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Consumer Product Data from the US EPA's Exposure Forecasting (ExpoCast) Project

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"Measurement and Prediction of Chemicals in Consumer Products"
Society of Toxicology Annual Meeting
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Conflict of Interest Statement

I have no conflicts of interest to disclose

The views expressed in this presentation are those of the author and do not necessarily reflect the views or policies of the U.S. EPA

Introduction

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

Park *et al*. (2012):

At least 3221 chemicals in humans, many appear to be exogenous

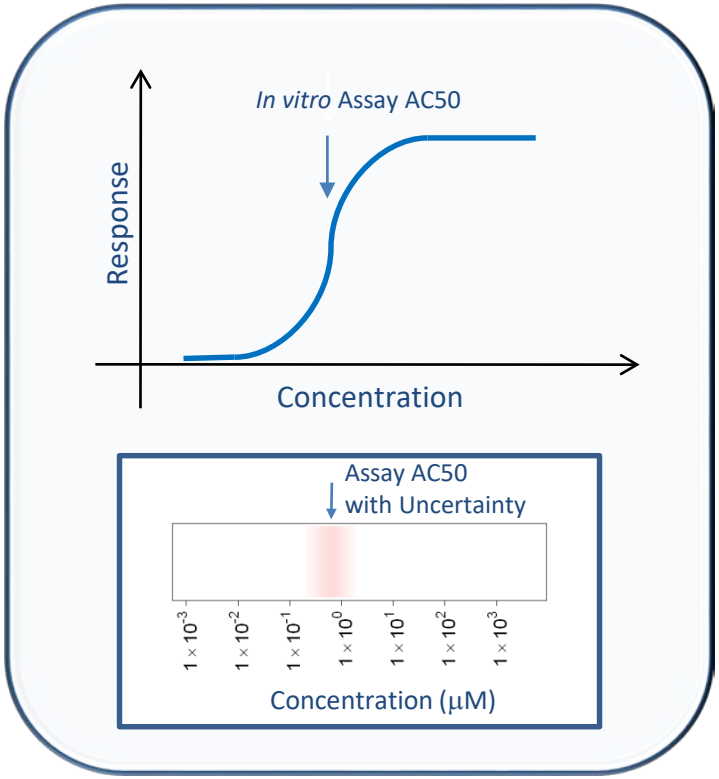
November 29, 2014

High-Throughput Bioactivity

- **Tox21**: Examining >10,000 chemicals using ~50 assays intended to identify interactions with biological pathways (Schmidt, 2009)

- **EPA Toxicity Forecaster (ToxCast)**:

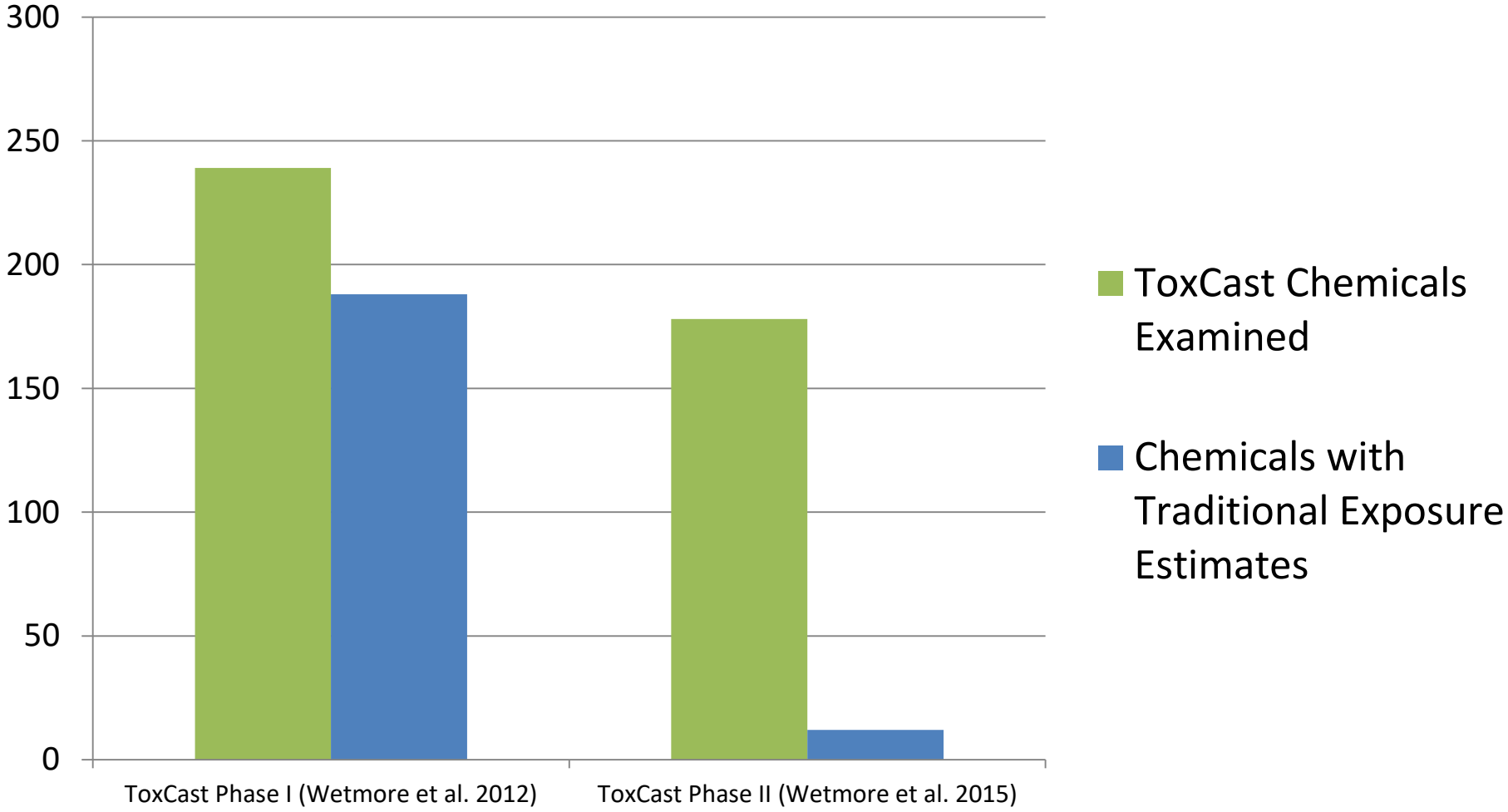
  For a subset (>3000) of Tox21 chemicals run >1000 additional assay endpoints (Judson et al., 2010)



- Most assays conducted in dose-response format (identify 50% activity concentration – AC50 – and efficacy if data described by a Hill function)
- Data are being revised, new chemicals tested, new assays added
- All data are made public:

http://comptox.epa.gov/dashboard/

Limited Available Data for Exposure Estimations



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

Using 21st Century Science to Improve Risk-Related Evaluations

- **January, 2017 National Academies of Science report:**
  - "Improving the amount and quality of the data that are needed to develop parameters for the computational exposure tools is critically important; without such data, the applicability of the tools is limited."
  - "Continued efforts to measure and estimate concentrations in multimedia sources—such as indoor air, indoor surfaces, dust, and consumer products—are required to address uncertainty in near-field exposures and pathways.
  - *"Recommendation:* Current efforts to obtain and organize information on chemical quantities in and rates of release from products and materials, particularly consumer products and materials in the indoor environment, should be expanded substantially."

