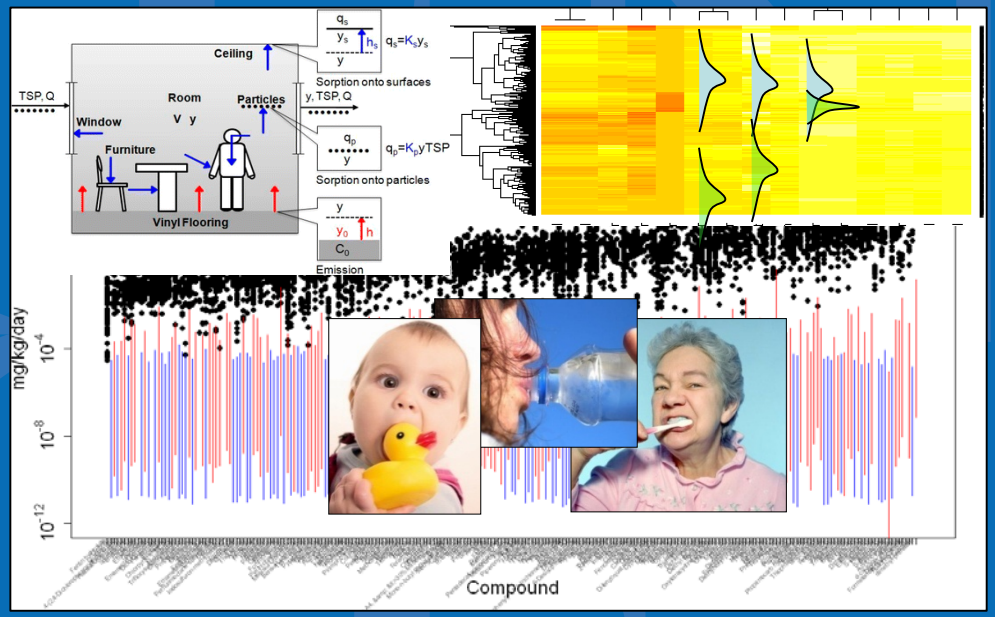
High Throughput Exposure Modeling of Semi-Volatile Chemicals in Articles of Commerce

Chantel I. Nicolas
ORISE Postdoctoral Chemist
U.S. EPA, ORD, National Center for Computational Toxicology



ACS-ENVR Presentation
August 11, 2014

Consumer Ingredient Database

Goldsmith et al. (2014), Food and Chem. Tox., ***65*****,** 269-279

- Created dataset of chemicals in consumer products (CP) with the help of chemical product categories list (CPCAT)

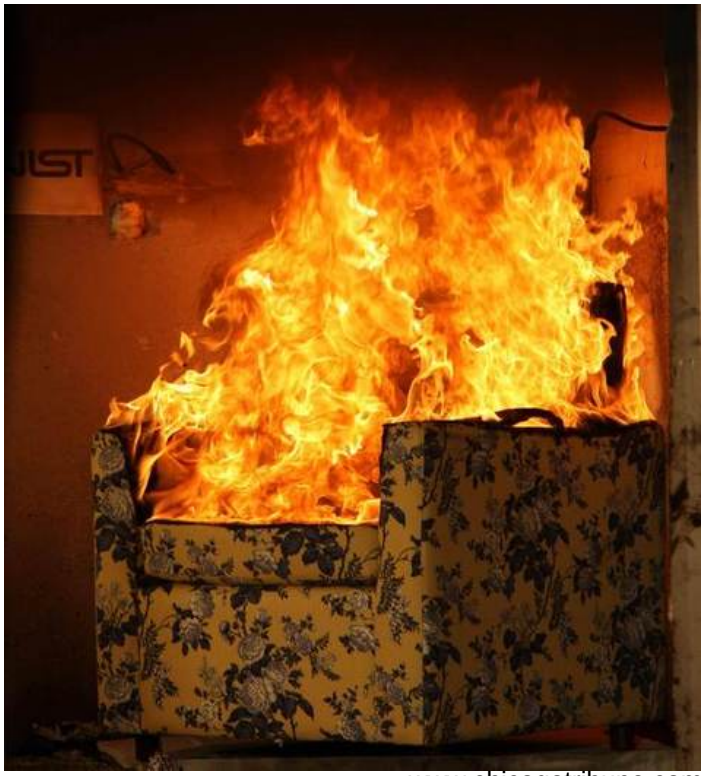
- Mapped ~1800 unique chemicals to ~9000 CP with MSDSs

www.quoteko.com

Predicting Exposures

Challenge: Predict exposures due to chemicals found in articles of commerce

- Industry is not required to provide formulation information (no MSDS)
- Observational studies are limited
- Analytical evidence is lacking
- Current models and techniques to model and predict near-field exposures may help

