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United States Environmental Protection Agency

Annual Meeting & ToxExpo
VIRTUAL EVENT • MARCH 2021

Prediction of Population Exposures to Chemicals in the Indoor Residential Environment

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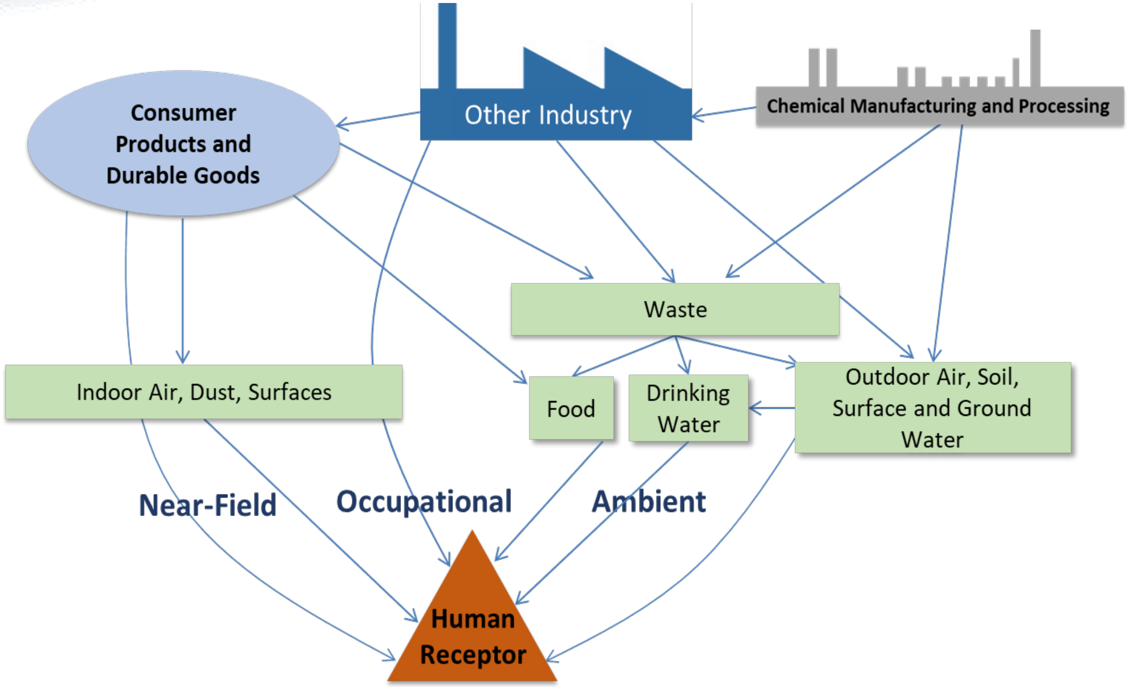
ExpoCast: Understanding Chemical Exposure Pathways

- The U.S. Environmental Protection Agency must prioritize thousands of commercial chemicals for further study: which have the highest potential risk?
  - Requires both ***exposure*** and ***hazard*** information
  - Many of these chemicals are data-poor with respect to exposure
- EPA Office of Research and Development's ExpoCast project is charged with characterizing ***exposure pathways*** for thousands of chemicals



ExpoCast: Understanding Chemical Exposure Pathways

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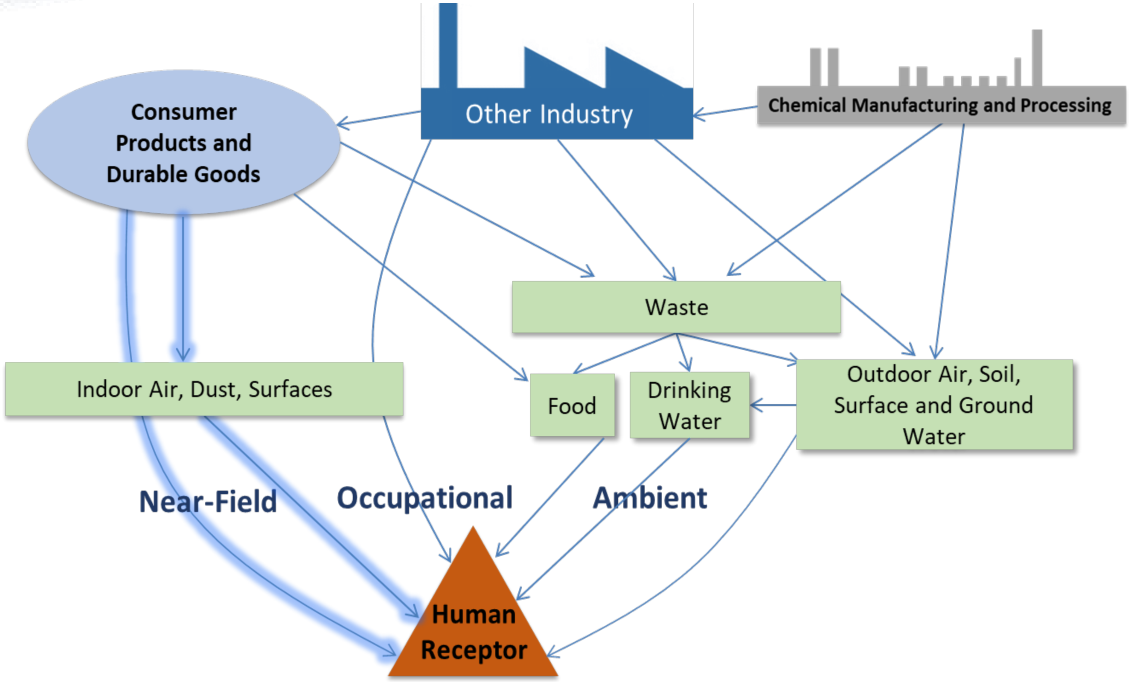
  - Requires both ***exposure*** and ***hazard*** information
  - Many of these chemicals are data-poor with respect to exposure
- EPA Office of Research and Development's ExpoCast project is charged with characterizing ***exposure pathways*** for thousands of chemicals
- Chemicals used in a "near-field" or residential context have higher observed concentrations in biomonitoring studies (Wambaugh et al. 2013, 2014)
- ExpoCast has been addressing several critical research questions around characterizing near-field (residential) exposures to many chemicals




Environmental Science & Technology

Article

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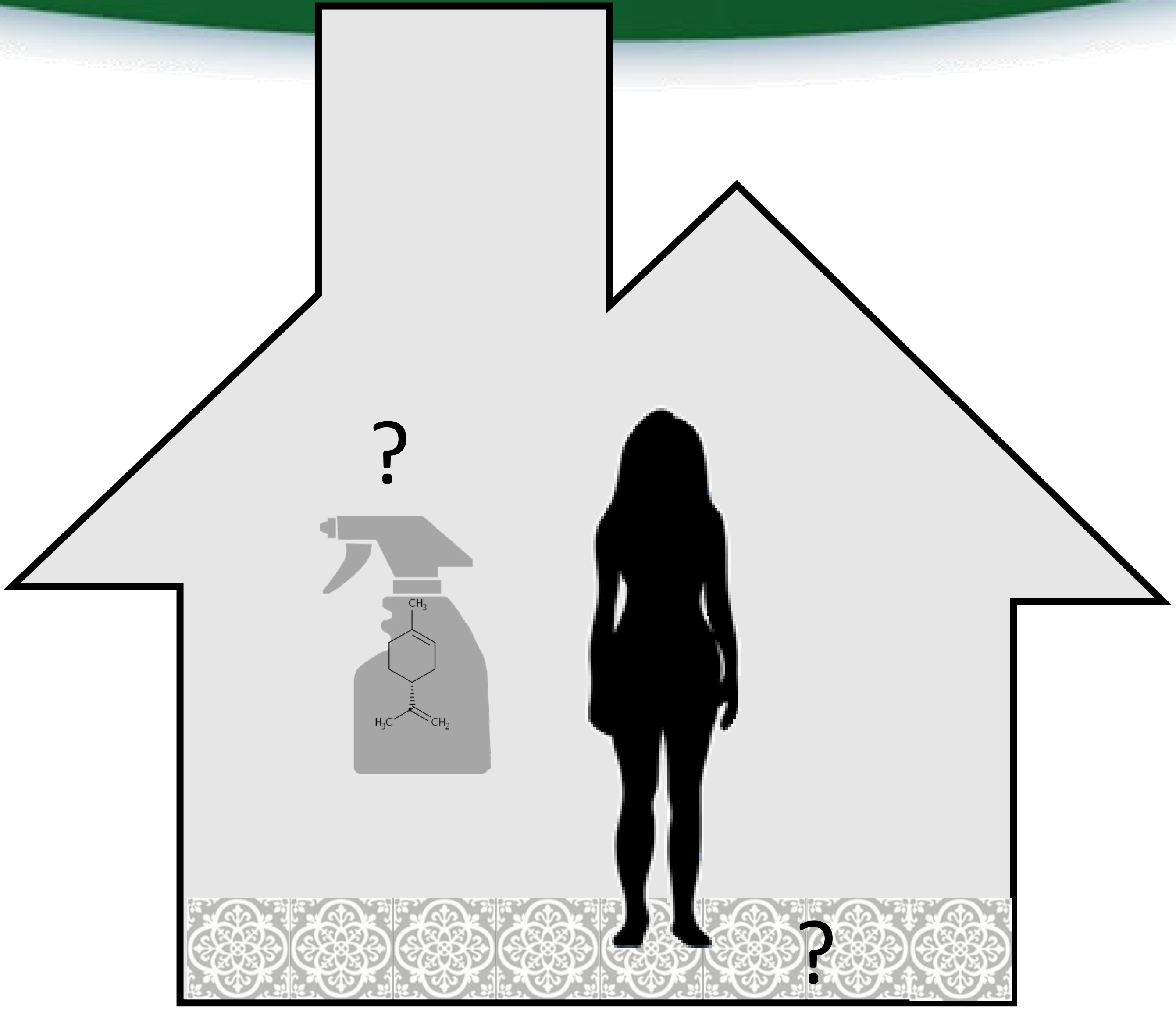
High Throughput Heuristics for Prioritizing Human Exposure to Environmental Chemicals

