Generating Exposure-Relevant Measurement Data for Potential Use in Support of TSCA Requirements

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International Society of Exposure Science
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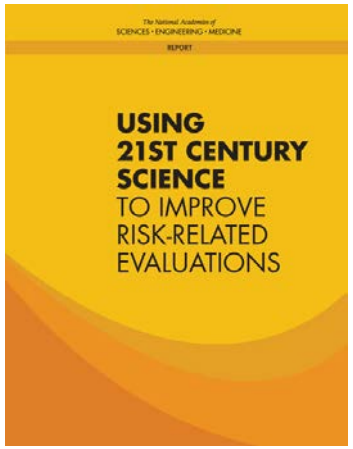
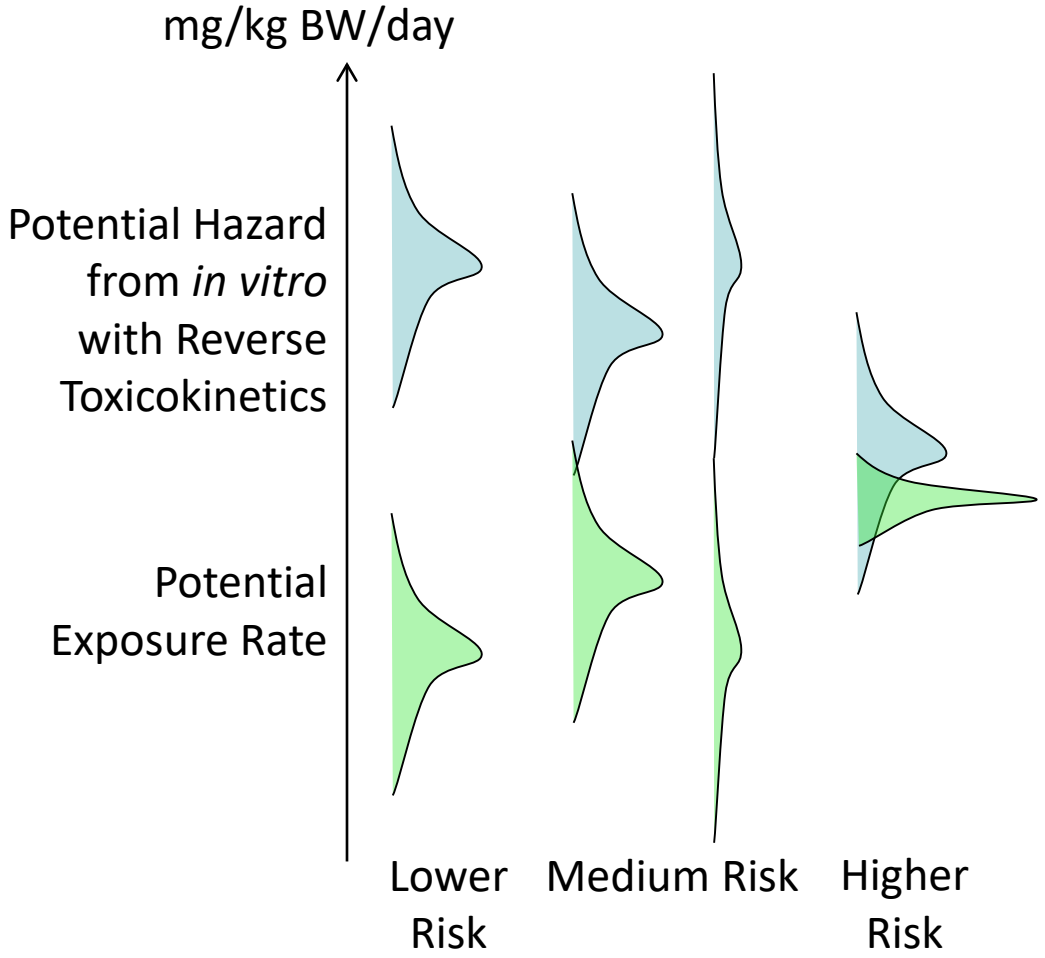
High Throughput Risk Prioritization



National Academy of Sciences, January, 2017:
"Translation of high-throughput data into risk-based rankings is an important application of exposure data for chemical priority-setting. Recent advances in high-throughput toxicity assessment, notably the ToxCast and Tox21 programs… and in high-throughput computational exposure assessment… have enabled first-tier risk-based rankings of chemicals on the basis of margins of exposure…"

High throughput risk prioritization needs:

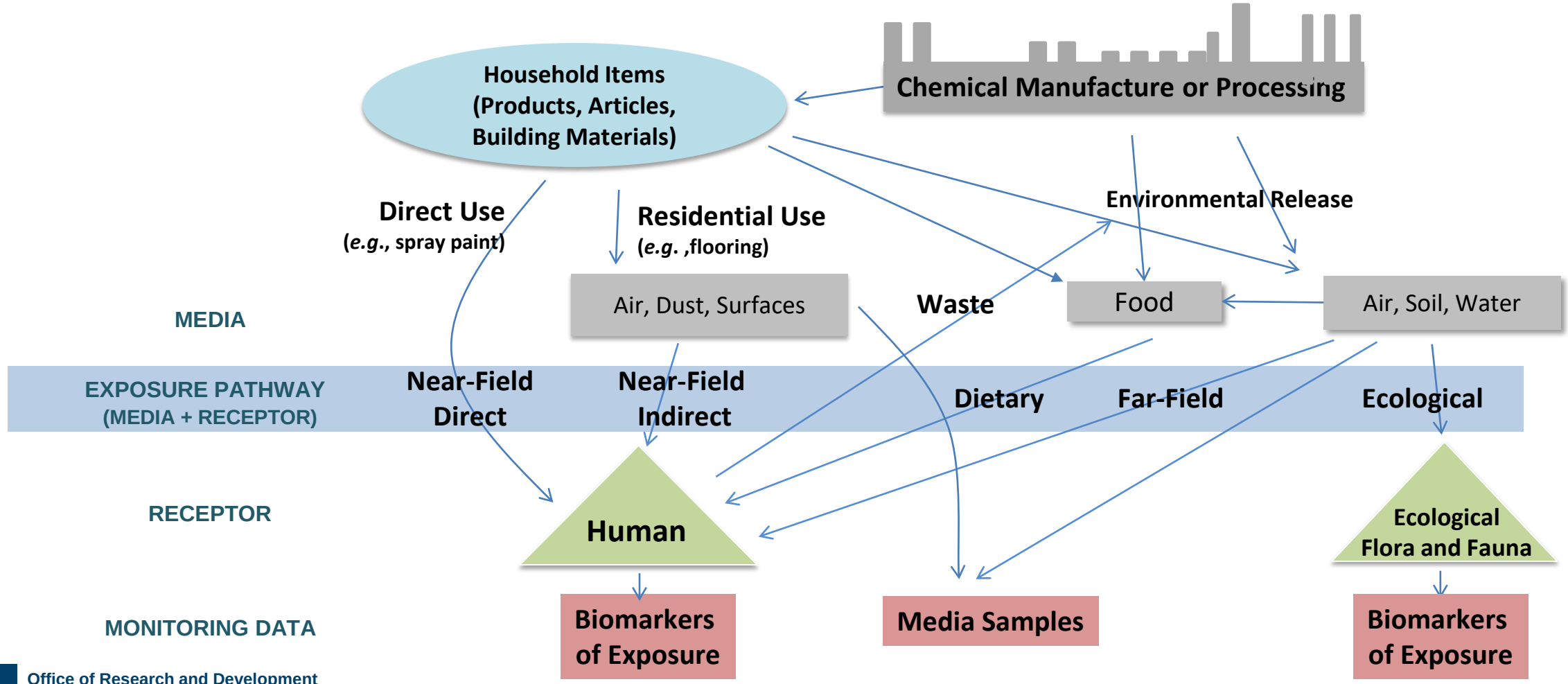
1. high throughput **hazard** characterization (e.g., ToxCast, Tox21)
2. high throughput **exposure** forecasts
3. high throughput **toxicokinetics** (*i.e.*, dosimetry)



Egeghy *et al*. (2012) – Most chemicals lack exposure data

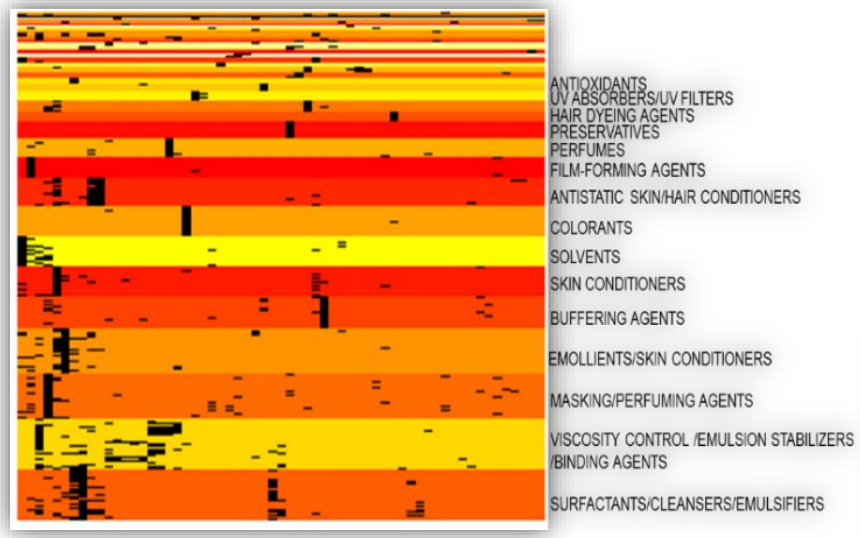
Chemical Use Identifies Relevant Pathways