Thinking About Exposure

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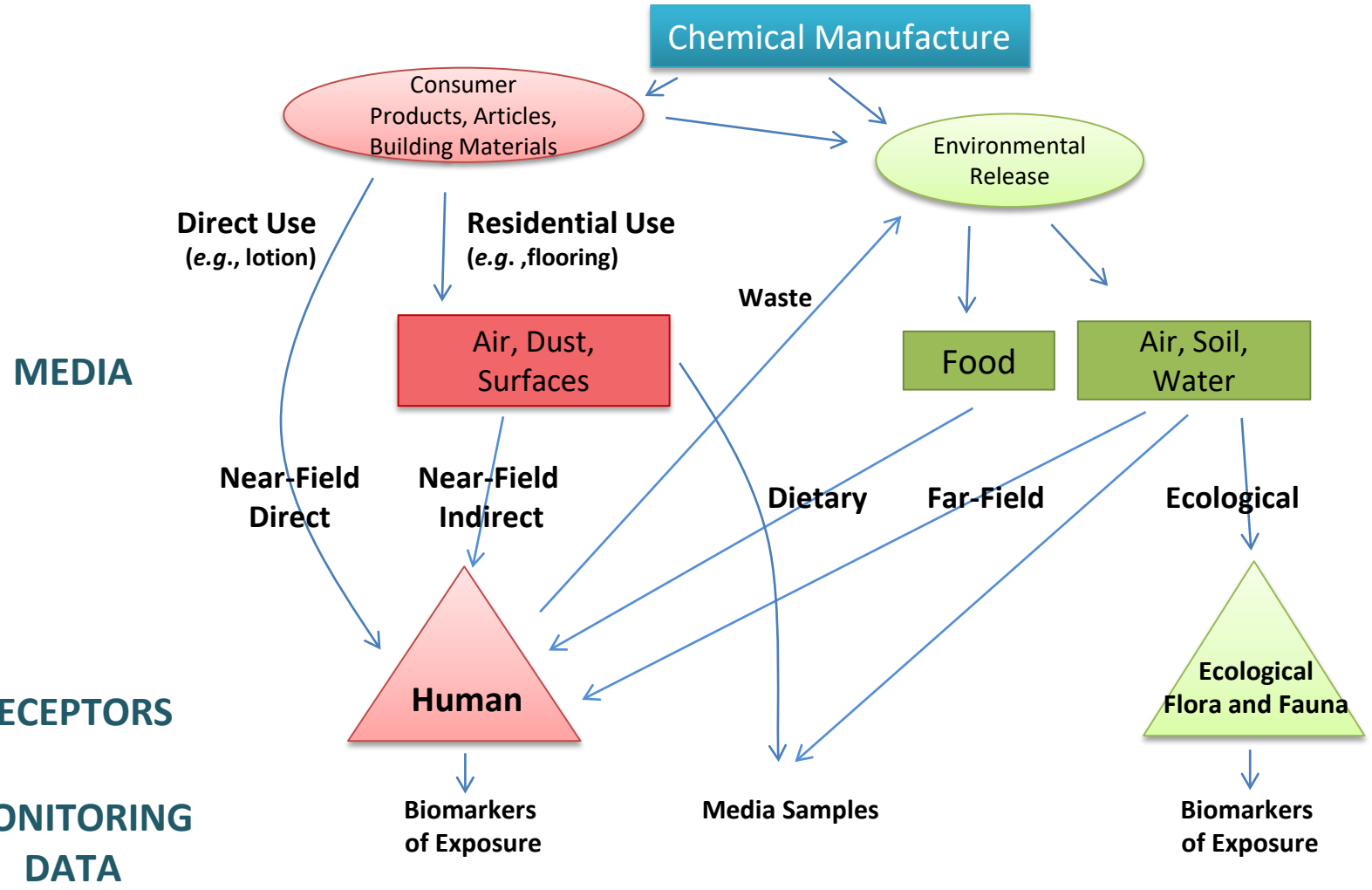