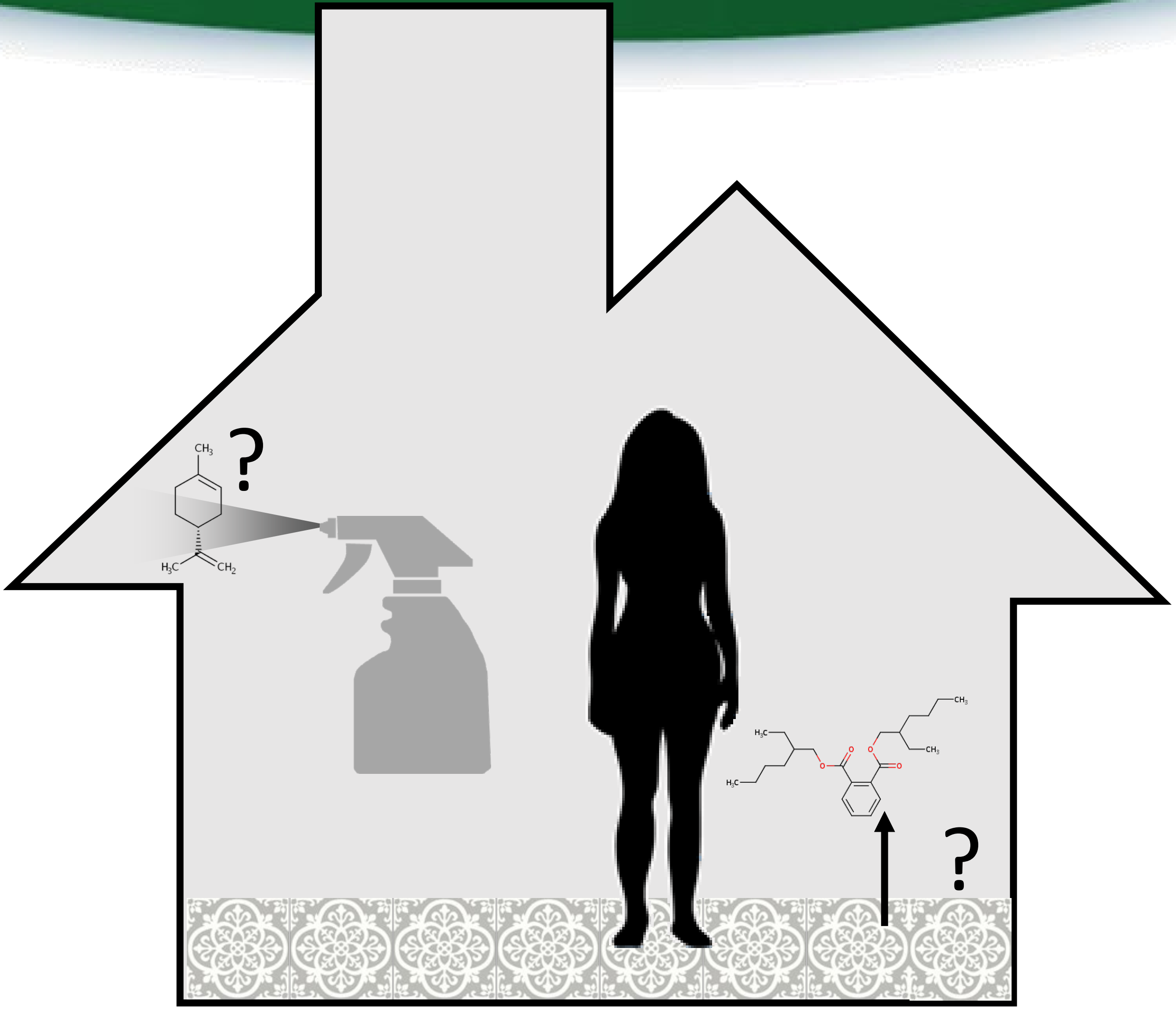
John F. Wambaugh,*[,†] Anran Wang,[†,§,‖] Kathie L. Dionisio,[‡] Alicia Frame,[†,‖] Peter Egeghy,[‡] Richard Judson,[†] and R. Woodrow Setzer[†]

Near-Field Exposure: Critical Questions



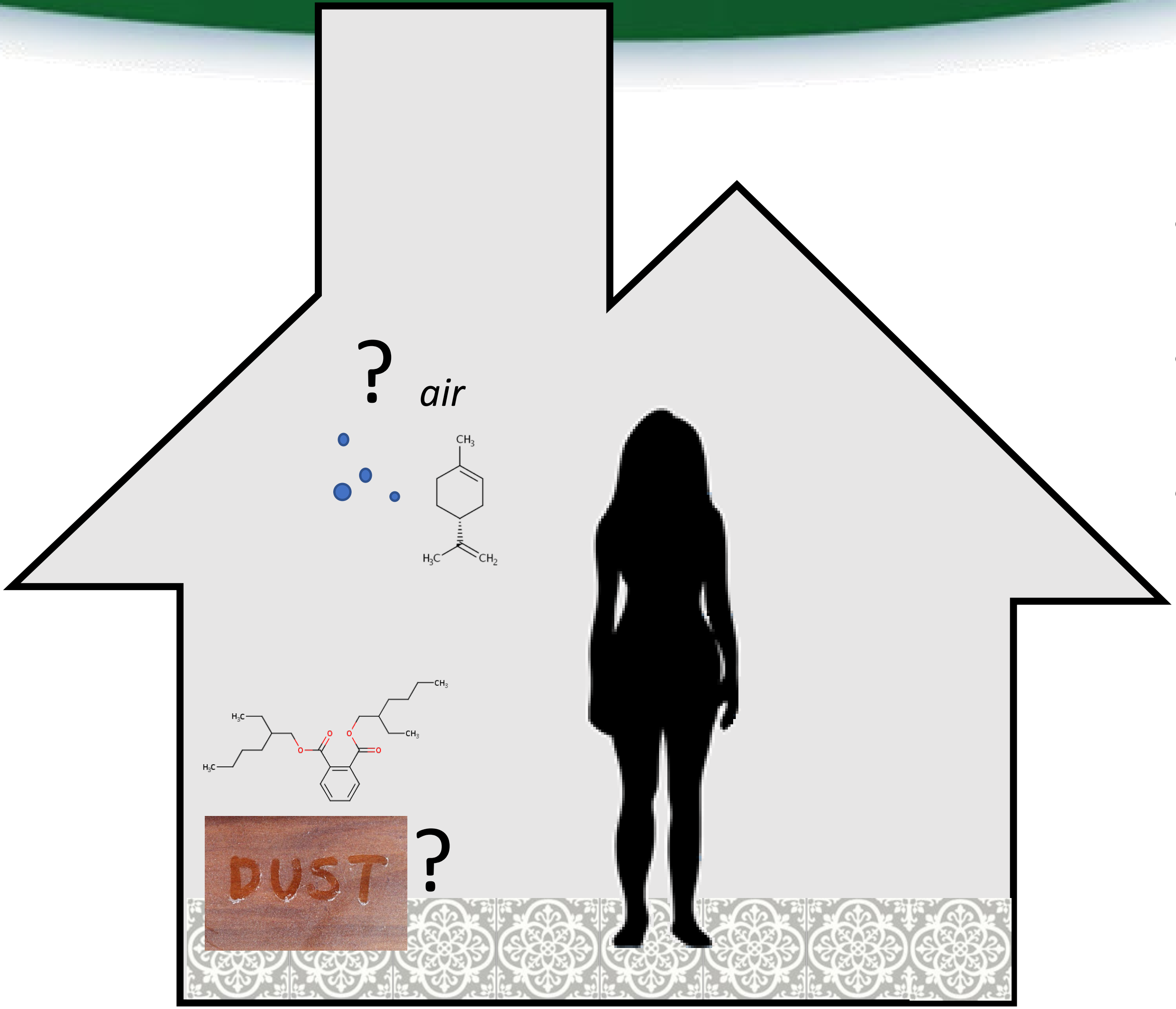
- What chemicals are in products (formulations and household articles)?

Near-Field Exposure: Critical Questions



- What chemicals are in products (formulations and household articles)?
- Which of these chemicals are released, how, and how much?