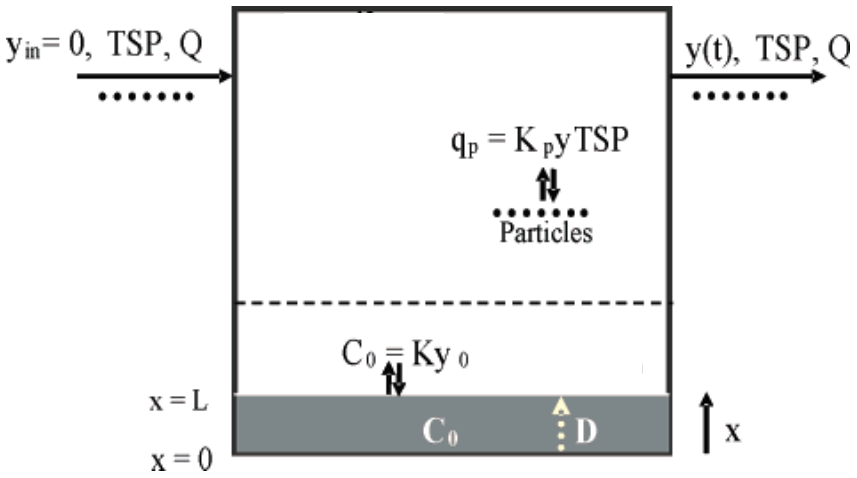


www.chicagotribune.com

Articles of Commerce

www.gmindy.com

Existing Models



Xu and Little (2006), Environ. Sci. Technol. ***40***, 456-451

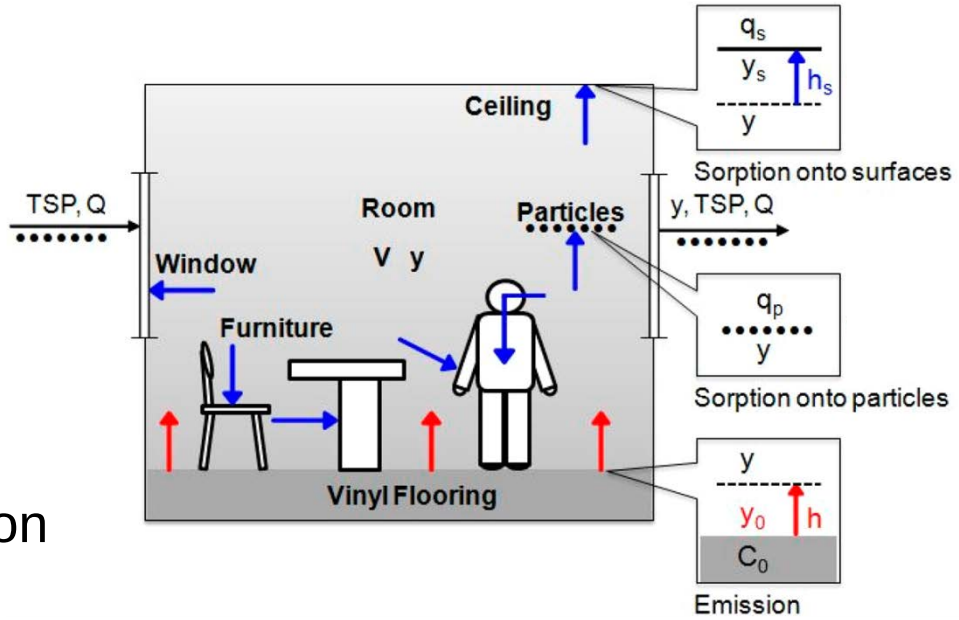
Xu and Little (2006)

1. Used vinyl flooring chamber to measure:
   a. Emission rate
   b. Surface adsorption
   c. Airborne particle adsorption

Little *et al*. (2012)

1. Proposed HTP methods to estimate exposure due to FRs

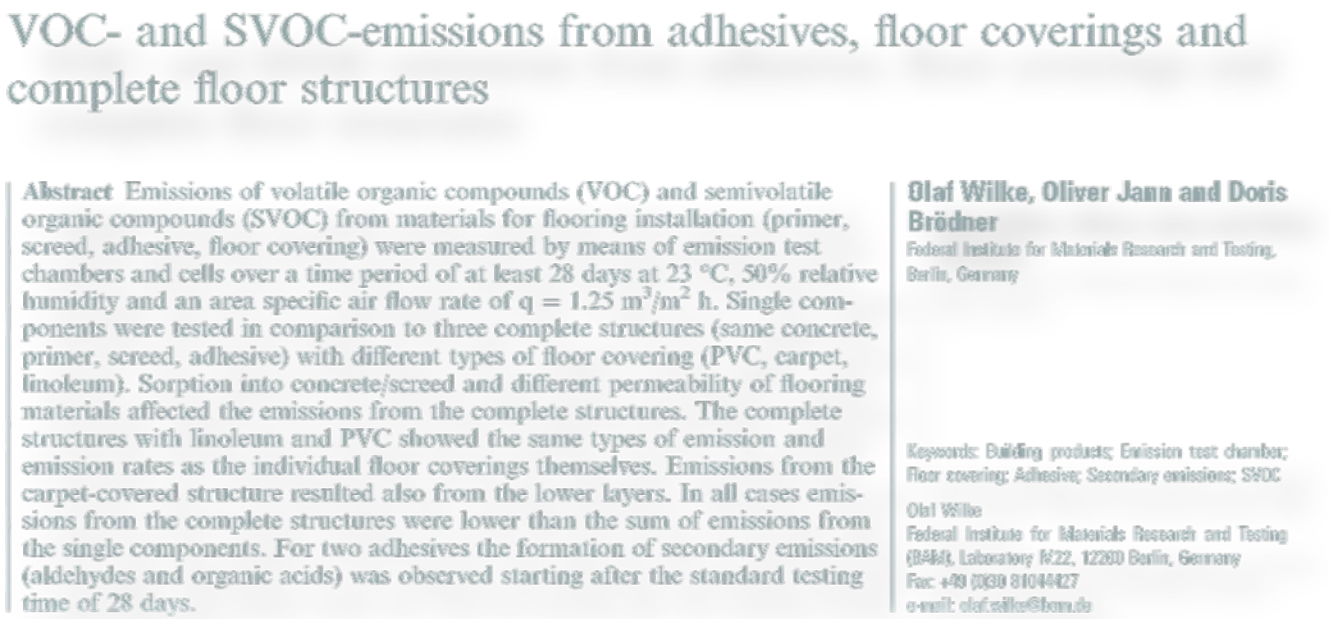
2. Proposed four main exposure parameters due to dermal absorption, air/particle inhalation, and dust ingestion



Little *et al.* (2012), Environ. Sci. Technol., ***46***, 11171-11178

Wilke et al. (2004) Training Set

- Analytical measurements of gas-phase concentrations (y_o) in flooring
- Key parameters for Little *et* al. (2006) model to estimate exposure
- How predictive will this experimental evidence be for other chemicals?



