High Throughput Modeling of Indoor Exposures to Chemicals

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Abstract

Risk due to chemical exposure is a function of both chemical hazard and exposure. Near-field exposures to chemicals in consumer products are identified as the main drivers of exposure and yet are not well quantified or understood. The ExpoCast project is developing a model that estimates indoor exposures to chemical additives in textiles, such as flame retardants, which are found in flooring, upholstery, and articles of clothing. Physicochemical properties of chemicals largely dictate how they may accumulate in the indoor environment at higher magnitudes than in the outdoor environment, which along with proximity of the sources, is correlated with high indoor exposure rates. Halogenated flame retardants, such as polybrominated diphenyl ethers (PBDEs), are semi-volatile compounds that are potentially harmful to humans. Given that chemical emission calculations principally depend on gas-phase concentration (y_0) and source surface area, we used a model (Little *et al.* 2012)[1] to assess the utility of physicochemical property information in predicting indoor emissions for these additives. Gas-phase concentrations were predicted using a regression model of experimental measurements of 74 chemicals found in 32 flooring materials by Wilke *et al.* (2004).[2] The flooring materials include a range of natural and synthetic floor coverings, installations, and adhesives. A linear regression yielded R^2- and p- values of approximately 0.3 and 2.0E-12, respectively, whereby logP and vapor pressure were significant predictors of y_0 along with its presence in adhesives and resilient flooring materials. These results potentially permit the forecasting of gas-phase concentrations of chemicals for which their analytical data in flooring materials are lacking. Predictions generated from using high throughput exposure methods were then combined with ToxCast high-throughput bioactivity screening data as a demonstration of high-throughput risk prioritization. *This abstract does not necessarily reflect EPA policy.*

Introduction: ToxCast + ExpoCast

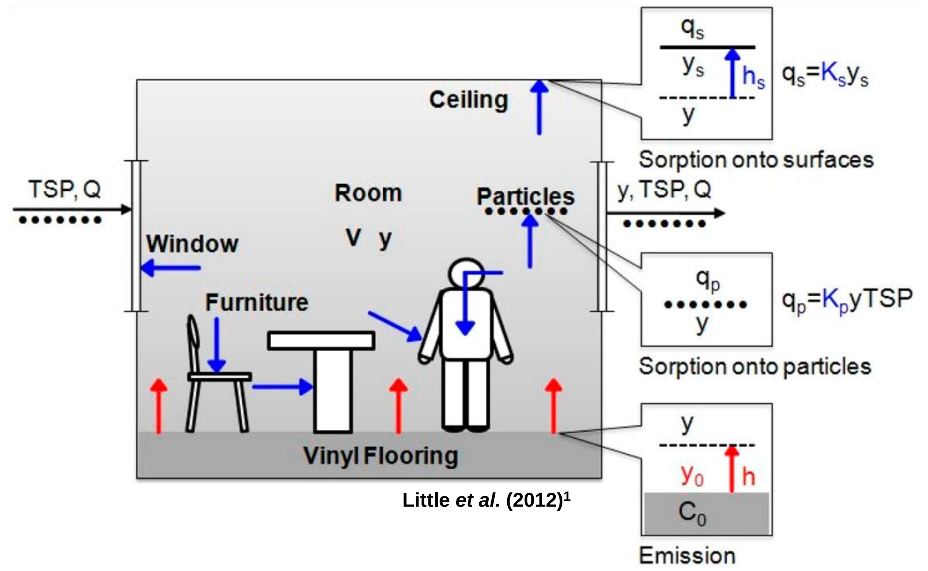
•The ToxCast program is working together with ExpoCast to develop a comprehensive approach towards risk-based prioritization of commercial chemicals using high throughput screening methods.

•Less than 20% of the 108,443 ACToR chemicals that have some hazard data, also have exposure data, which is due in part to limited time and resources as well as a lack of a federal mandate for companies to provide formulation data for chemical additives in articles of commerce, which may contain semi-volatile organic compounds (SVOCs).

•SVOCs such as polybrominated diphenyl ethers (PBDEs), are semi-volatile organic compounds that are potentially harmful to humans.