Near-Field Exposure: Critical Questions



- What chemicals are in products (formulations and household articles)?
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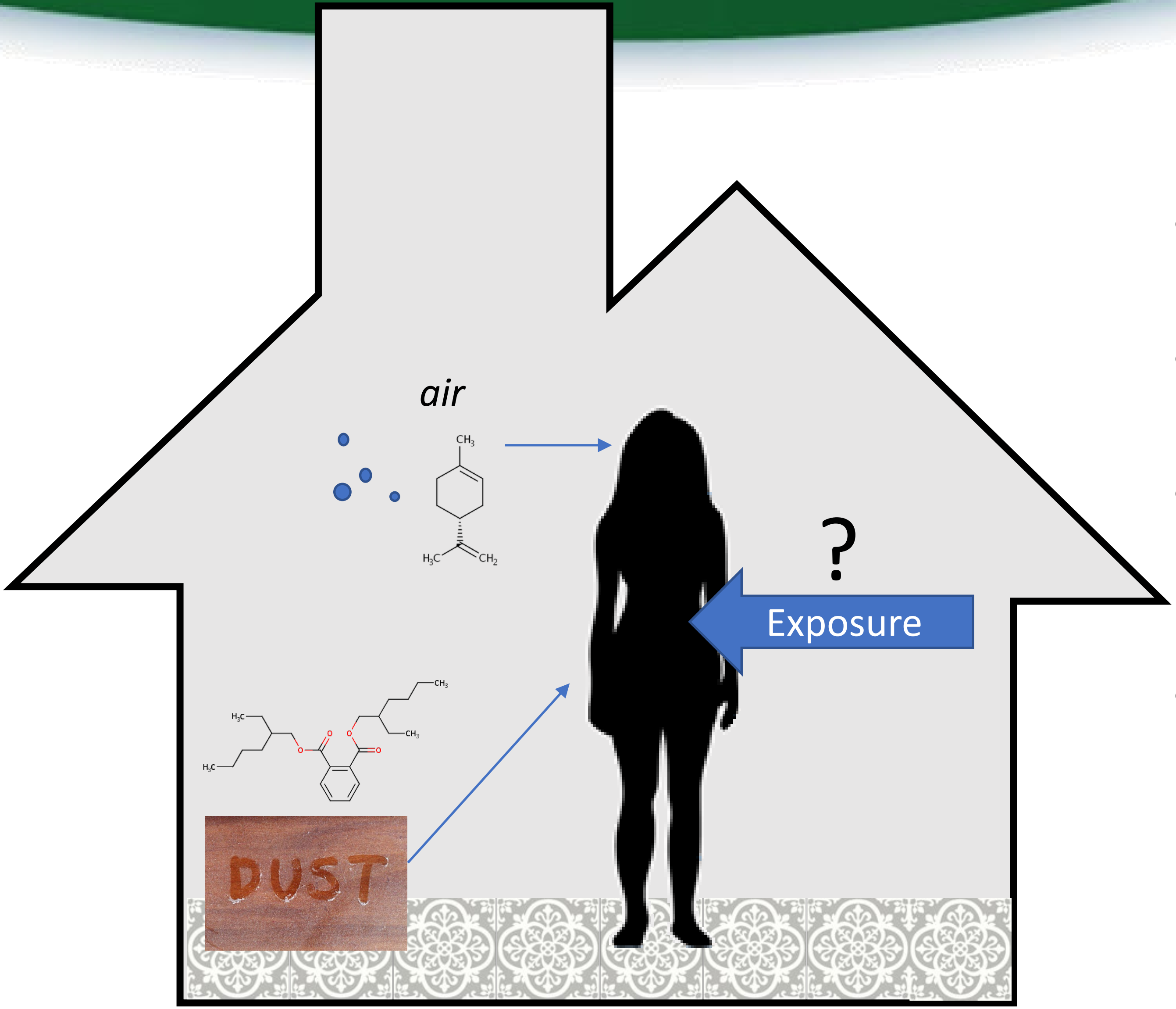
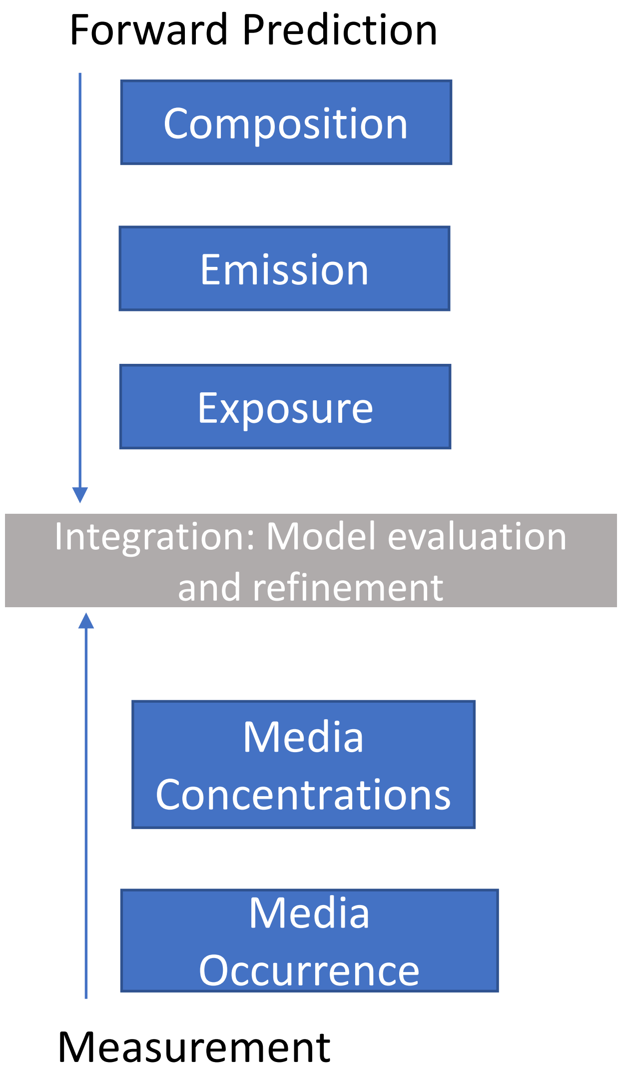
- Where do these chemicals reside in the indoor environment (e.g., dust or air)?

Near-Field Exposure: Critical Questions



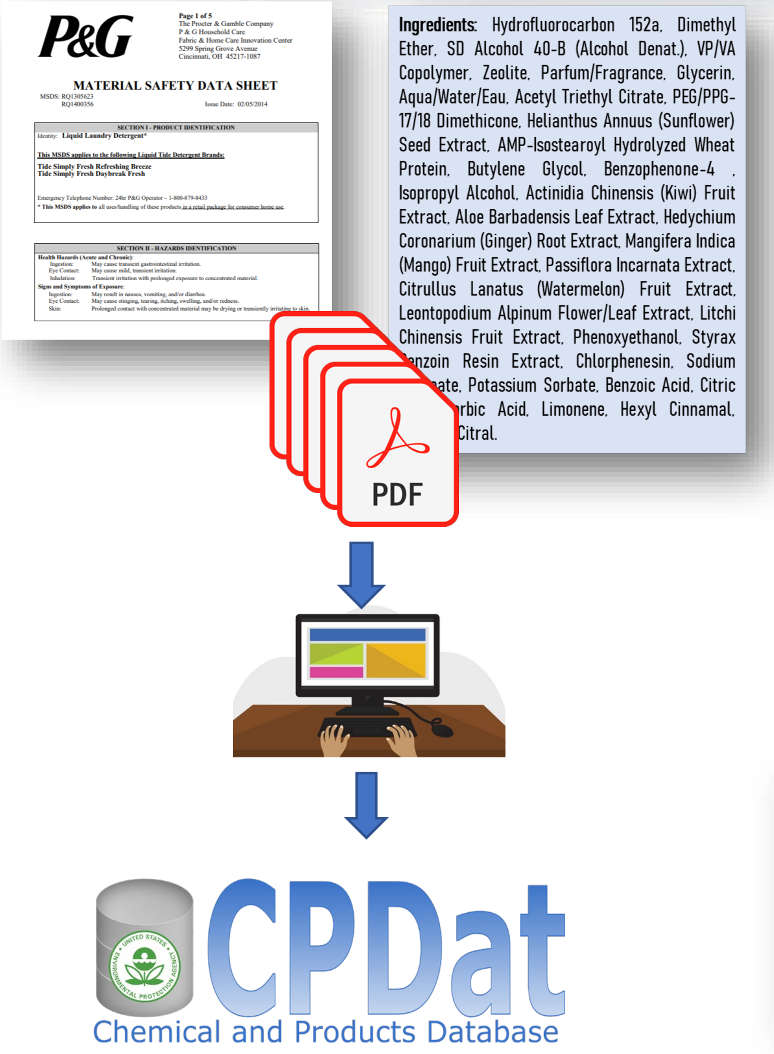
- What chemicals are in products (formulations and household articles)?
- Which of these chemicals are released, how, and how much?
- Where do these chemicals reside in the indoor environment (e.g., dust or air)?
- What exposures result (single chemicals, co-exposures?)

Overview



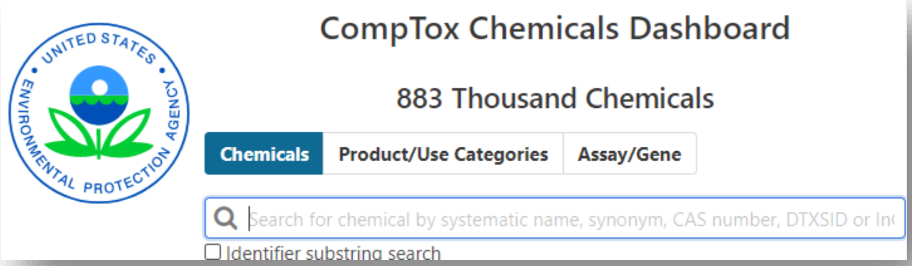
- Characterization of chemicals in consumer products
- Characterization of emission processes
- High-throughput exposure modeling
- HT measurement of chemicals in air, dust, and biological media

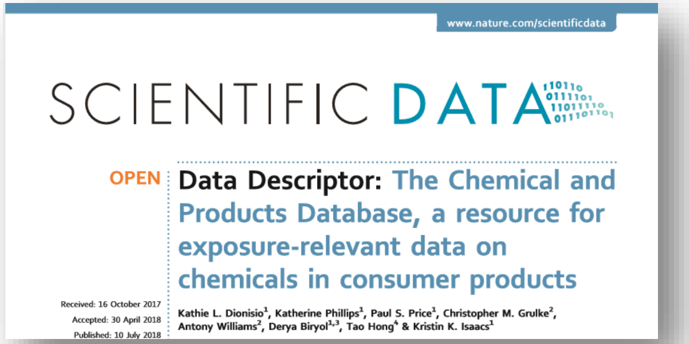
Characterization of Chemicals in Consumer Products