VOC- and SVOC-emissions from adhesives, floor coverings and complete floor structures

Abstract Emissions of volatile organic compounds (VOC) and semivolatile organic compounds (SVOC) from materials for flooring installation (primer, screed, adhesive, floor covering) were measured by means of emission test chambers and cells over a time period of at least 28 days at 23 °C, 50% relative humidity and an area specific air flow rate of q = 1.25 m^3/m^2 h. Single components were tested in comparison to three complete structures (same concrete, primer, screed, adhesive) with different types of floor covering (PVC, carpet, linoleum). Sorption into concrete/screed and different permeability of flooring materials affected the emissions from the complete structures. The complete structures with linoleum and PVC showed the same types of emission and emission rates as the individual floor coverings themselves. Emissions from the carpet-covered structure resulted also from the lower layers. In all cases emissions from the complete structures were lower than the sum of emissions from the single components. For two adhesives the formation of secondary emissions (aldehydes and organic acids) was observed starting after the standard testing time of 28 days.

Olaf Wilke, Oliver Jann and Doris Brödner
Federal Institute for Materials Research and Testing, Berlin, Germany

Keywords: Building products; Emission test chamber; Floor covering; Adhesive; Secondary emissions; SVOC

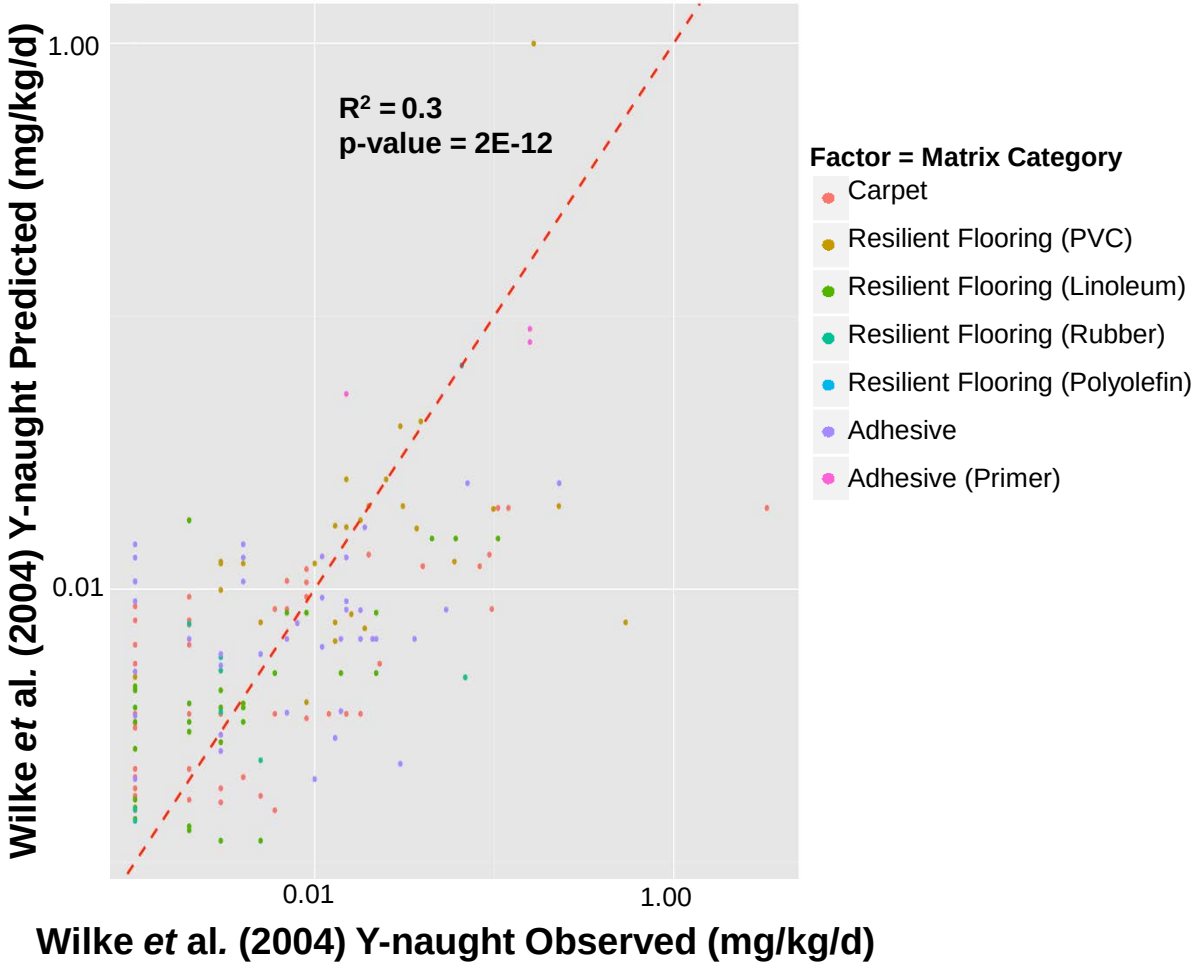
Olaf Wilke
Federal Institute for Materials Research and Testing (BAM), Laboratory V.22, 12200 Berlin, Germany
Fax: +49 (0)30 81044127
e-mail: olaf.wilke@bam.de

Wilke *et* al., (2004) Indoor Air, ***14***, 98-107

Gas-Phase Concentration Model

- 73 chemicals in model including SVOCs[1]
- 41 FRs in ToxCast (CPCat)
- 2 main properties that model data (LogP and VP)
- 1 novel house model used to estimate exposures[2]