•Human exposures SVOCs, are at a much higher rate indoors than outdoors because humans tend to spend more time indoors.

•Engaging in exposure-based prioritization for 1000's of chemicals requires the use of models that estimate exposures in a time and cost effective manner.



•Little *et al.* (2012)[1] provide a rapid method to estimate exposure to SVOCs by combining use information with emissions data and properties of chemicals.

•This model estimates exposure in mg/kg/d due to particle ingestion, dermal air absorption, as well as a dust inhalation; it requires the concentration of the SVOC in the air in contact with the source (gas-phase concentration (y_0)) as well as the source surface area.

•Concentration data from Wilke *et al.* (2004) was utilized to predict the gas-phase concentrations of chemicals found in various flooring materials based on their physical chemical properties.

•The indoor exposures for 41 ToxCast Phase II chemicals were predicted using the Little model and then compared with available hazard data.

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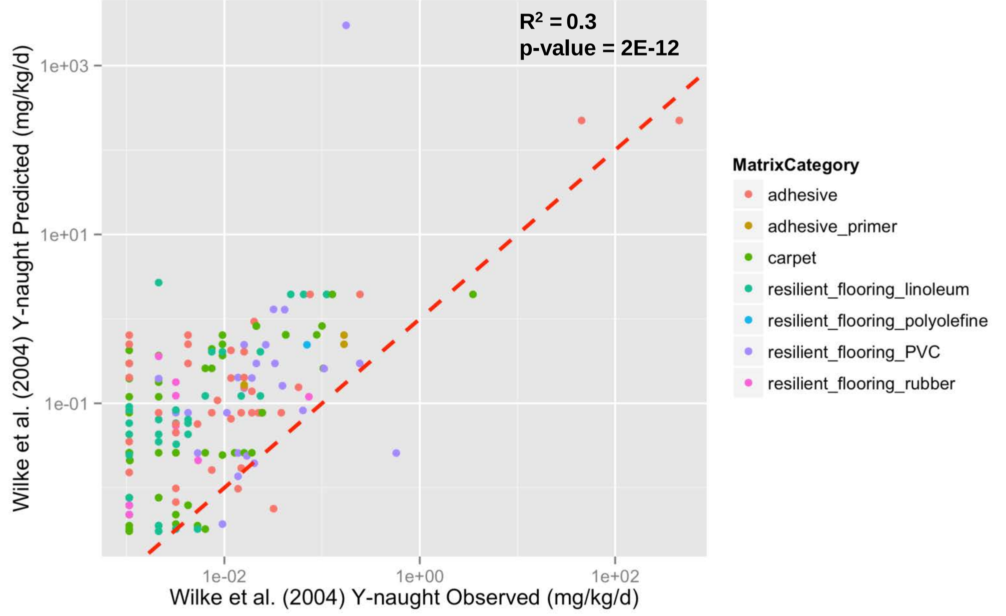
High Throughput Indoor Exposure Modeling