- We have collected over **400,000** documents describing composition of consumer products
- Material Safety Data Sheets, ingredient lists, manufacturer disclosures
- Data are curated (text extraction, cleaning, categorization, harmonization of chemical identifiers) using our Factotum curation application
- Harmonized data are released in the **Chemical and Products Database (CPDat)** (Dionisio et al., 2018)
- Organized around a set of consumer product use categories (PUCs) optimized for exposure modeling

https://comptox.epa.gov/dashboard





https://www.epa.gov/chemical-research/chemical-and-products-database-cpdat

Product Categories in CPDat

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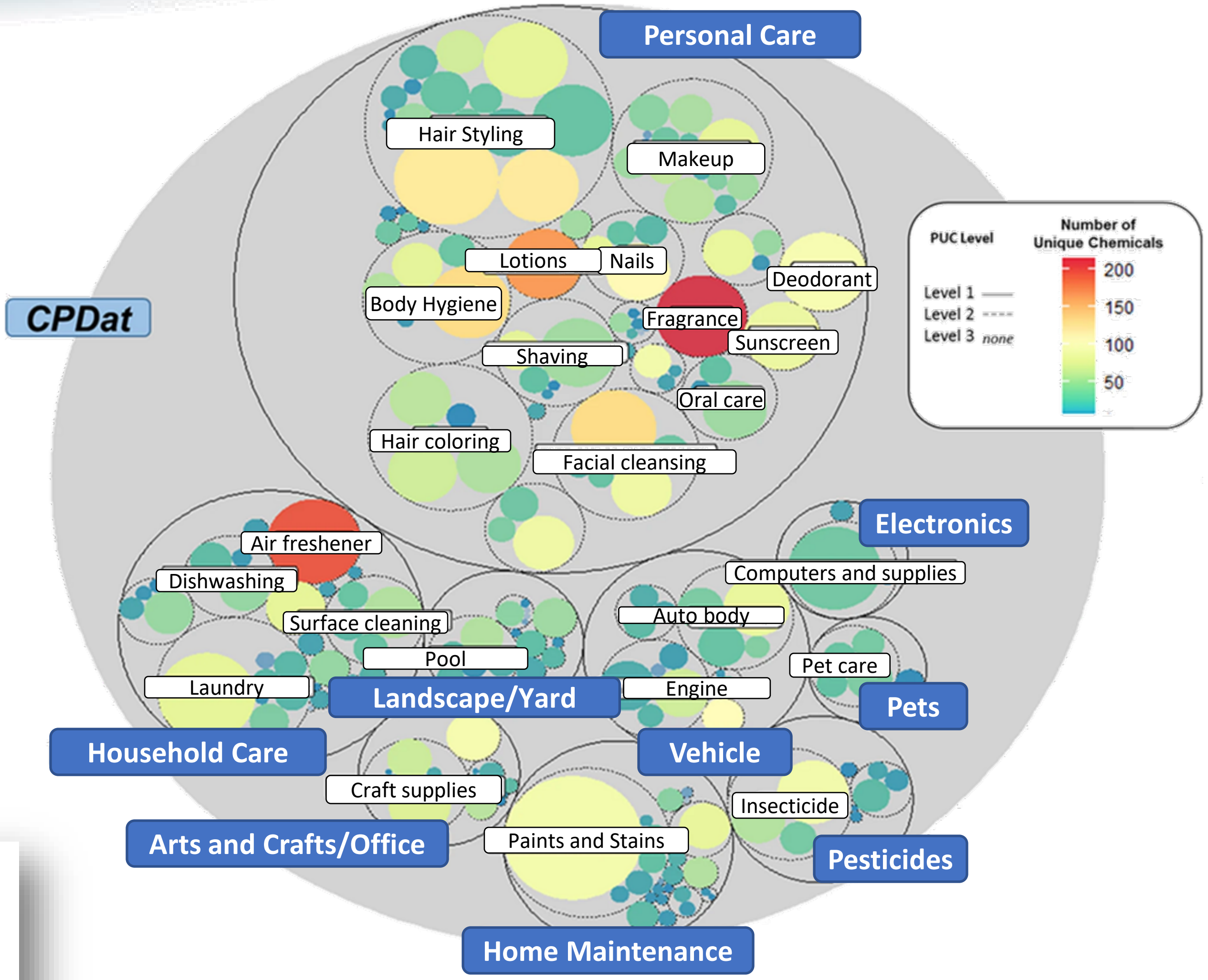
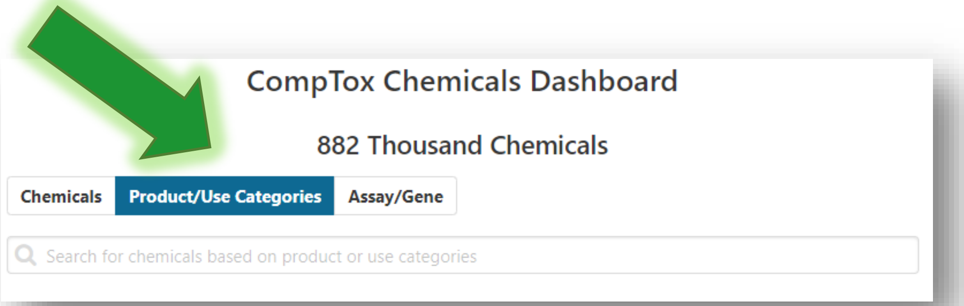
- Allows for linking to consumer product exposure models
  - *Maps to **habits and practices** (product use) data*
  - *Chemical **release***
    - *How much?*
    - *Compartment of release*
  - *Maps to exposure algorithms – if chemical and product are known, models can be rapidly parameterized*

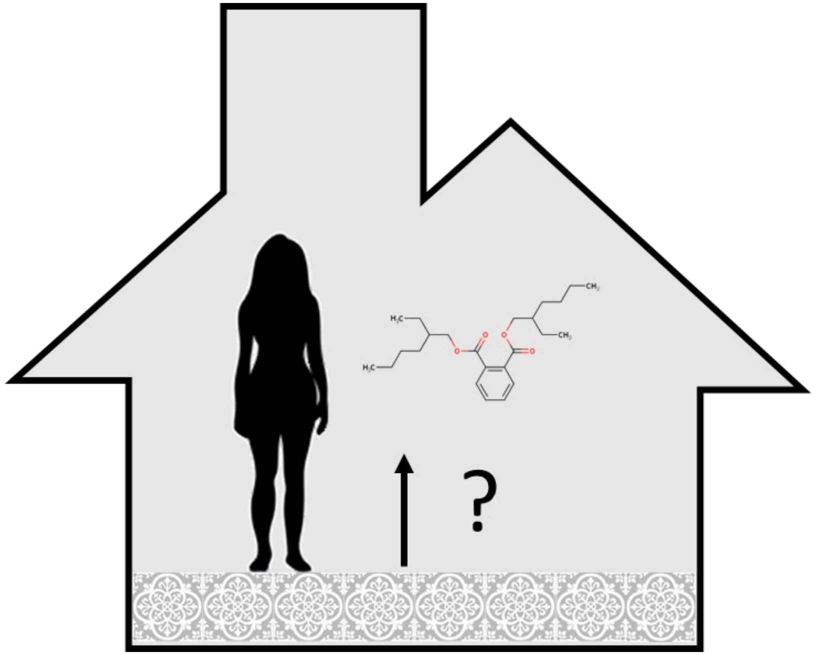




Isaacs et al., 2020

Characterization of Emission Processes

- Many mass-transfer models are available for modeling emission sources for volatile and semivolatile organic compounds (VOCs and SVOCs) in indoor materials such as flooring under different conditions
- Detailed modeling of emission sources depend on parameters such as material/air partition coefficients, solid-phase diffusion coefficients, adsorption/desorption rate constants, mass-transfer coefficients, and initial material phase concentrations (weight fraction in the material)
- Often these parameters can only be estimated using experimental systems (e.g., chamber studies)
- Such work is ongoing in EPA ORD for chemical classes of interest: organophosphate flame retardant and per- and polyfluoroalkyl substances (PFAS)



Contents lists available at ScienceDirect
Chemosphere
journal homepage: www.elsevier.com/locate/chemosphere
ELSEVIER

The influence of temperature on the emissions of organophosphate ester flame retardants from polyisocyanurate foam: Measurement and modeling

Yirui Liang [a,1], Xiaoyu Liu [b,*], Matthew R. Allen [c]

Contents lists available at ScienceDirect
Chemosphere
journal homepage: www.elsevier.com/locate/chemosphere
ELSEVIER

Determination of fluorotelomer alcohols in selected consumer products and preliminary investigation of their fate in the indoor environment

Xiaoyu Liu [a,*], Zhishi Guo [a], Edgar E. Folk IV [b], Nancy F. Roache [b]