Figure from Kristin Isaacs

Exposure Pathways

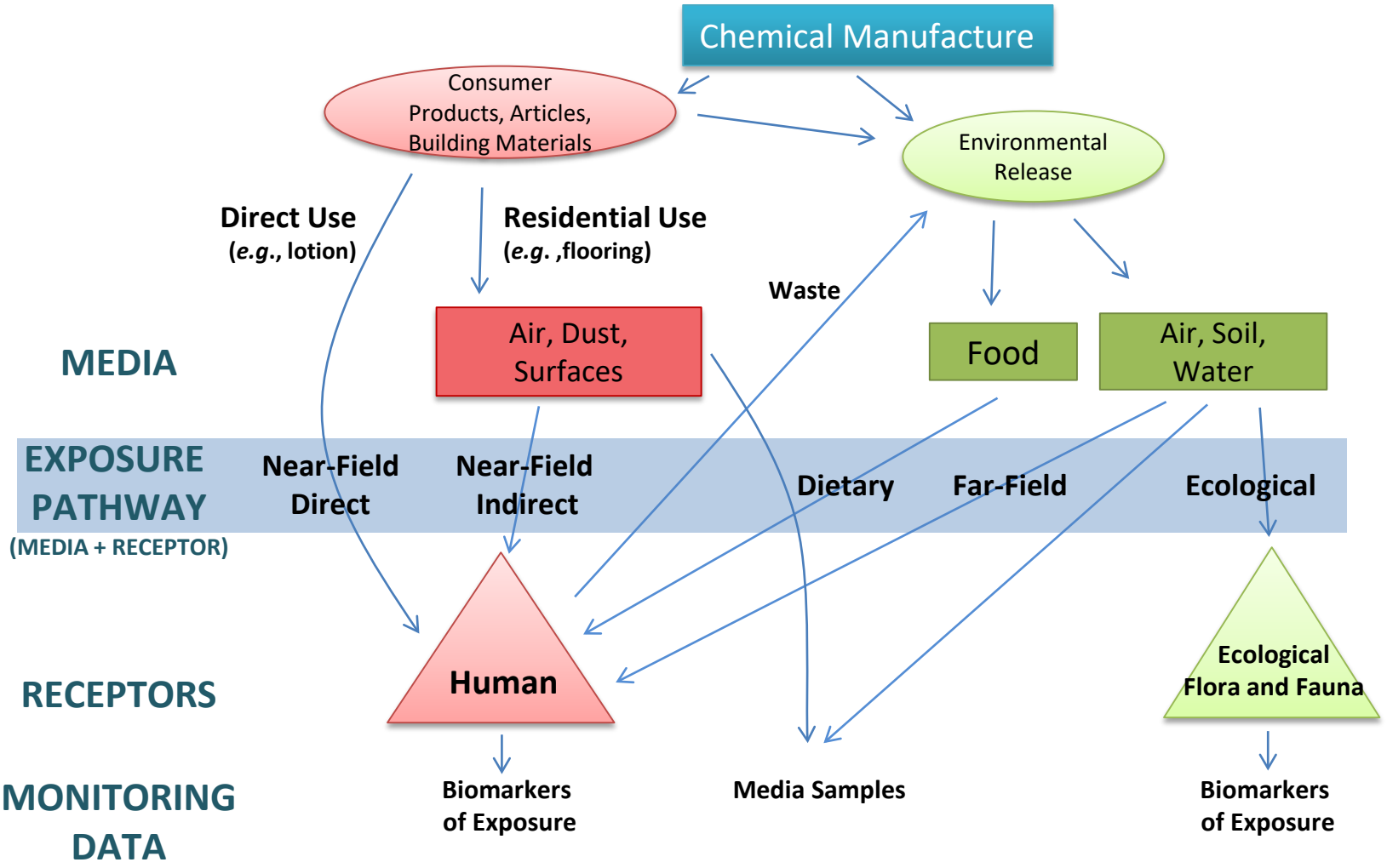
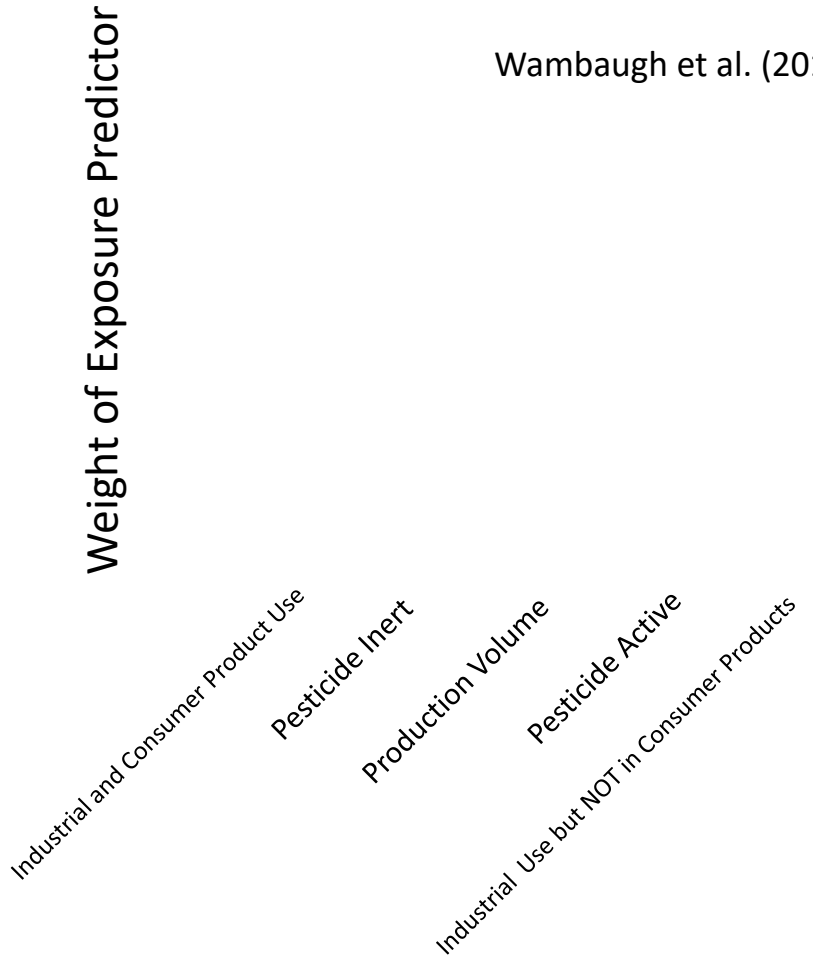