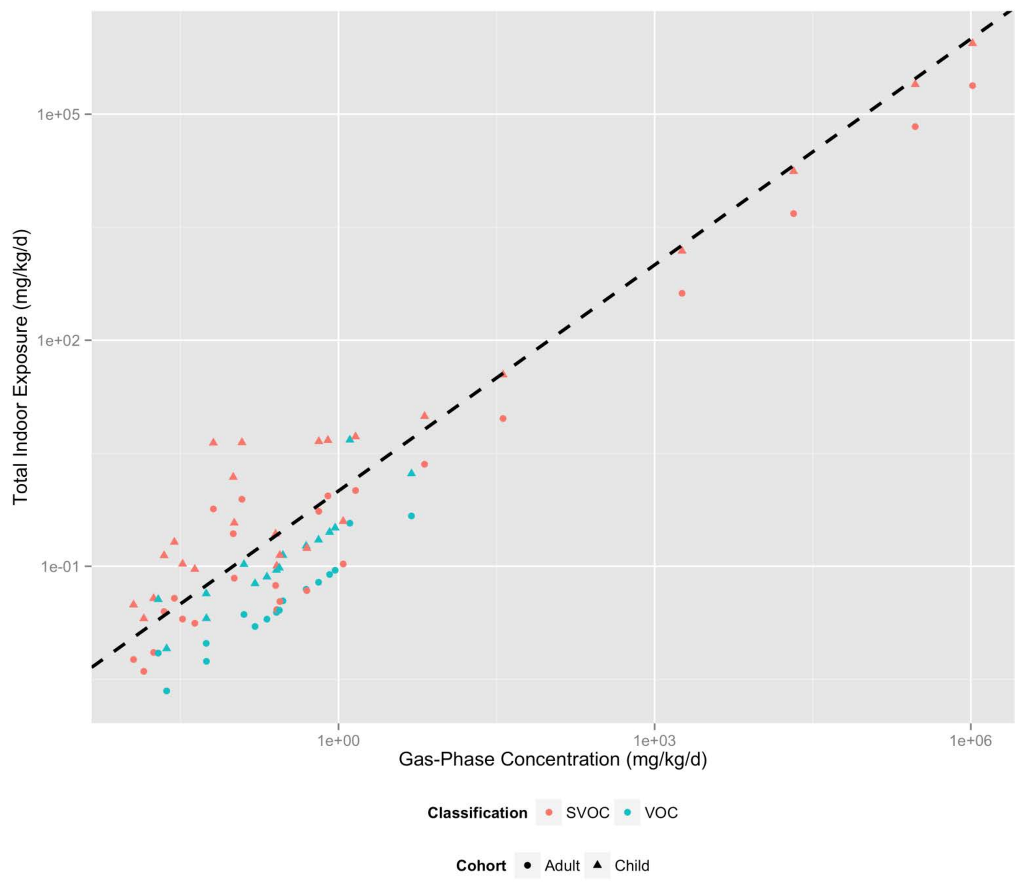
Figure 1. Regression Model for Predicting Y_0



•The physicochemical properties of a total of 72 chemicals were found in various flooring materials, which include various carpet types, adhesives, and resilient flooring materials[2], were utilized in order to determine whether gas-phase concentrations of chemicals found in textiles could be predicted. (Figure 1)

•The properties utilized in this model were logP, vapor pressure (VP), Henry's law, and molecular weight.

Figure 3: Predicted Total Indoor Exposures for Adults and Children

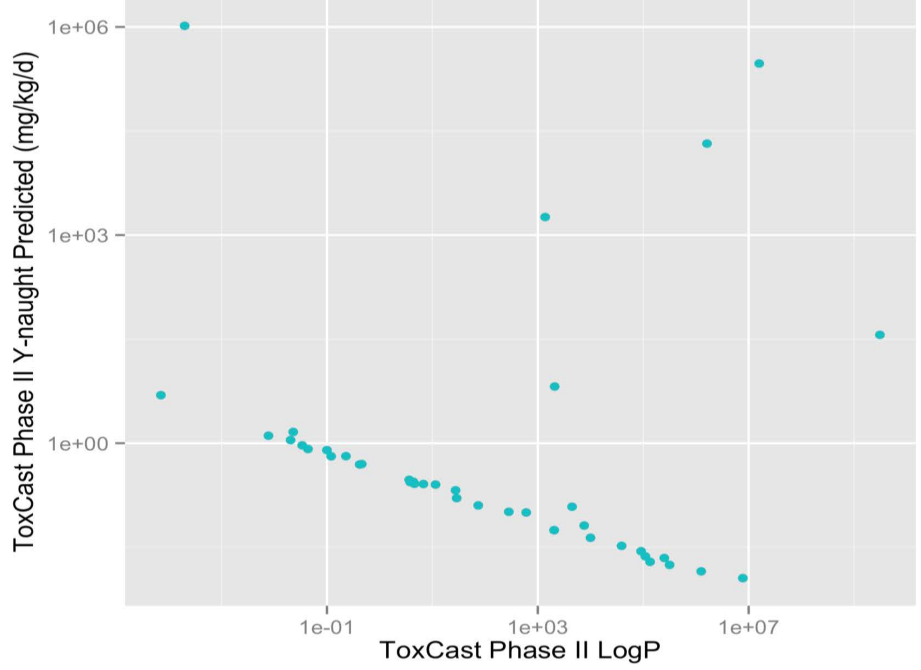


•In Figure 3 are the predicted total indoor exposures due to 41 ToxCast Phase II flame retardants that lack exposure data.