Exposure data are limited (Egeghy *et al*., 2012) but some pathways have much higher average exposures! (Wallace *et al*., 1987)



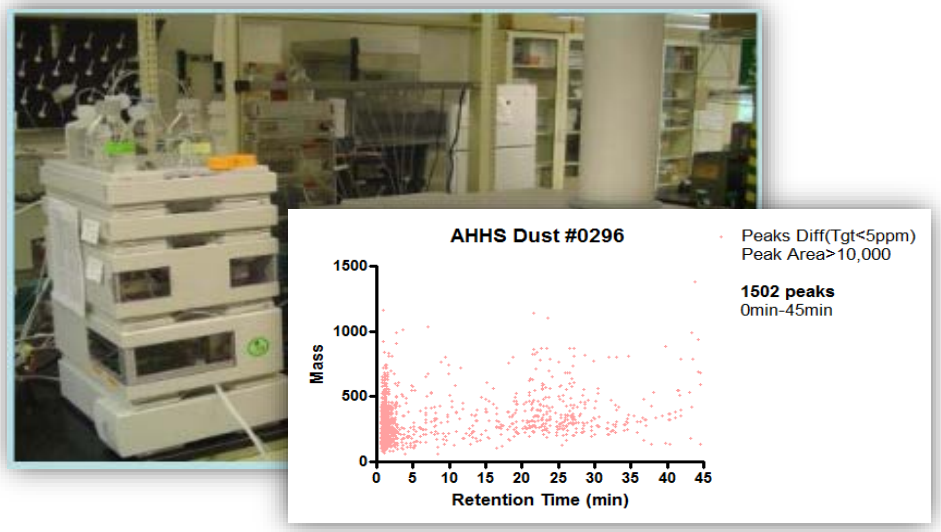
New Exposure Related Data

United States Environmental Protection Agency



Chemical Use Information

Data on chemicals within and emission from household items



Monitoring Data

nielsen

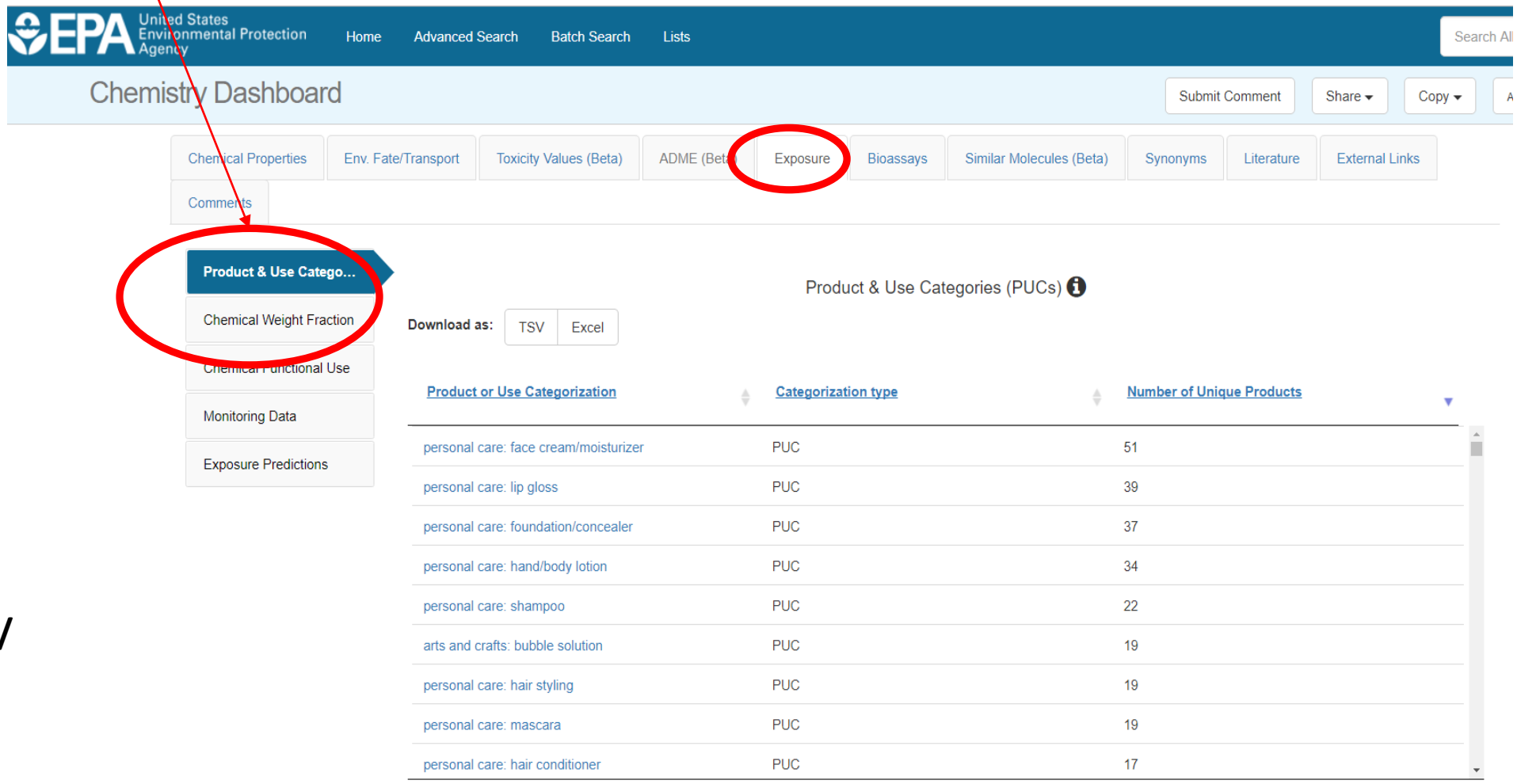
Habits and Practices (Behavior) Information

Data on physico-chemical properties

Chemical Use Information for ~30,000 Chemicals

CPDat

- Chemical-Product database (CPDat) maps many different types of use information and ontologies onto each other
- Includes CPCPdb (Goldsmith, et al., 2014) with information on ~2000 products from major retailors
- Available through the Chemistry Dashboard **http://comptox.epa.gov/**



Product or Use Categorization	Categorization type	Number of Unique Products
personal care: face cream/moisturizer	PUC	51
personal care: lip gloss	PUC	39
personal care: foundation/concealer	PUC	37
personal care: hand/body lotion	PUC	34
personal care: shampoo	PUC	22
arts and crafts: bubble solution	PUC	19
personal care: hair styling	PUC	19
personal care: mascara	PUC	19
personal care: hair conditioner	PUC	17

Dionisio *et al.* (2015)