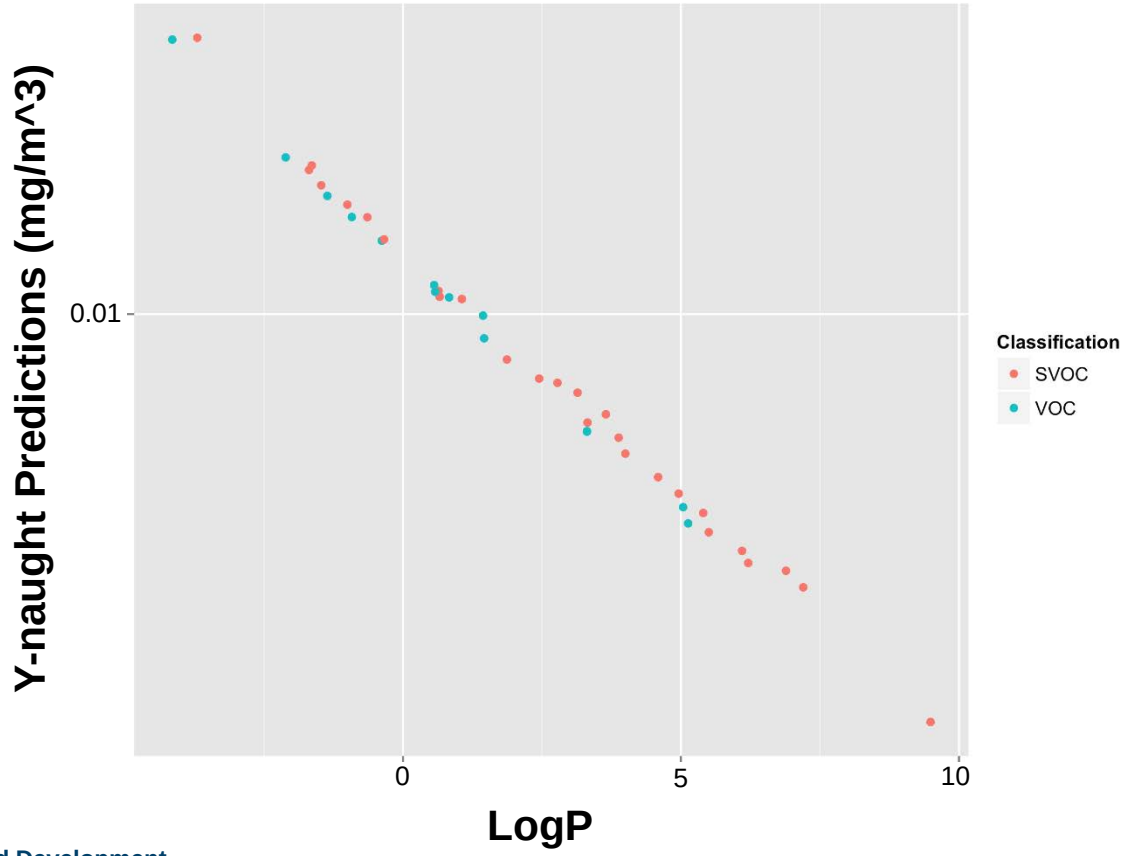
Acronyms:
- SVOCs = Semivolatile Organic Compounds
- FRs = Flame Retardants
- VP = Vapor Pressure
- LogP= Octanol:water partition coefficient
- Y_0 = Gas-phase concentration



References:
1. Wilke *et al.* (2004)
2. Little *et al.* (2012)

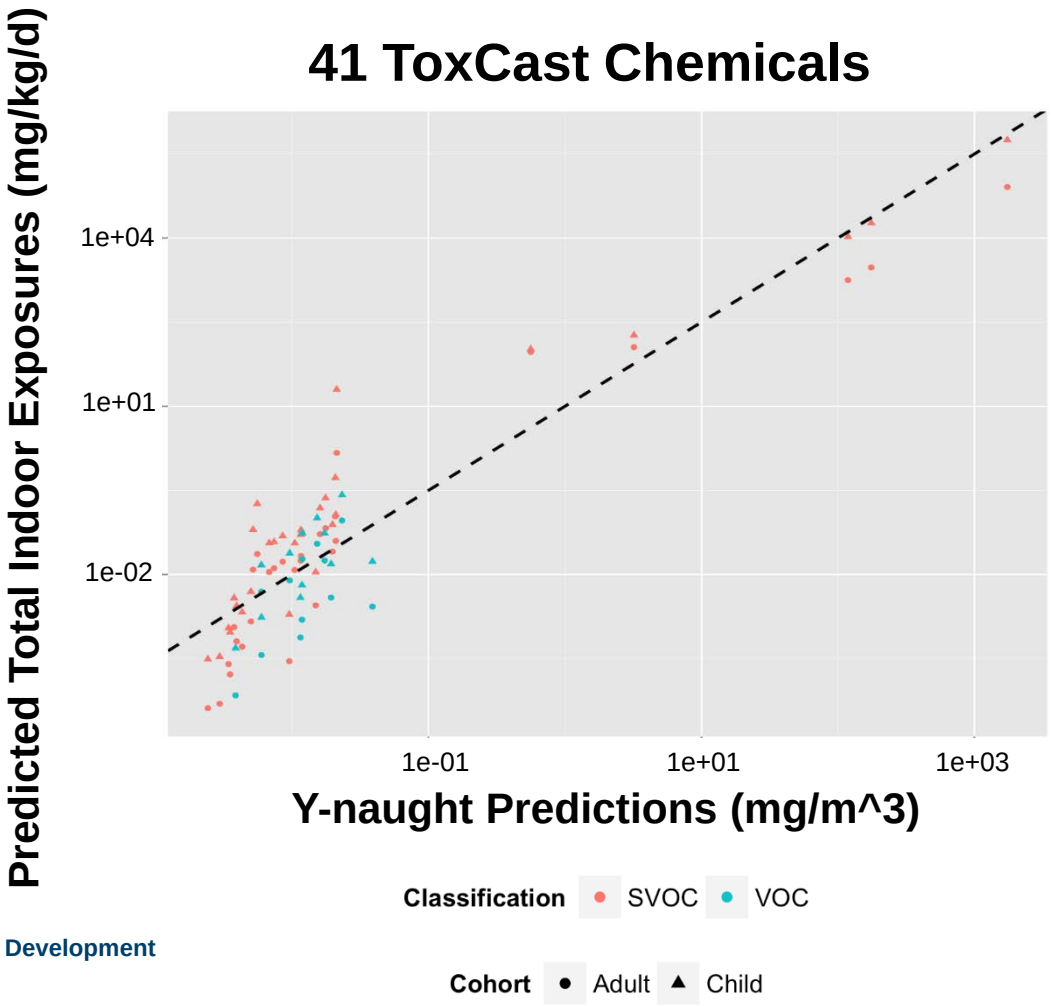
Y-naught Predictions

- Gas-phase concentration (y-naught) predictions for 41 ToxCast chemicals based on Wilke *et* al. (2004) training set