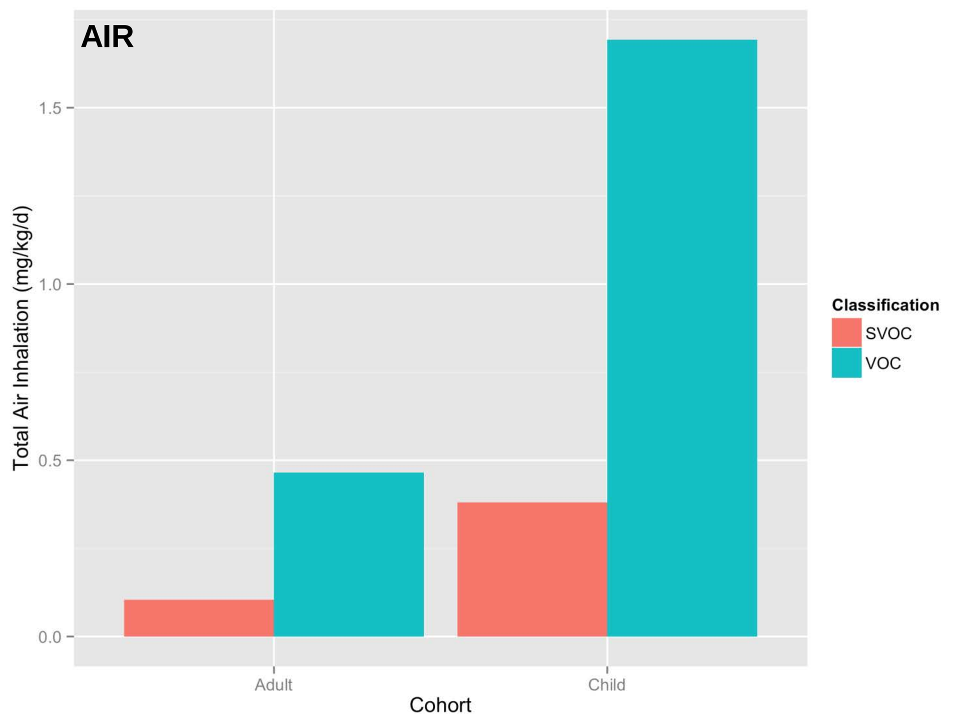
•The exposure estimates of children are much higher than that of adults and SVOCs tend to have higher indoor exposure rates because children have higher inhalation rates.[1,3,4]

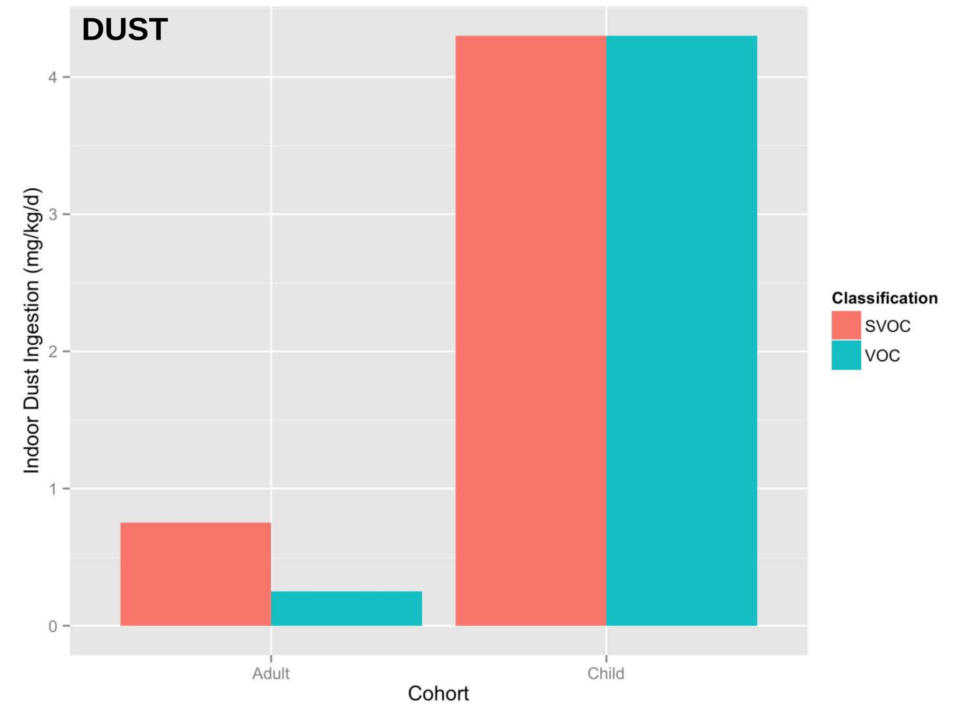
*CPCat = Chemical and Product Categories

