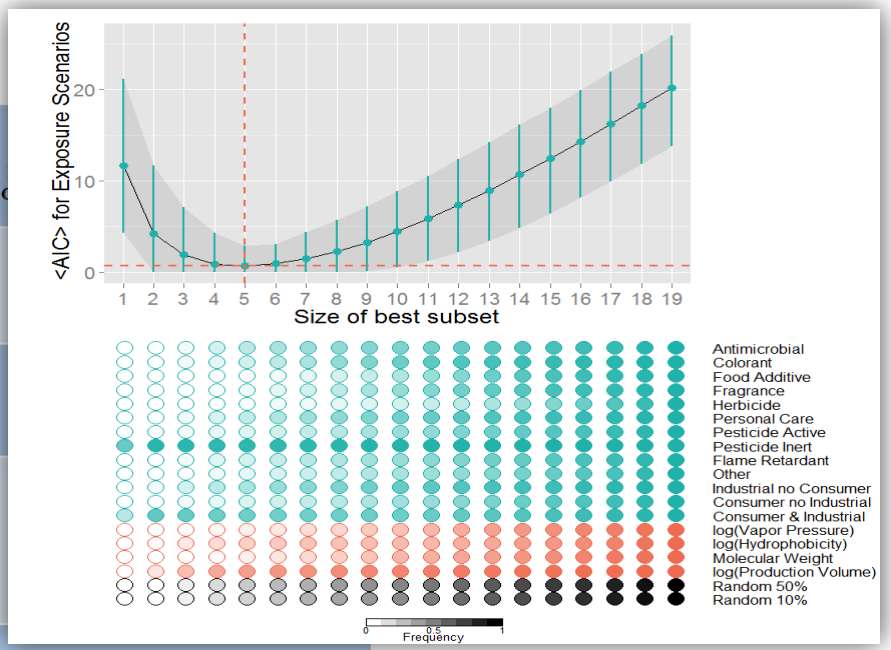

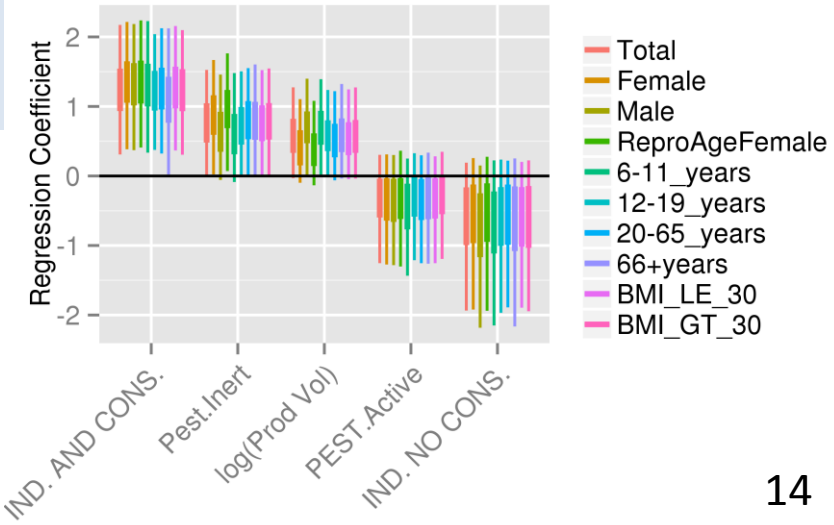

Wambaugh *et al.*, 2014

Probabilistic Human Exposure Modeling

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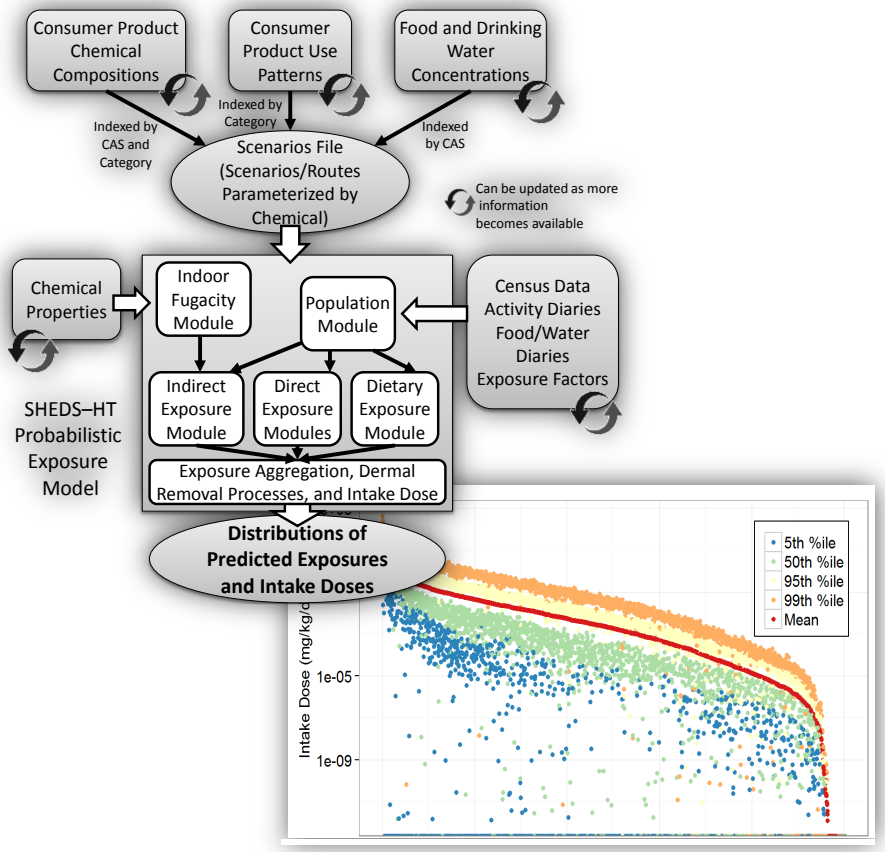
- By taking information from disparate datastreams, can we simulate demographics, activities, consumer product use, indoor chemical fate and transport, and resulting exposures and doses for thousands of individuals for thousands of chemicals?