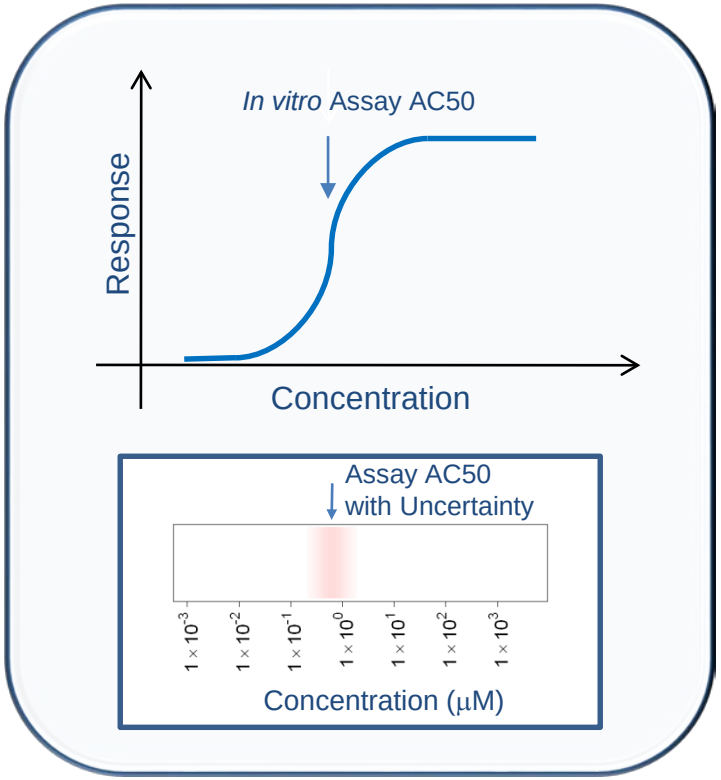
Indoor Exposure Predictions

- Little *et* al. (2012) model used to predict indoor exposures to ToxCast chemicals



High-Throughput Bioactivity

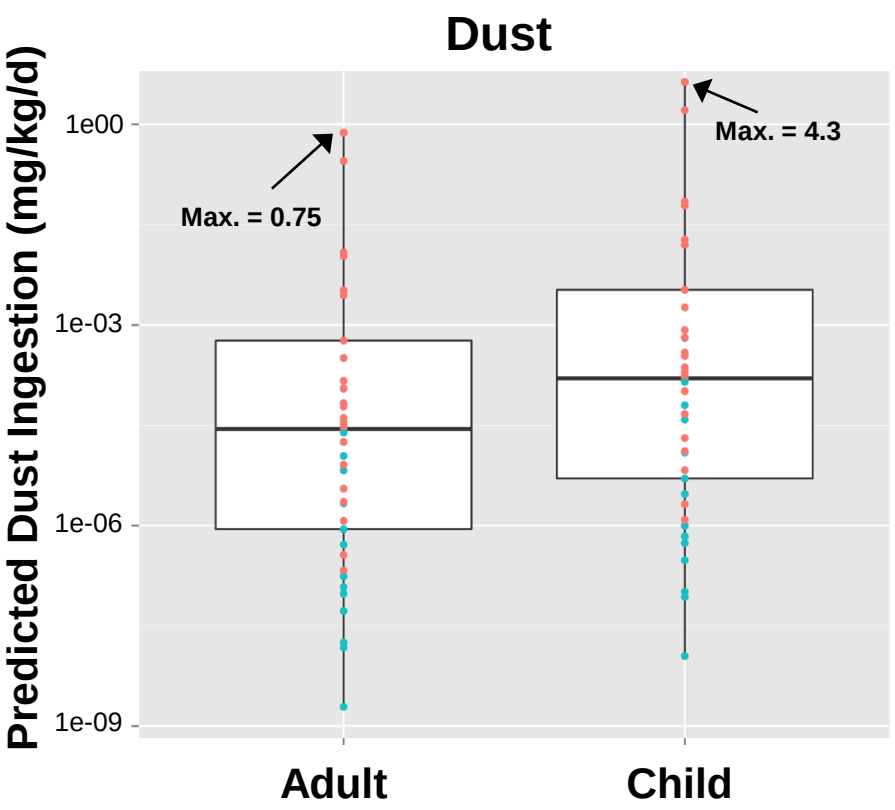
- **Tox21**: Examining ~10,000 chemicals using ~50 assay-endpoints intended to identify interactions with biological pathways (Schmidt, 2009)
- **ToxCast**: For a subset (~2000) of Tox21 chemicals ran >600 additional assay-endpoints (Judson et al., 2010)
- Most assay-endpoints conducted in dose-response format (identify 50% activity concentration – AC50 – and efficacy if data described by a Hill function)
- All data is public: http://actor.epa.gov/