Characterization of Emission Processes

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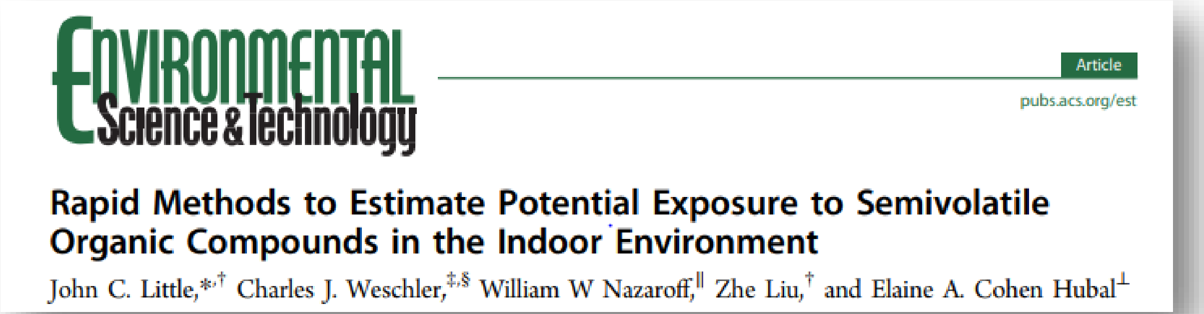
- For SVOCs with low volatility, emission source models can be simplified in such a way that they depend on a critical parameter, y_0, the steady-state gas phase concentration at the material surface.
- This parameter can be used to parameterize high-throughput exposure models.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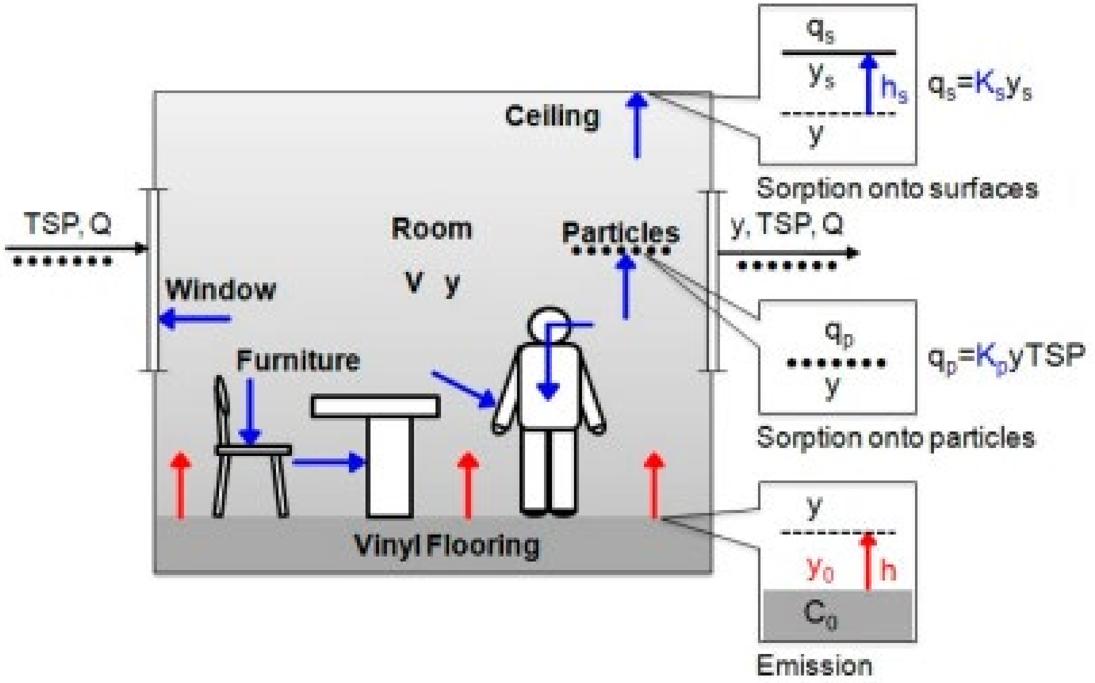
Rapid Methods to Estimate Potential Exposure to Semivolatile Organic Compounds in the Indoor Environment

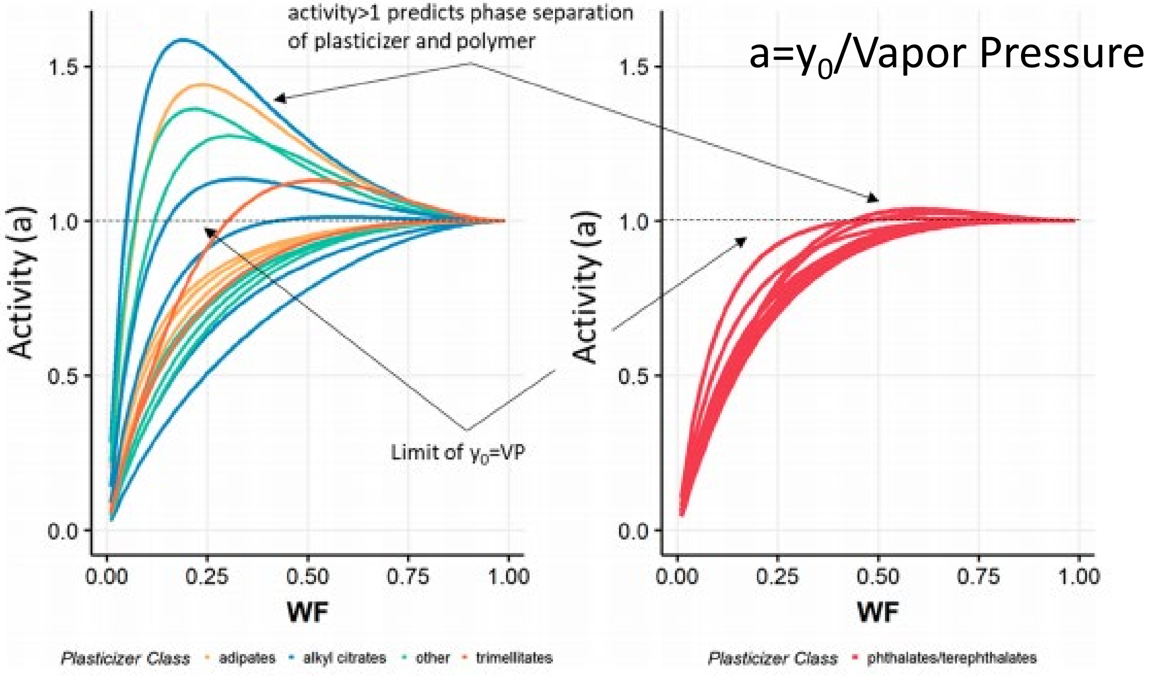
John C. Little,*,† Charles J. Weschler,‡,§ William W Nazaroff,∥ Zhe Liu,† and Elaine A. Cohen Hubal⊥

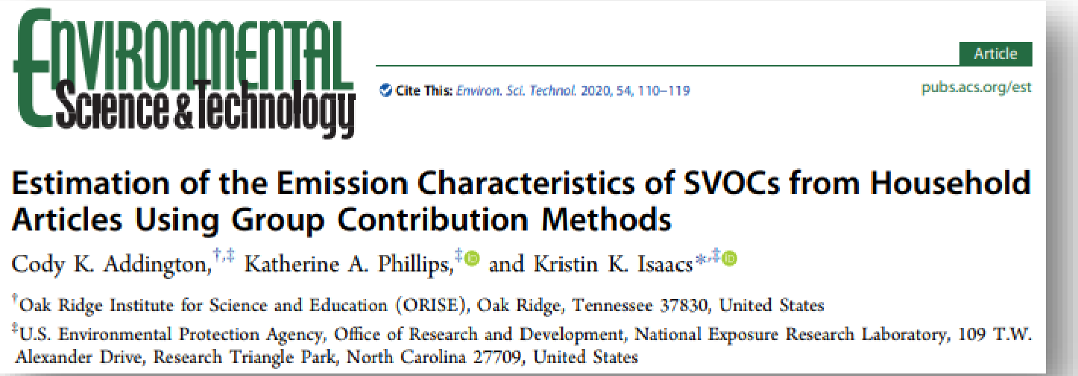


Characterization of Emission Processes

United States Environmental Protection Agency

- For SVOCs with low volatility, emission source models can be simplified in such a way that they depend on a critical parameter, y_0, the steady-state gas phase concentration at the material surface.
- This parameter can be used to parameterize high-throughput exposure models.
- We recently applied structure-based group contribution models to estimate polymer-chemical interactions (as quantified by the activity, a: the ratio of the steady state gas phase concentration to vapor pressure) and y_0 for a variety of plasticizers in PVC as a function of material weight fractions.
- This allowed us to estimate high-throughput exposures associated with several different types of products in CPDat.