- Stochastic Human Exposure and Dose Simulation Model-High Throughput (**SHEDS-HT**)

- Modular R-based probabilistic human exposure model



Isaacs et al., 2014

- Population exposure distributions for >2500 chemicals in consumer products

- Expansion to 1000s more chemicals in other products and articles via new exposure data (e.g. use information) and expansion of exposure pathways modeled

Development of HT Models for Ecological Exposure and Corresponding Monitoring Data

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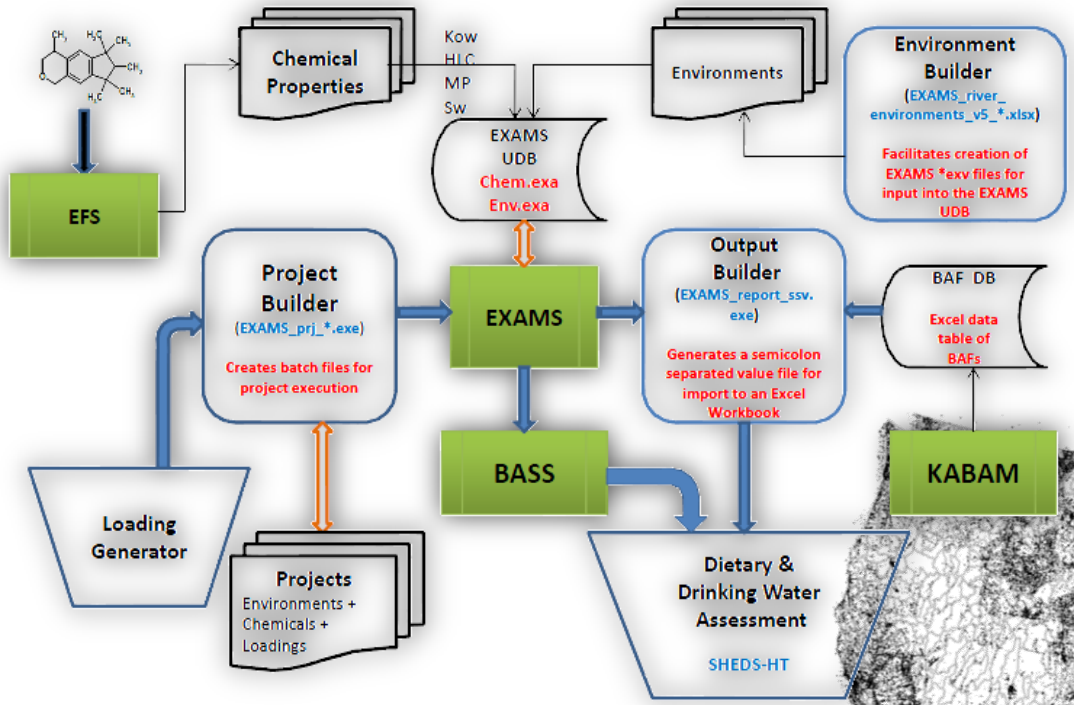
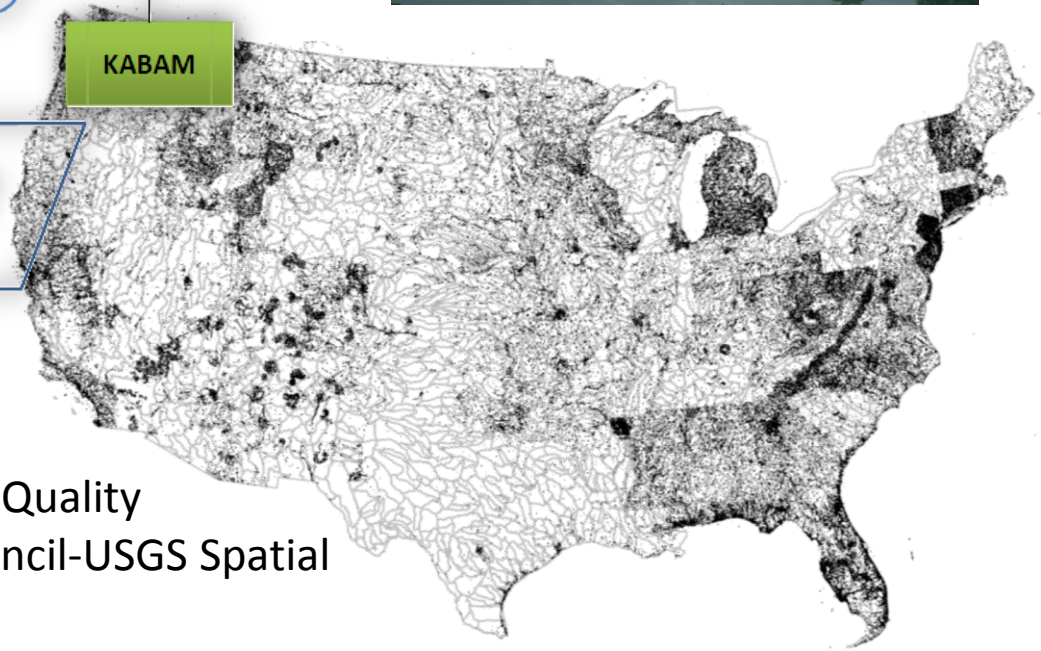