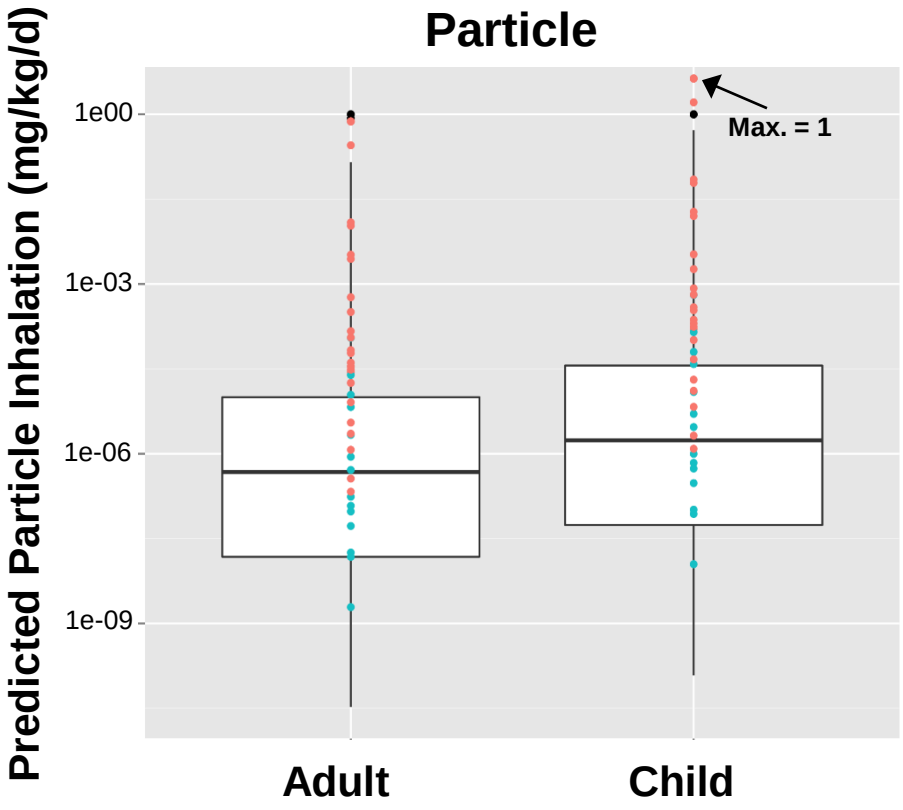


- Translation from *in vitro* concentration to steady-state oral equivalent doses by Wetmore *et al*. (2012)