Environmental Science & Technology
Article
Cite This: Environ. Sci. Technol. 2020, 54, 110–119
pubs.acs.org/est

Estimation of the Emission Characteristics of SVOCs from Household Articles Using Group Contribution Methods

Cody K. Addington,[†,‡] Katherine A. Phillips,[‡] and Kristin K. Isaacs*[‡]

[†]Oak Ridge Institute for Science and Education (ORISE), Oak Ridge, Tennessee 37830, United States

[‡]U.S. Environmental Protection Agency, Office of Research and Development, National Exposure Research Laboratory, 109 T.W. Alexander Drive, Research Triangle Park, North Carolina 27709, United States

Identification of Co-Exposures Indoors

- EPA Office of Research and Development entered a collaboration with the Nielsen company
- Nielsen provided consumer product purchasing data for 60,000 U.S. households from their National Consumer Panel Study (“Homescan”)

Identification of Co-Exposures Indoors

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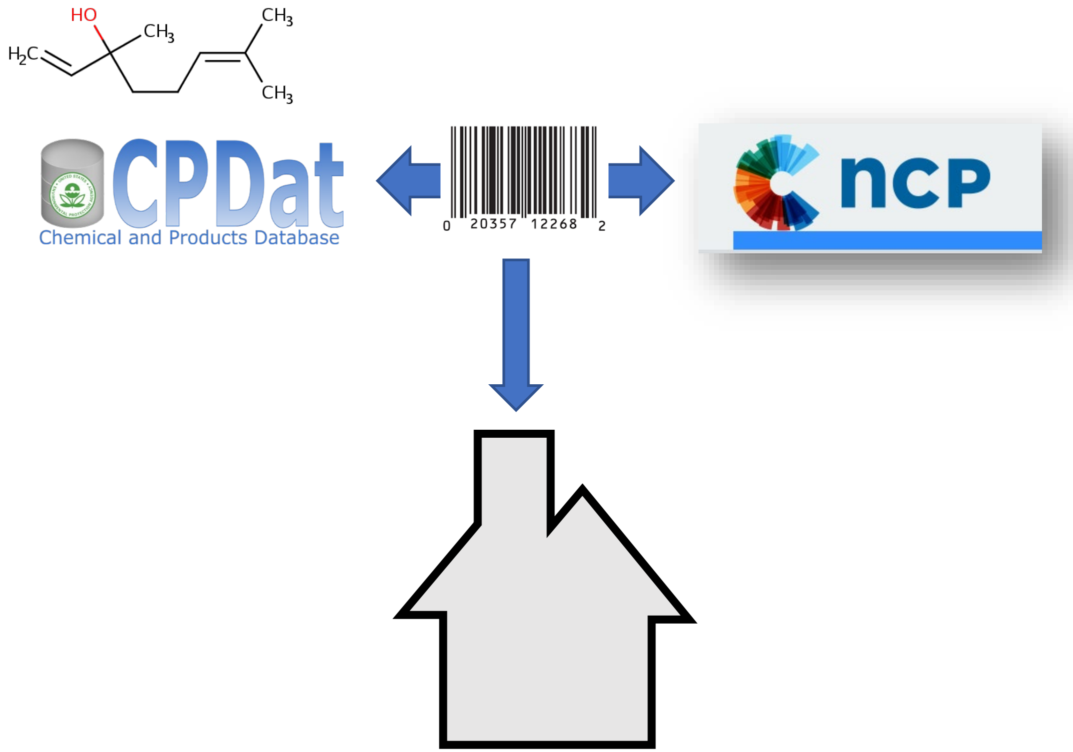
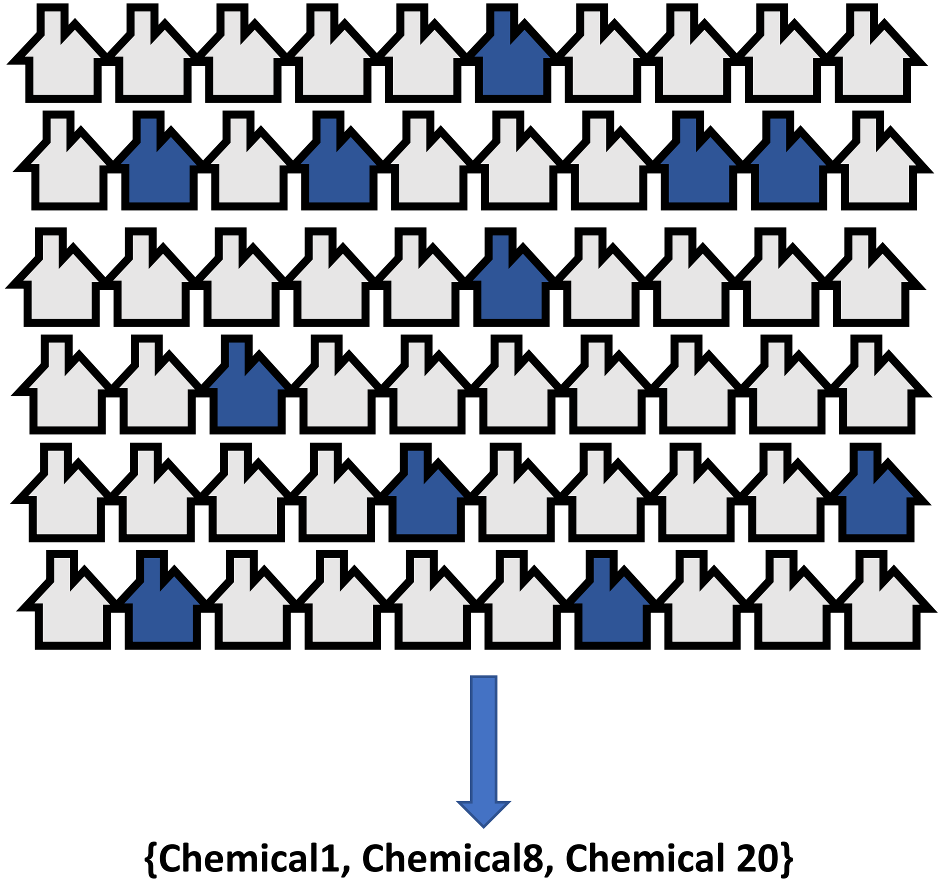
- Data were integrated with CPDat ingredient data by Universal Product Code
- We identified the chemicals being introduced into homes within the same month (and thus had potential co-exposure)



{Chemical1, Chemical2…..Chemical 50}

Identification of Co-Exposures Indoors

- EPA Office of Research and Development entered a collaboration with the Nielsen company
- Nielsen provided consumer product purchasing data for 60,000 U.S. households from their National Consumer Panel Study (“Homescan”)
- Data were integrated with CPDat ingredient data by Universal Product Code
- Used a data-mining technique (Frequent Itemset Mining) to identify frequently-occurring combinations of chemicals across households (broad group of chemicals and potential endocrine-active chemicals)
- Were able to examine impact of demographics (race, household size, income, education) on frequent combinations



Identification of Co-Exposures Indoors

United States Environmental Protection Agency

- Here demographics and chemical sets are clustered to indicate the similarity of rankings of chemical combinations
- Cell color reflects relative prevalence of the chemical combination (rank across all prevalent combinations) for the demographic versus total population
- We could identify patterns in chemical co-occurrence in both the broad chemical group and potential endocrine active chemicals
- Results can be used to prioritize chemicals for testing in *in vitro* systems