Courtesy of Craig Barber



National Water Quality Monitoring Council-USGS Spatial Data

Courtesy of Woody Setzer

Parameterization, Application, and Evaluation of CSS and Other Existing HT Models for Human Exposure to Large Numbers of Chemicals

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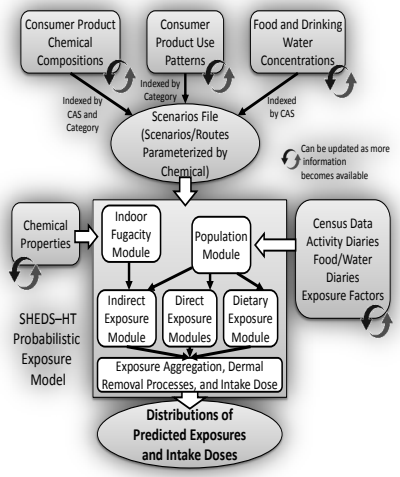
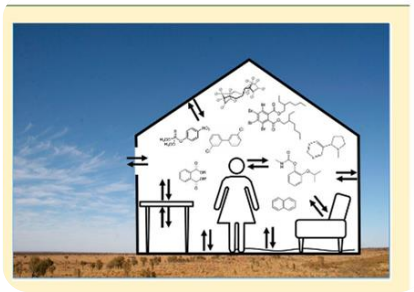
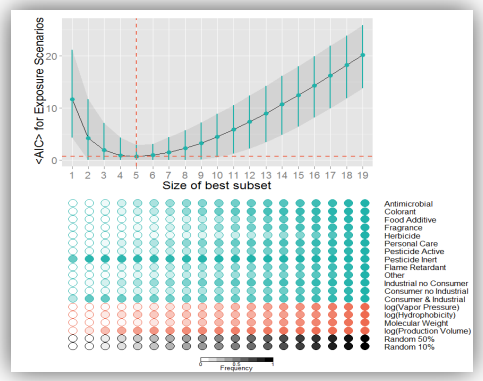


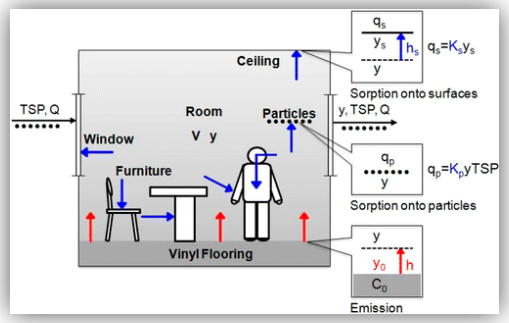
Isaacs et al., 2014



Zhang et al., 2014

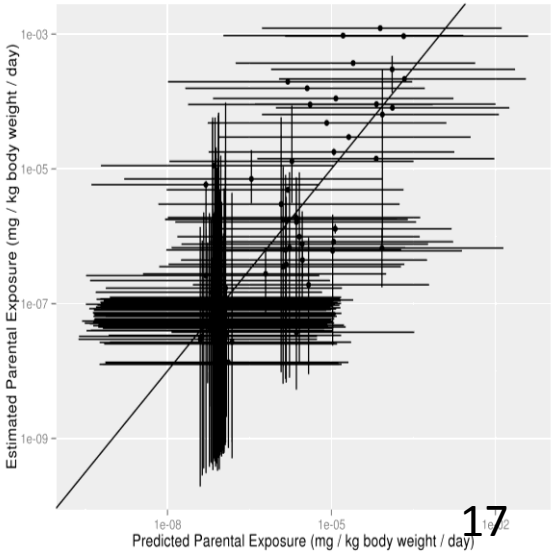


Wambaugh et al., 2014



Little et al., 2012

- Evaluation with NHANES biomonitoring data to build consensus models and exposure predictions
- Merge with hazard information to develop risk-based metrics for prioritization



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Chemical Safety for Sustainability (CSS) Rapid Exposure and Dosimetry (RED) Project

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