Figure 2: Predicted Y_0 for Adults and Children



•Figure 2 shows the relationship between the octanol:water partition coefficient (LogP) of 41 ToxCast Phase II flame retardants, classified by CPCat*, and their predicted gas-phase concentrations.





High Throughput Risk Prioritization

•Of the 41 ToxCast Phase II flame retardants classified via CPCAT, ToxCast *in vitro* hazard data were available for only 8 of them, including dieldrin, heptachlor, and bisphenol A (BPA), to name a few.

•BPA exposure rates were at least two orders of magnitude higher than its estimated equivalent applied dose in mg/kg/day** for some of the assays. (Figure 4).

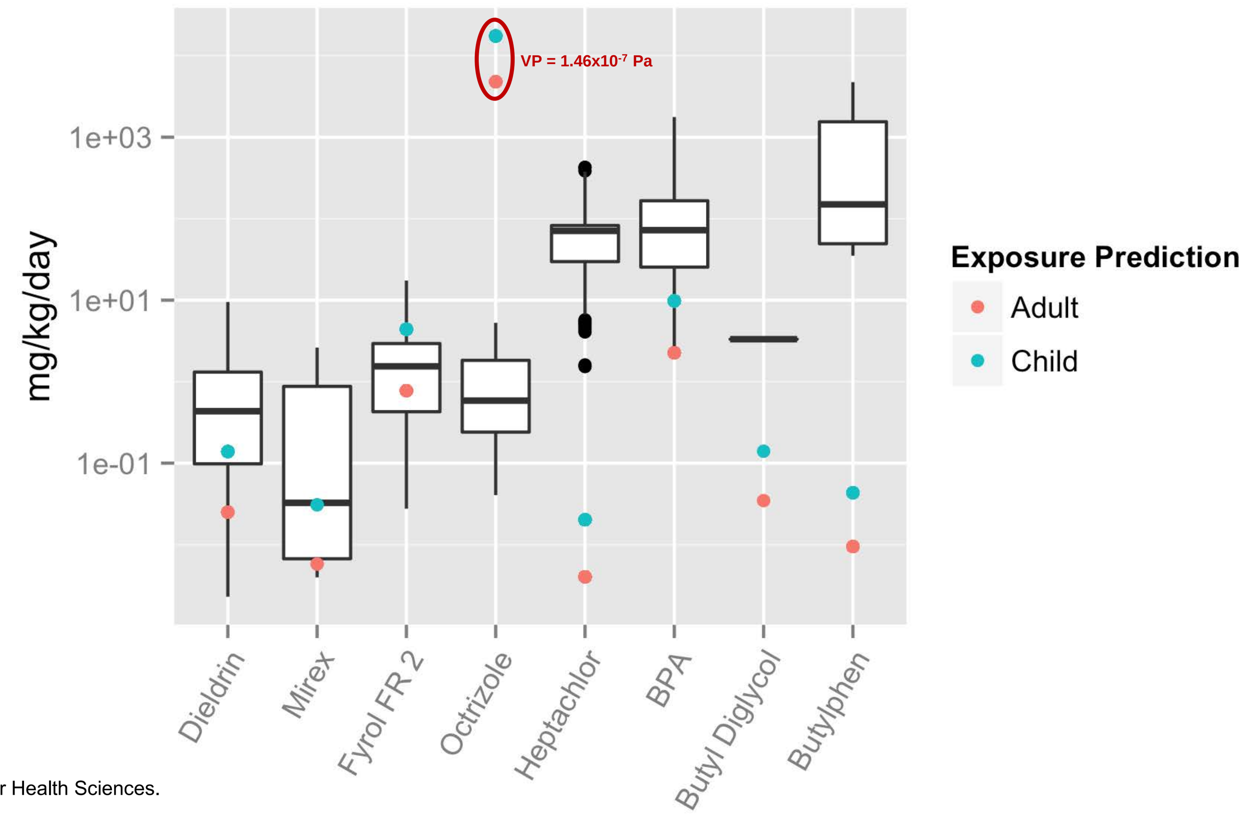
•The upper and lower edges correspond to the 25th and 75th percentiles.