Broad TSCA Inventory

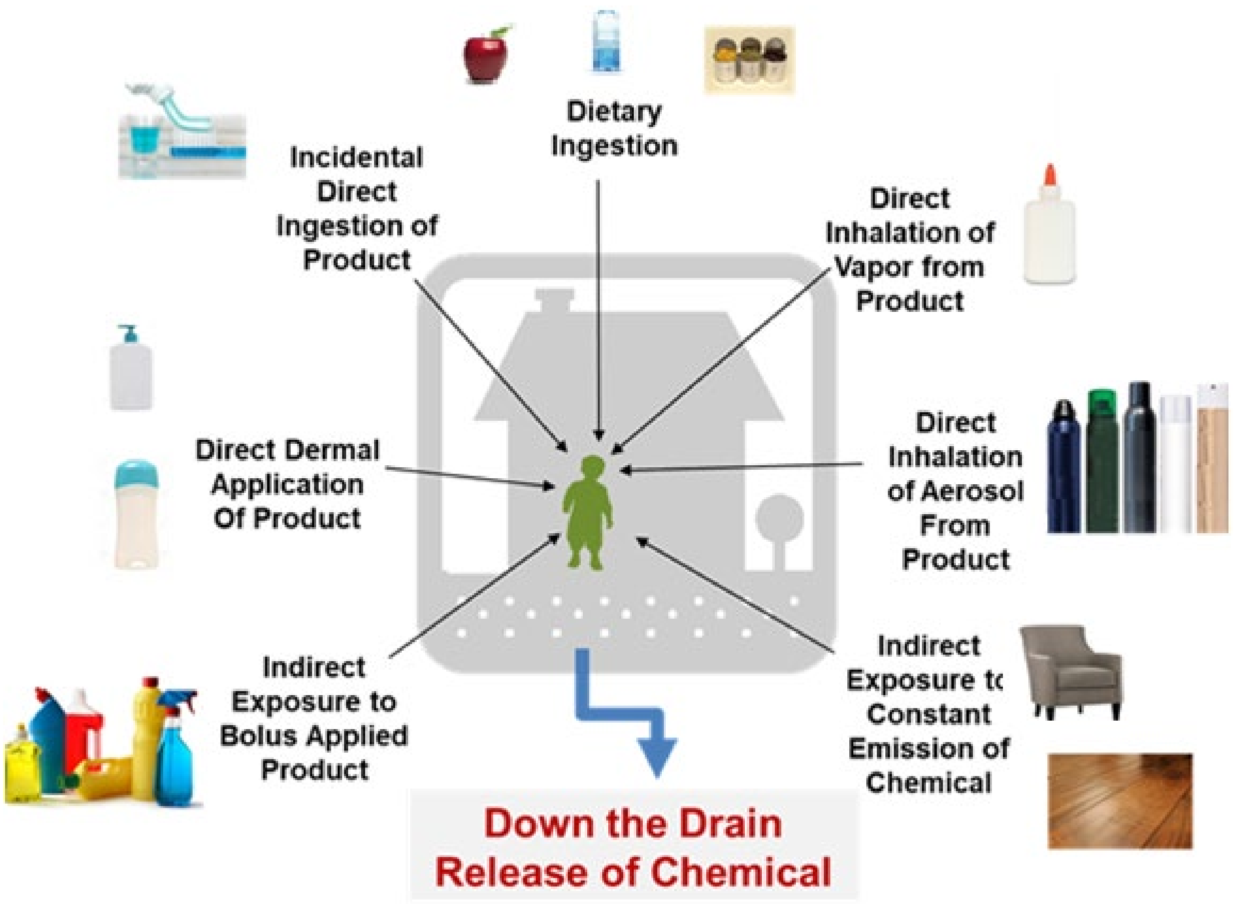
Grade And High School	African American	Mid Higher	Lower	Mid Lower	White	No Child	Non-Childbearing	Asian	Post College	Childbearing	Higher	Under 13	Under 18	College	Hispanic	Under 6	Chemical set
-5	-5	-6	-4	-6	0	0	0	4	1	-1	0	-1	-1	0	0	3	{Sulfuric acid, mono-C10-16-alkyl esters, sodium salts | Poly(oxy-1,2-ethanediyl), .alpha.-sulfo-.omega.-hydroxy-, C10-16-alkyl ethers, sodium salts | Ethanol | 1,2-Propylene glycol}
-1	-2	-5	-3	-6	0	0	0	4	0	-1	0	-1	-1	0	-1	2	{Sulfuric acid, mono-C10-16-alkyl esters, sodium salts | Poly(oxy-1,2-ethanediyl), .alpha.-sulfo-.omega.-hydroxy-, C10-16-alkyl ethers, sodium salts | 1,2-Propylene glycol}
-2	-3	-5	-4	-6	0	0	0	4	2	-1	0	-1	-1	0	0	2	{Poly(oxy-1,2-ethanediyl), .alpha.-sulfo-.omega.-hydroxy-, C10-16-alkyl ethers, sodium salts | Ethanol | 1,2-Propylene glycol}
-1	-7	-3	-5	-6	0	0	0	4	1	-1	0	-1	0	0	-1	1	{Sulfuric acid, mono-C10-16-alkyl esters, sodium salts | Ethanol | 1,2-Propylene glycol}
-1	-4	-2	-4	-6	0	0	0	3	3	-1	0	0	0	0	-1	1	{Sulfuric acid, mono-C10-16-alkyl esters, sodium salts | 1,2-Propylene glycol}
-1	-2	-2	-4	-6	0	0	0	4	3	-1	0	-1	0	0	-1	1	{Poly(oxy-1,2-ethanediyl), .alpha.-sulfo-.omega.-hydroxy-, C10-16-alkyl ethers, sodium salts | 1,2-Propylene glycol}
-1	-5	0	-4	-2	0	-1	-1	1	1	1	1	0	1	1	2	-1	{Ethanol | Sodium dodecyl sulfate}
-8	0	0	-3	-5	0	0	0	4	4	2	1	3	2	0	2	4	{Sodium dodecyl sulfate | Glycerol} A
-1	-2	-1	-1	-1	-1	-1	-1	3	3	2	2	2	2	0	2	2	{Ethanol | 1,2-Propylene glycol}
0	1	0	0	0	0	0	0	4	3	5	1	5	5	0	5	5	{Ethanol | Glycerol}
0	1	0	0	0	0	0	0	-2	-2	-2	-1	-2	-2	0	-2	-2	{Poly(oxy-1,2-ethanediyl), .alpha.-sulfo-.omega.-hydroxy-, C10-16-alkyl ethers, sodium salts | Ethanol}
1	1	1	1	1	1	1	1	-1	-1	-1	-1	-1	-1	0	-1	-1	{Sulfuric acid, mono-C10-16-alkyl esters, sodium salts | Poly(oxy-1,2-ethanediyl), .alpha.-sulfo-.omega.-hydroxy-, C10-16-alkyl ethers, sodium salts | Ethanol}
0	0	0	0	0	0	0	0	-2	-1	-2	0	-2	-2	0	-2	-2	{Sulfuric acid, mono-C10-16-alkyl esters, sodium salts | Poly(oxy-1,2-ethanediyl), .alpha.-sulfo-.omega.-hydroxy-, C10-16-alkyl ethers, sodium salts}
0	-1	0	0	0	0	0	0	-2	-2	-2	-1	-2	-2	0	-2	-2	{Sulfuric acid, mono-C10-16-alkyl esters, sodium salts | Ethanol}
0	1	1	1	1	0	1	0	-13	-9	-2	-3	-5	-3	-2	-2	-7	{Propane | Isobutane}
7	8	6	10	10	0	0	0	-10	-19	-11	-2	-4	-4	0	-2	2	B {Sulfuric acid, mono-C10-16-alkyl esters, sodium salts | C10-16-Alkyldimethylamines oxides}
7	10	6	11	10	0	0	0	-9	-18	-11	-2	-4	-4	0	-1	3	{Poly(oxy-1,2-ethanediyl), .alpha.-sulfo-.omega.-hydroxy-, C10-16-alkyl ethers, sodium salts | C10-16-Alkyldimethylamines oxides}
8	10	7	12	11	1	0	0	-8	-18	-10	-1	-3	-3	1	0	4	{Sulfuric acid, mono-C10-16-alkyl esters, sodium salts | Poly(oxy-1,2-ethanediyl), .alpha.-sulfo-.omega.-hydroxy-, C10-16-alkyl ethers, sodium salts | C10-16-Alkyldimethylamines oxides}
0	-5	-1	-2	-3	0	-1	0	-9	-4	0	0	0	0	0	-1	0	{Ethanol | Isobutane}
1	2	0	-2	-5	0	1	1	-4	-2	-1	1	-1	0	1	-1	1	{Ethanol | Sodium hydroxide}

Stanfield et al., submitted

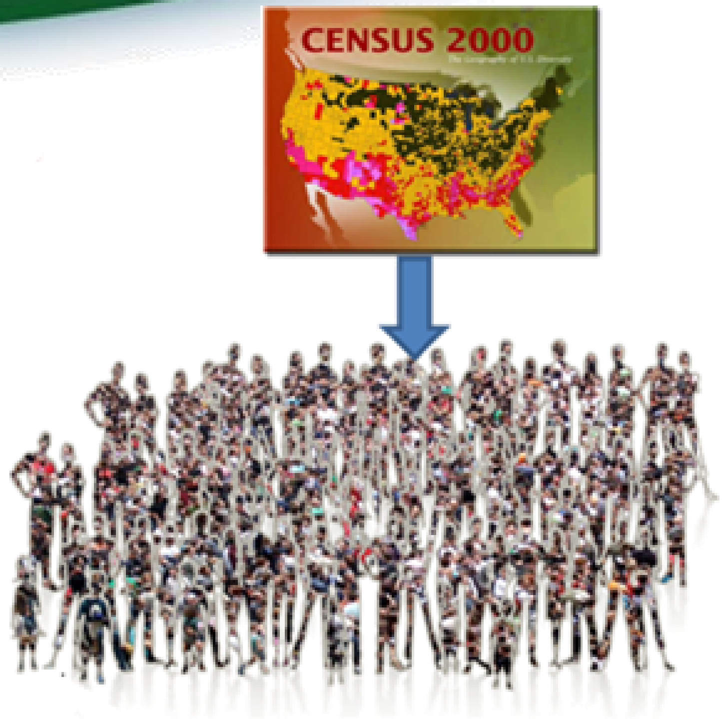
High-Throughput Consumer Exposure Model (SHEDS-HT)

- CPDat has allowed for rapid parameterization of consumer exposure models, like the High-throughput Stochastic Human Exposure Model (SHEDS-HT, Isaacs et al. 2014)
- SHEDS-HT predicts ***aggregate*** population-based human exposures to thousands of commercial chemicals in consumer products, consumer articles, and foods via inhalation, dermal, ingestion, and dietary pathways in a **high-throughput manner**
- Includes a fugacity-based indoor fate and transport model to predict indoor chemical concentrations in air (particles and gas-phase) and on surfaces (particles and residues).

SHEDS-HT



SHEDS-HT: Overview



SHEDS-HT: Overview

SHEDS-HT: Overview

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Chemical Residues in Foods

nhanes

Food Intakes

CPDat
Chemical and Products Database

Chemical Weight Fractions

Consumer Product Use Patterns

Relevant exposure factors (e.g. weight, bathing and hand washing behaviors, hand-to mouth behaviors)

Daily-level activity diary
- Time spent in microenvironments
- Energy expenditure (ventilation)

Indoor Chemical Emission from Articles (y_0)

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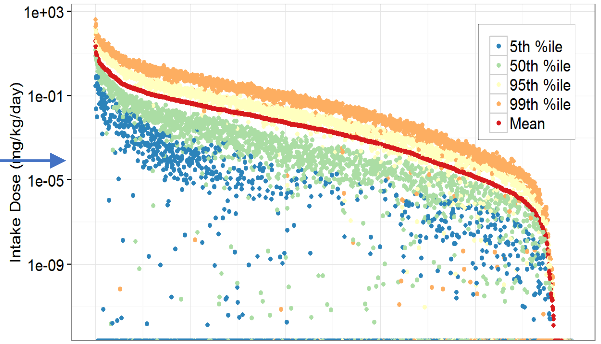