*Slide from John Wambaugh

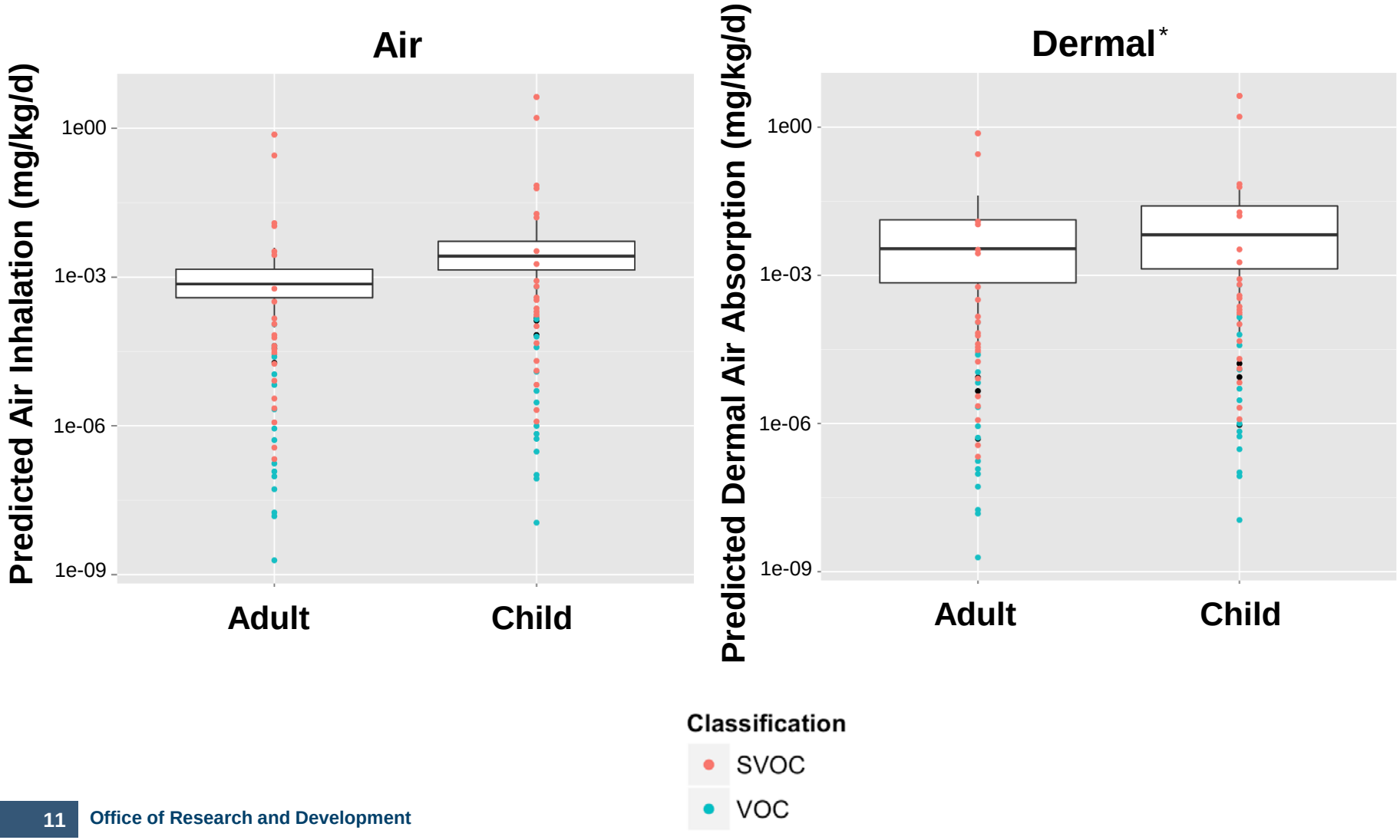
Indoor Exposure Contributions I





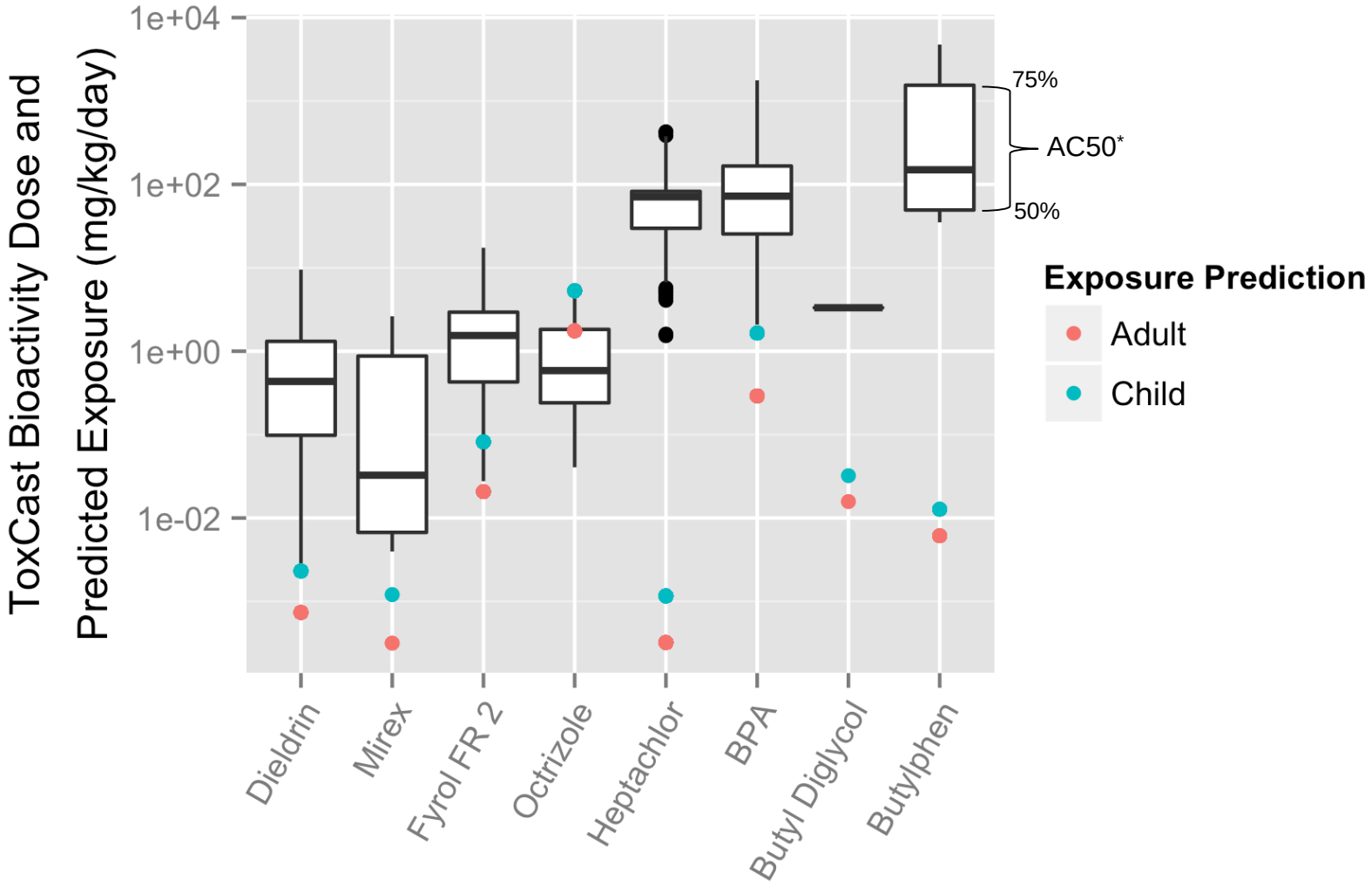
Classification
SVOC
VOC

Indoor Exposure Contributions II



*Mitragotri *et* al., (2002) J. Pharm. Sci.***91***, 744-752

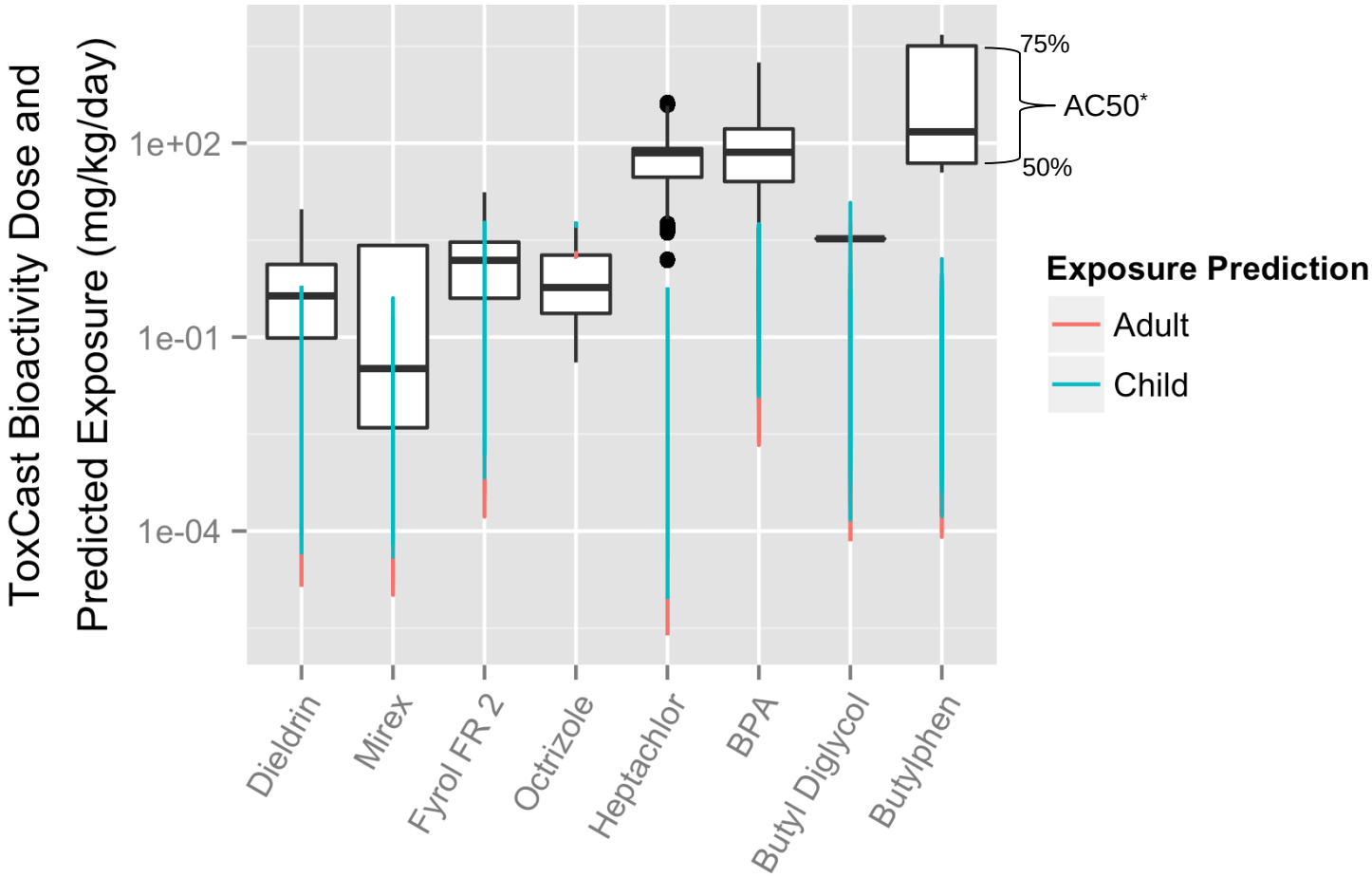
Total Indoor Exposures versus Equivalent Applied Doses