•These eight chemicals have been tested using *in vitro* assays that include:

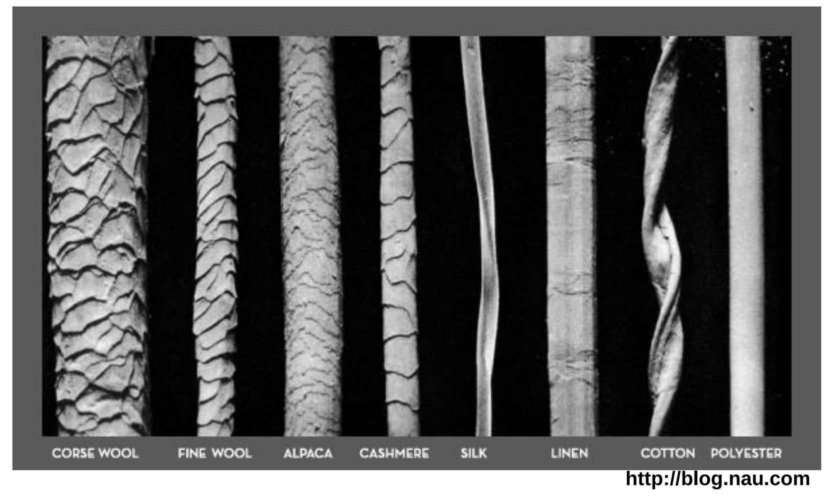
- •Attagene (ATG)
- •Bioseek (BSK)
- •Novascreen (NVS)
- •Appredica (APR)

**Assay data provided by Barbara A. Wetmore at The Hamner Institutes for Health Sciences.

Figure 4: Total Indoor Exposures versus Equivalent Applied Doses



The Importance of Twill Type and Textile Descriptors



•The image to the left illustrates the noticeable differences between various textile fibers.

•Surface areas of materials thus vary and this will further impact how chemicals may partition out of them into the air and onto surfaces.

•Descriptors under consideration for use in better defining these textiles are based on their capacity to affect the rate at which chemicals partition out of the material phase and may include:

- •Fugacity Potential
- •Crystallinity
- •Surface Area
- •Pore Size
- •Material Type

Conclusion

•Using the physicochemical properties of chemicals and their observed gas-phase concentrations in various flooring materials[2], a regression model predicting the concentrations of SVOCs in the air in contact with their sources (y_0) of a test-set of chemicals was generated. An R^2 value of ~0.3 showed that LogP and vapor pressure were among the most significant predictors for y_0.

•Of the eight flame retardants that have available bioactivity data, five of them have an overlap between their predicted indoor exposures and their equivalent applied doses, while three of them were predicted to have a margin of exposure greater than ten (assuming steady-state has been reached).

•Future work includes the improvement of the regression model to include descriptors that identify properties that may be specific to various articles of commerce such as their fugacity potential, which may largely affect the partitioning of SVOCs into the air and other media.