Improving Exposure Pathway Characterization and Model Evaluation

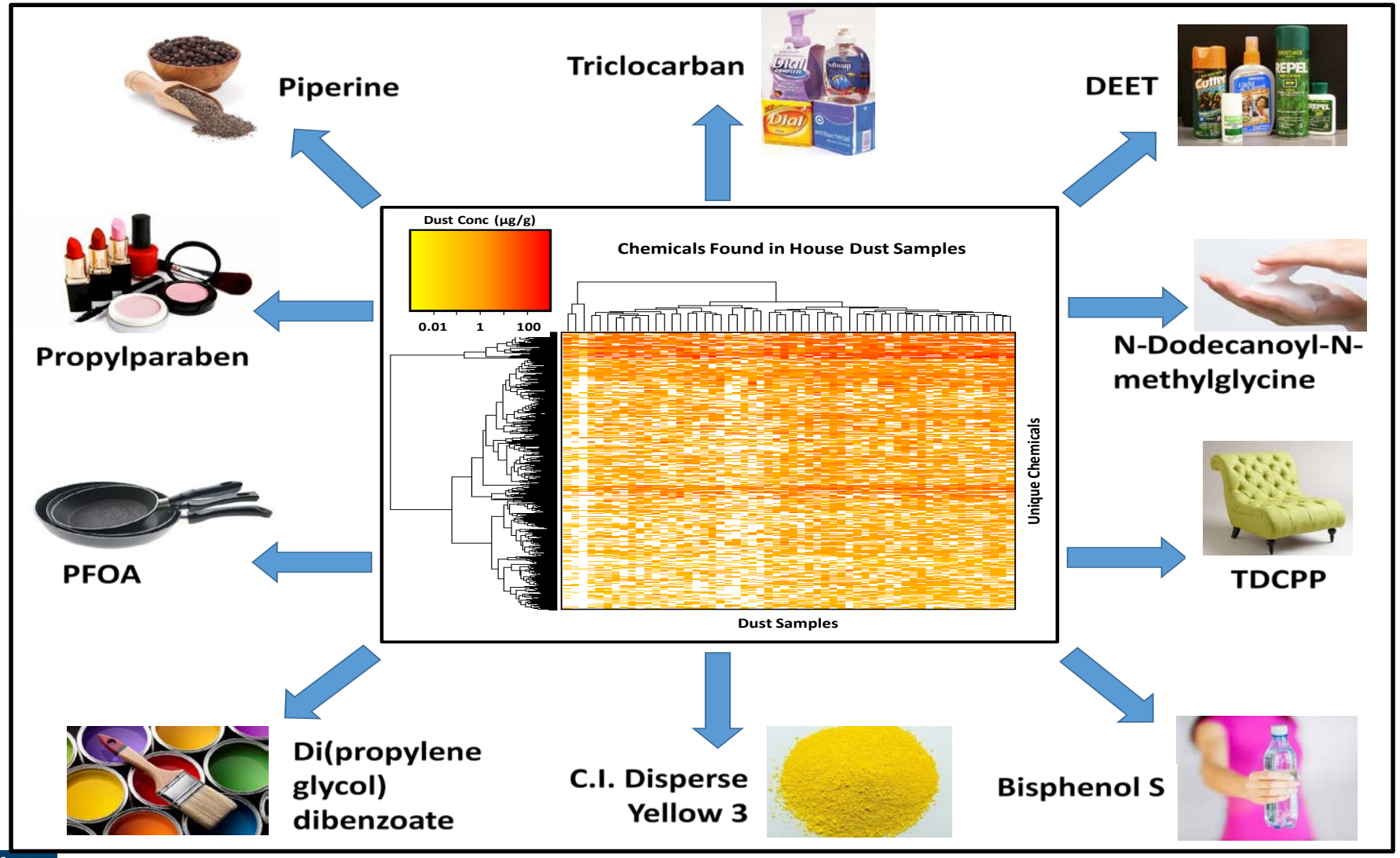
- Targeted Analysis:
  - We know the chemical for which we are looking
  - 10s – 100s of chemicals
- Non-Targeted Analysis (NTA):
  - We have no preconceived lists
  - 1,000s – 10,000s of chemicals
- Ongoing development of methods for various matrices including environmental and biological media

- Goal is to develop tools, databases, and workflows for rapid analysis of any sample for chemicals of interest, i.e. ***exposure forensics***
- These monitoring data (and others) are being pushed into EPA/ORD's public databases, along with other data being curated with program office partners

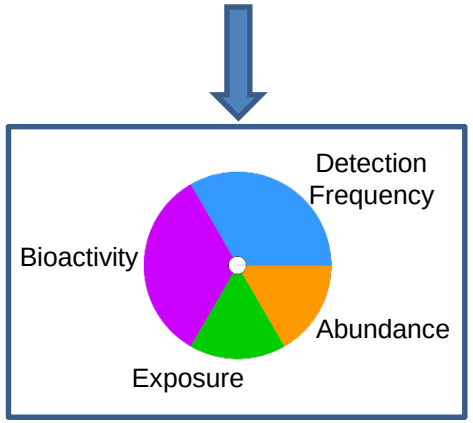
See Sobus et al. "Integrating Tools for Non-Targeted Analysis Research and Chemical Safety Evaluations at the US EPA" (JESEE, *in press*)

House Dust Pilot Study

Dust samples from 56 homes (American Health Homes Survey)