*Unpublished data provided by Barbara Wetmore

Uncertainty Analysis

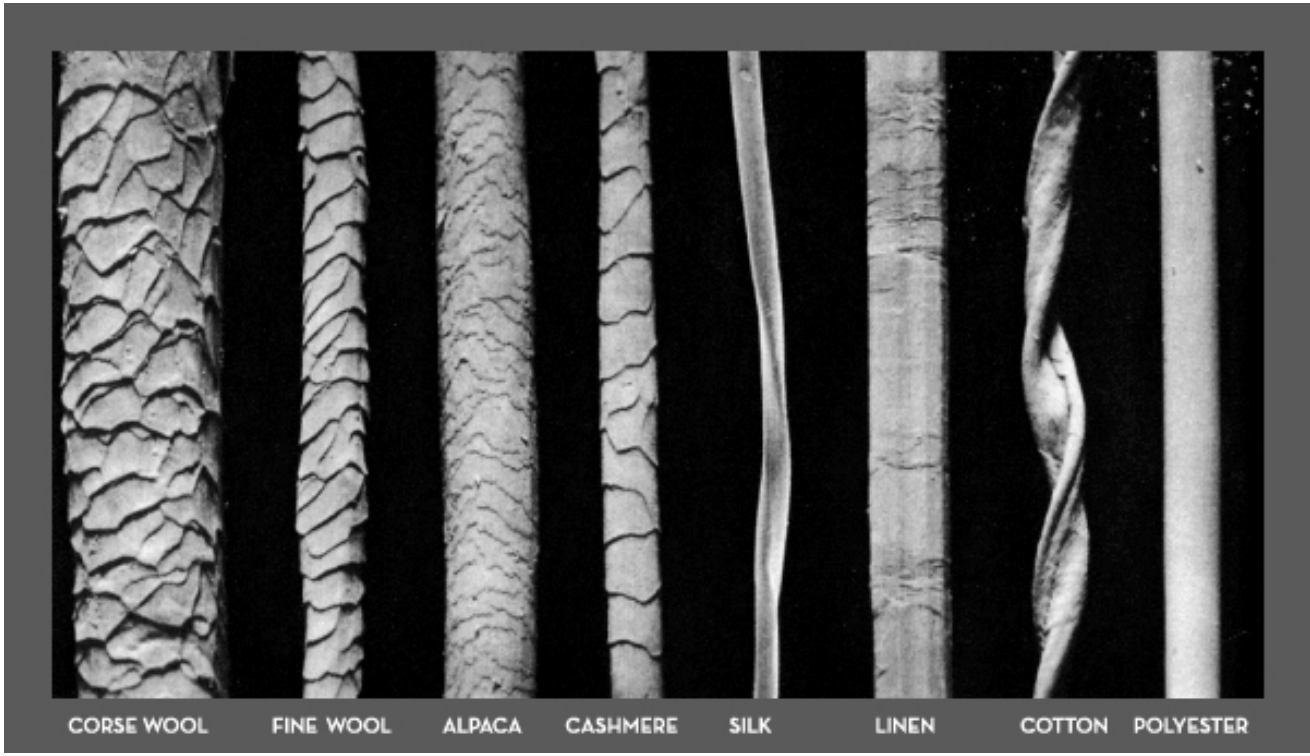
- Monte Carlo Simulations



*Unpublished data provided by Barbara Wetmore

Refining the Model

- Pore size
- Crystallinity
- Material type
- Surface area
- Fugacity potential



http://blog.nau.com

Conclusions

- A regression model predicting the concentrations of SVOCs in the air in contact with their sources (y_0) of a test-set of chemicals were generated

- An R^2 value of ~0.3 resulted showing that LogP and VP were most significant predictors

- Little *et* al. (2012) model allows us to potentially predict indoor exposures for chemicals with parse analytical data in carpet

- Statistical analysis will help us assess domain of applicability, sensitivity, and uncertainty (MC)

Future Work

1. Utilize statistical methods to
    a. Assess domain of applicability
    a. Perform uncertainty analysis on other parameters (Monte Carlo simulation)

2. Improve gas-phase concentration model by
    a. Including descriptors for textile properties
    a. Narrowing down scope of model to specific types of materials or chemicals
    a. Validating model via wet lab analysis (contracts)

Acknowledgements

ExpoCast™

Kathie Dionisio
Peter Egeghy
Kristin Isaacs
Xiaoyu Liu
Chantel Nicolas
Robert Pearce
Woody Setzer
Cory Strope
Dan Vallero
John Wambaugh*

ToxCast™

Bhavesh Ahir
Richard Judson
Thomas Knudsen
Kamel Mansouri
James Rabinowitz

External Collaborators

Rocky Goldsmith (Chemical Computing Group)
Barbara Wetmore (Hamner Institutes)
New contracts to be awarded soon

*Principal Investigator

The views expressed in this presentation are those of the author and do not necessarily represent the views or policies of the U.S. Environmental Protection Agency.