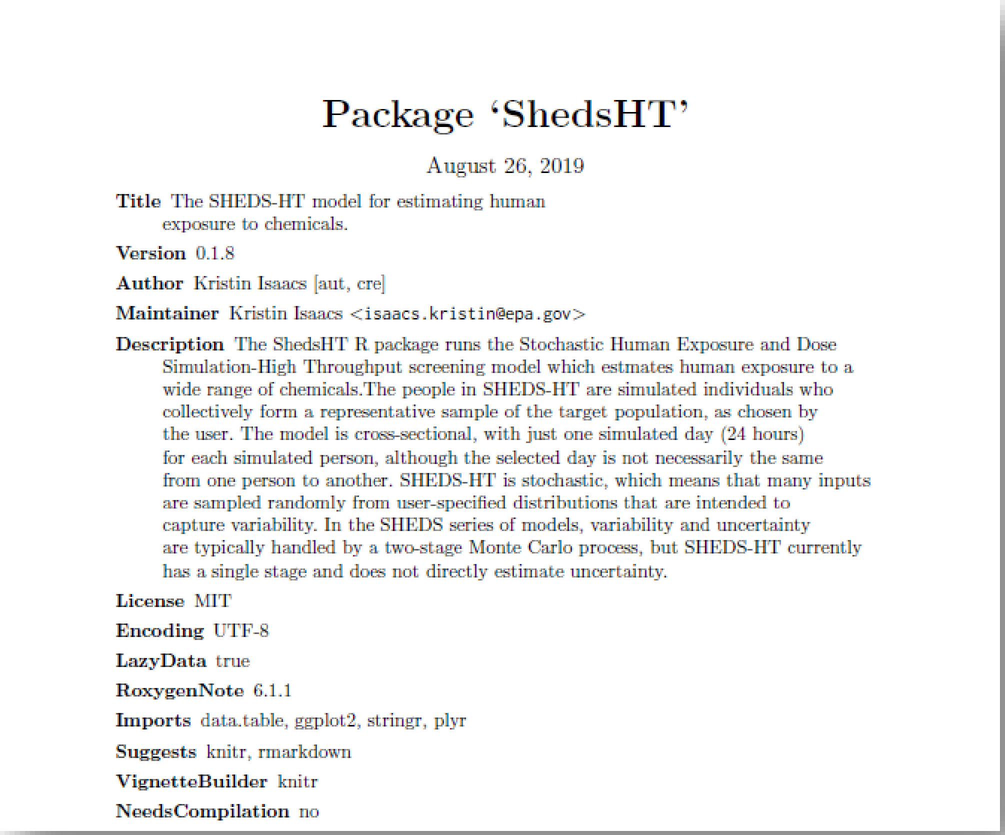
Population Exposures
mg/kg-BW/day

Relevant exposure factors (e.g. weight, bathing and hand washing behaviors, hand-to mouth behaviors)

Daily-level activity diary
- Time spent in microenvironments
- Energy expenditure (ventilation)

Indoor Chemical Emission from Articles (y_0)

R package ‘ShedsHT”



Package ‘ShedsHT’

August 26, 2019

Title The SHEDS-HT model for estimating human exposure to chemicals.

Version 0.1.8

Author Kristin Isaacs [aut, cre]

Maintainer Kristin Isaacs <isaacs.kristin@epa.gov>

Description The ShedsHT R package runs the Stochastic Human Exposure and Dose Simulation-High Throughput screening model which estmates human exposure to a wide range of chemicals.The people in SHEDS-HT are simulated individuals who collectively form a representative sample of the target population, as chosen by the user. The model is cross-sectional, with just one simulated day (24 hours) for each simulated person, although the selected day is not necessarily the same from one person to another. SHEDS-HT is stochastic, which means that many inputs are sampled randomly from user-specified distributions that are intended to capture variability. In the SHEDS series of models, variability and uncertainty are typically handled by a two-stage Monte Carlo process, but SHEDS-HT currently has a single stage and does not directly estimate uncertainty.

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Encoding UTF-8

LazyData true

RoxygenNote 6.1.1

Imports data.table, ggplot2, stringr, plyr

Suggests knitr, rmarkdown

VignetteBuilder knitr

NeedsCompilation no

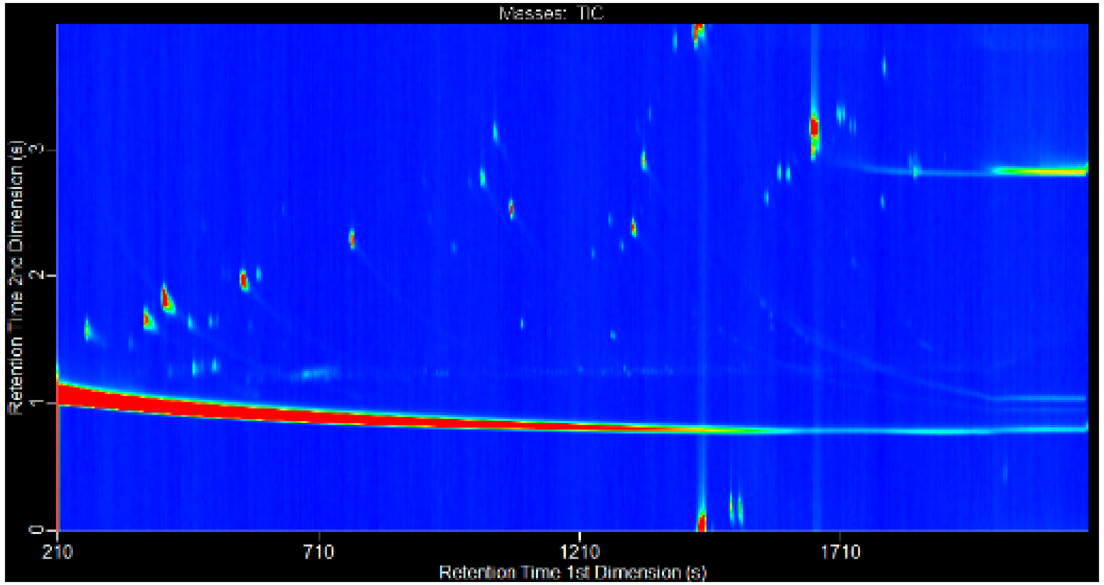
- R Package with help documentation and User’s Guide
- Current model release
- Default input files (e.g. population, food diaries, CPDat data)
- Example run-specific input files
- Training materials
- Example current applications
  - Solvent emissions from consumer products for government inventories
  - Dietary exposures to process-formed chemicals
  - Exposures for chemical-product combinations to inform state decision-making

https://github.com/HumanExposure/SHEDSHTRPackage

Non-Targeted Analysis of Environmental and Biological Media

- Targeted Analysis:
  - We know exactly what we're looking for
  - 10s – 100s of chemicals
- Non-Targeted Analysis (NTA) or Suspect Screening Analysis (SSA)
  - We have no preconceived lists
  - 1,000s – 10,000s of chemical
- Can supplement and evaluate predicted concentrations in consumer products, concentrations in indoor media and, estimated exposures (e.g., blood concentrations)

High Resolution Mass Spectrometry



Published and Ongoing NTA Studies in the ExpoCast Project

United States Environmental Protection Agency

Consumer Products

- Phillips *et al., Env. Sci. Tech.* 2018

Consumer Product Emissions from Different Substrates


Residential Dust

- Rager *et al., Env. Int.,* 2016

Recycled Consumer Materials

Residential Air

Comparison against known chemicals used in the home (Using CPDat and inventory of products in the home)

Pooled Human Blood

Summary

- In ExpoCast, we are developing data and models necessary for characterizing near-field (residential) exposures associated with thousands of chemicals
  - Consumer product ingredients
  - Emission processes
  - Aggregate and combined exposures
- We are using new analytical measurement data to evaluate and refine these datasets and models
- Estimates of population exposures associated with near-field sources and pathways feed existing ORD consensus exposure models that integrate many different pathway-specific estimates into a population median exposure
- These consensus estimates are being used in multiple decision-making contexts to prioritize chemicals for further study

References

- Addington CK, Phillips KA, Isaacs KK. Estimation of the Emission Characteristics of SVOCs from Household Articles Using Group Contribution Methods. Environ Sci Technol. 2020 Jan 7;54(1):110-119.
- Dionisio KL, Phillips K, Price PS, Grulke CM, Williams A, Biryol D, Hong T, Isaacs KK. The Chemical and Products Database, a resource for exposure-relevant data on chemicals in consumer products. Scientific data. 2018 Jul 10;5:180125.
- Isaacs KK, Glen WG, Egeghy P, Goldsmith MR, Smith L, Vallero D, Brooks R, Grulke CM, Özkaynak H. SHEDS-HT: an integrated probabilistic exposure model for prioritizing exposures to chemicals with near-field and dietary sources. Environmental science & technology. 2014 Nov 4;48(21):12750-9.
- Isaacs KK, Dionisio K, Phillips K, Bevington C, Egeghy P, Price PS. Establishing a system of consumer product use categories to support rapid modeling of human exposure. Journal of exposure science & environmental epidemiology. 2020 Jan;30(1):171-83.
- Liang Y, Liu X, Allen MR. The influence of temperature on the emissions of organophosphate ester flame retardants from polyisocyanurate foam: Measurement and modeling. Chemosphere. 2019 Oct;233:347-354.
- Liu X, Guo Z, Folk EE 4th, Roache NF. Determination of fluorotelomer alcohols in selected consumer products and preliminary investigation of their fate in the indoor environment. Chemosphere. 2015 Jun;129:81-6. doi: 10.1016/j.chemosphere.2014.06.012. Epub 2014 Jul 2. PMID: 24997516.
- Little JC, Weschler CJ, Nazaroff WW, Liu Z, Cohen Hubal EA. Rapid methods to estimate potential exposure to semivolatile organic compounds in the indoor environment. Environ Sci Technol. 2012 Oct 16;46(20):11171-8.
- Phillips KA, Yau A, Favela KA, Isaacs KK, McEachran A, Grulke C, Richard AM, Williams AJ, Sobus JR, Thomas RS, Wambaugh JF. Suspect screening analysis of chemicals in consumer products. Environmental science & technology. 2018 Feb 6;52(5):3125-35.
- Rager JE, Strynar MJ, Liang S, McMahen RL, Richard AM, Grulke CM, Wambaugh JF, Isaacs KK, Judson R, Williams AJ, Sobus JR. Linking high resolution mass spectrometry data with exposure and toxicity forecasts to advance high-throughput environmental monitoring. Environ Int. 2016 Mar;88:269-280. doi: 10.1016/j.envint.2015.12.008. Epub 2016 Jan 23. PMID: 26812473.

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