Thousands of compounds prioritized using ToxPi



45% of confirmed compounds never before measured in dust

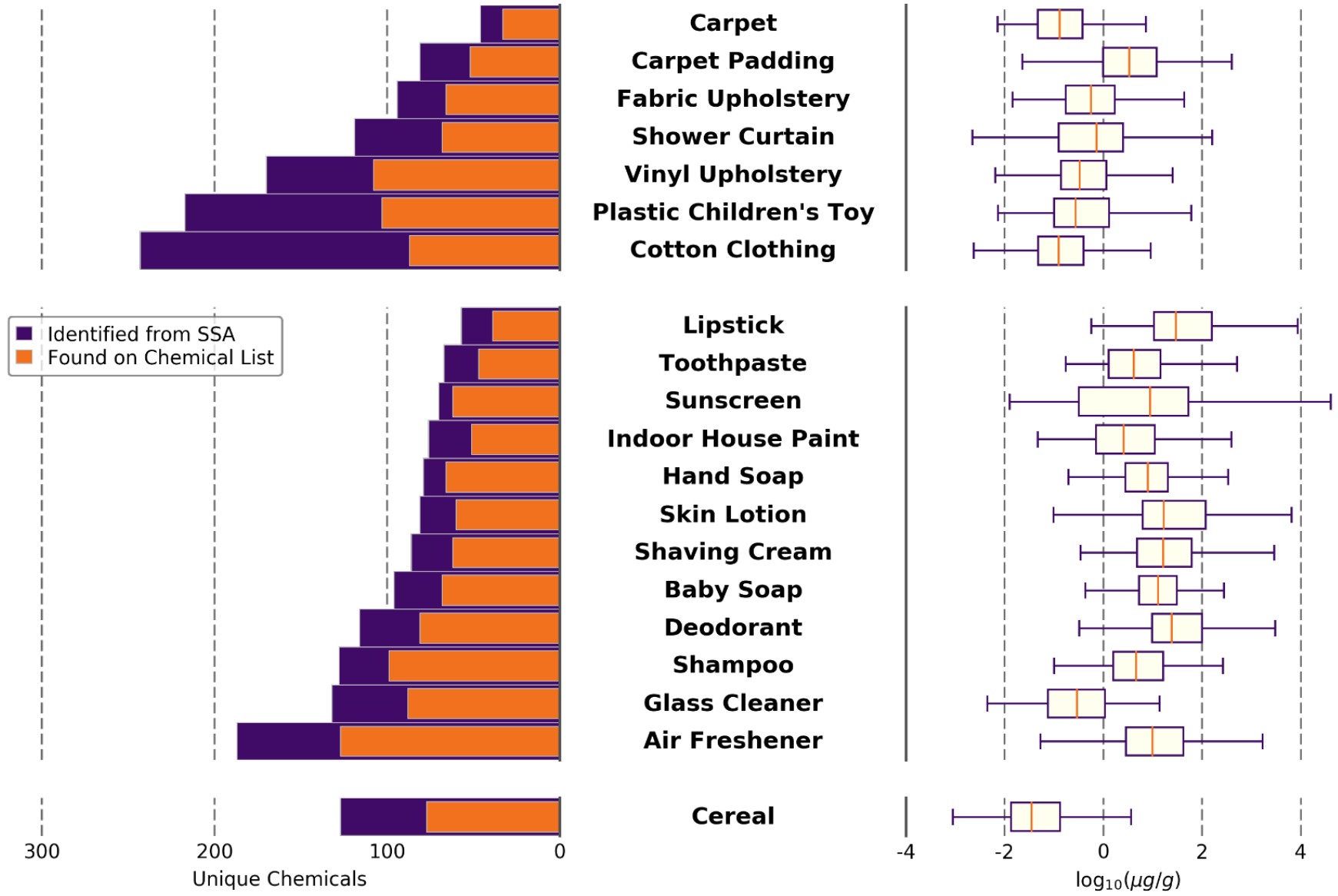
Rager et al., (2015)

Household Item Pilot Study

Analyzed 5 examples each of 20 diverse household items.

Not all categories relevant to TSCA, but included to illustrate the flexibility of the approach.

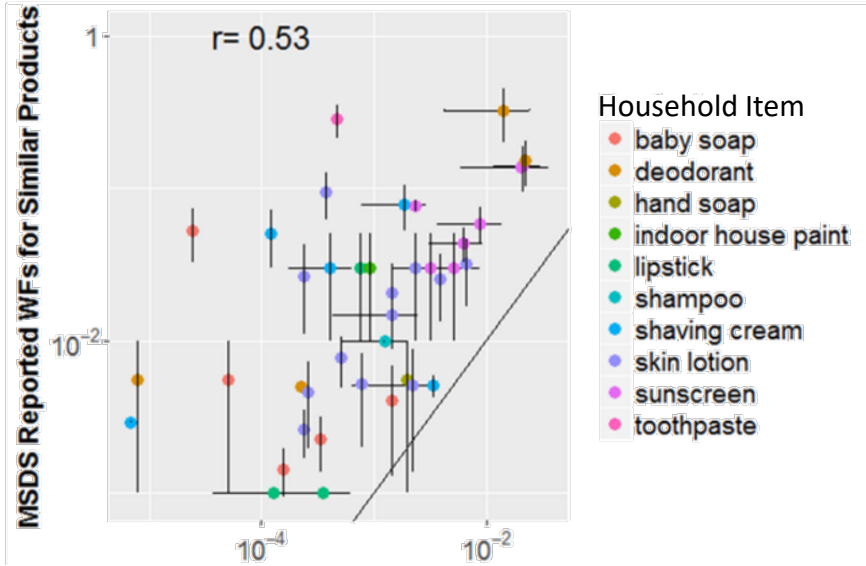
Of 1,632 chemicals confirmed or tentatively identified, 1,445 were not present in CPCPdb



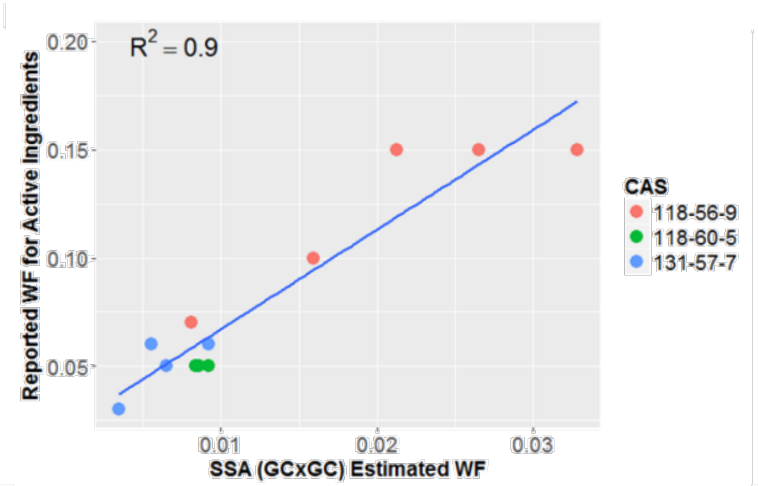
Phillips *et al.* (*submitted*)

Caveats to Non-Targeted Screening

- **Chemical presence in an object does not mean that exposure occurs**
- **Only some chemical identities are confirmed, *most are tentative***
  - Can use formulation databases and predictor models (e.g., Isaacs *et al.* (2016) and Phillips *et al.* (2017))
- **Chemical presence in an object does not necessarily mean that it is bioavailable**
  - Can build emission models (e.g., Biryol *et al.*, 2017)
- **Caveats specific to household item pilot:**
  - Samples are being homogenized and are extracted with a solvent (dichloro methane, DCM)
  - Only using one solvent (DCM, polar) and one method (GCxGC-TOF-MS)
  - Not all household items relevant to TSCA
- **Exposure alone is not risk, need hazard data**



Small range for quantitation may lead to lead inaccurate concentration



Phillips *et al.* (*submitted*)

EPA's Non-Targeted Analysis Collaborative Trial (ENTACT)

Led by Jon Sobus and Elin Ulrich (EPA/NERL)

ToxCast Chemicals →

Reference House Dust →

Reference Human Serum →

Reference Silicone Wristbands →

By Sector		By Location	
Academia	15	Canada	1
Government	8	Europe	3
Vendors	5	US	24

→ **Method Evaluation**

→ **Reference Libraries**

→ **Model Training Sets**

EPA's Non-Targeted Analysis Collaborative Trial (ENTACT)

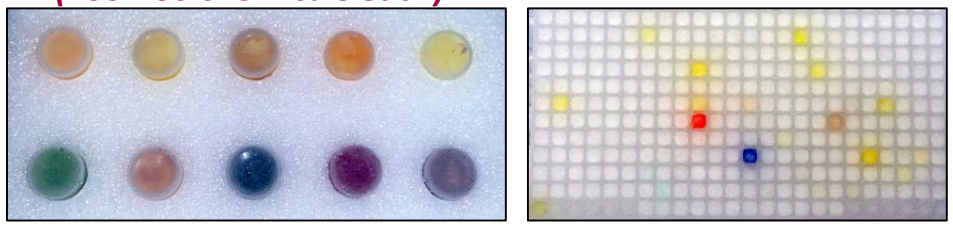
Part 1

Chemicals from ToxCast Library

~1200 ToxCast Chemicals (highest quality)

10 Mixtures (100-400 chemicals each)

*Multi-Well Plates**



~20 Collaborators & 5 Contractors*:

1st: Blinded analysis

2nd: Unveiling of chemicals

3rd: Unblinded evaluation

Part 2

Fortified Reference House Dust

100-200 chemicals

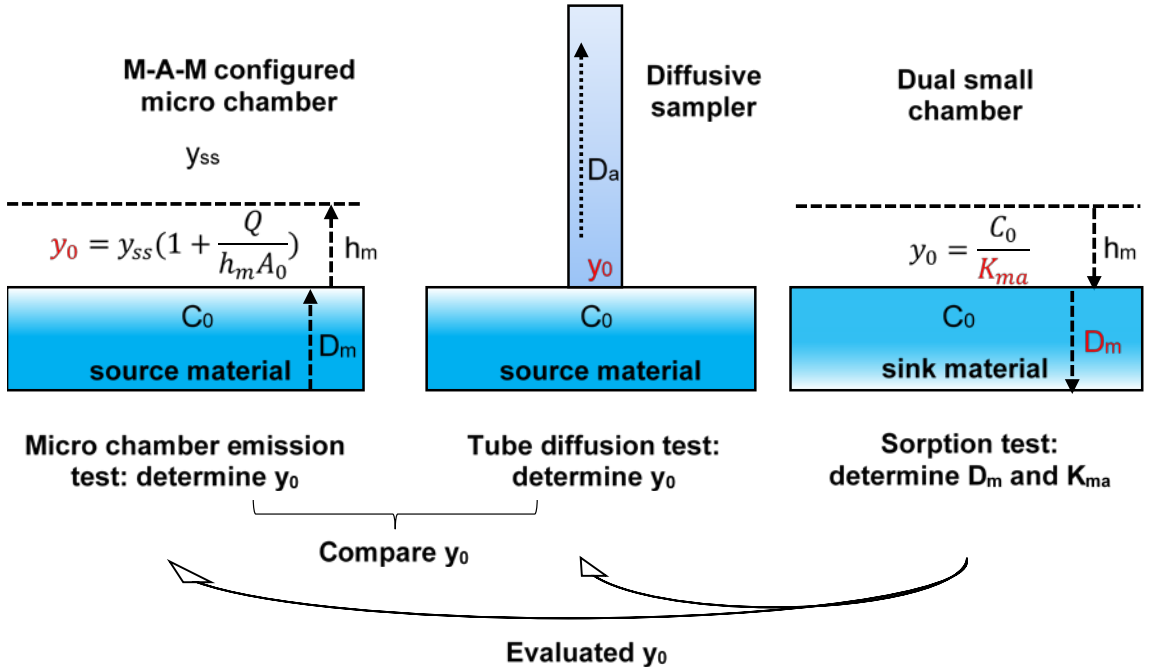
Fortified Reference Human Serum

100-200 chemicals

Fortified Reference Silicone Wristbands

100-200 chemicals

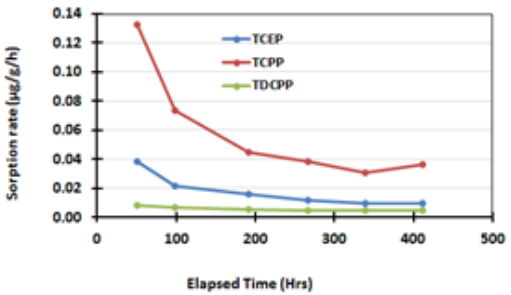
Experiments Characterizing Chemical Emission and Migration



Rough estimated K_{ds}

FRs	TCEP	TCPP	TDCPP
In dust (μg/g)	1.19	1.15	1.00
In foam (μg/g)	531.44	426.75	244.30
K_{ds}	2.23x 10^{-3}	2.68 x 10^{-3}	4.11 x 10^{-3}

Dust sorption rate



Carpet

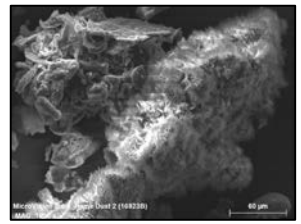
Vinyl flooring

Mattress pad

Painted wallboard

Baby pajamas

SPF foam


House dust

Xiaoyu Liu (EPA/NRMRL)

Conclusions

- We would like to know more about the potential risk posed by thousands of chemicals in the environment – which ones should we start with?
- Expanded monitoring data allows model parametrization and evaluation
  - Are chemicals missing that we predicted would be there?
  - Are there unexpected chemicals?
- While the amended TSCA provides an opportunity for ORD exposure measurements and databases to support OPPT risk evaluations, prior to any implementation the fitness-for purpose of these projects (e.g., for prioritization, scoping, or risk evaluation) must be evaluated in the context of TSCA requirements.
- All data being made public:
  - The Chemistry Dashboard (A search engine for chemicals) **http://comptox.epa.gov/**
  - Chemical-Product Database: http://actor.epa.gov/cpcat/
  - R package “httk”: https://CRAN.R-project.org/package=httk
  - R package “SHEDS-HT”

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