Figure from Kristin Isaacs

Predicting Exposure



We incorporate multiple computer models into consensus predictions for 1000s of chemicals

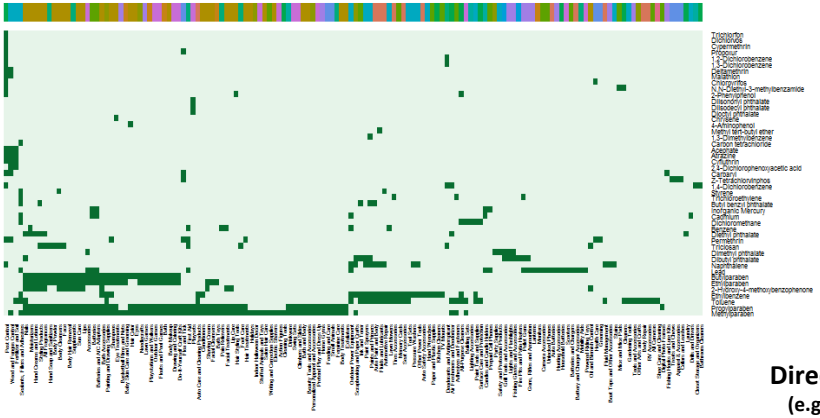
Same five predictors work for all NHANES demographic groups analyzed – stratified by age, sex, and body-mass index:

- Industrial and Consumer use
- Pesticide Inert
- Pesticide Active
- Industrial but no Consumer use
- Production Volume

Chemical Use Identifies Relevant Pathways

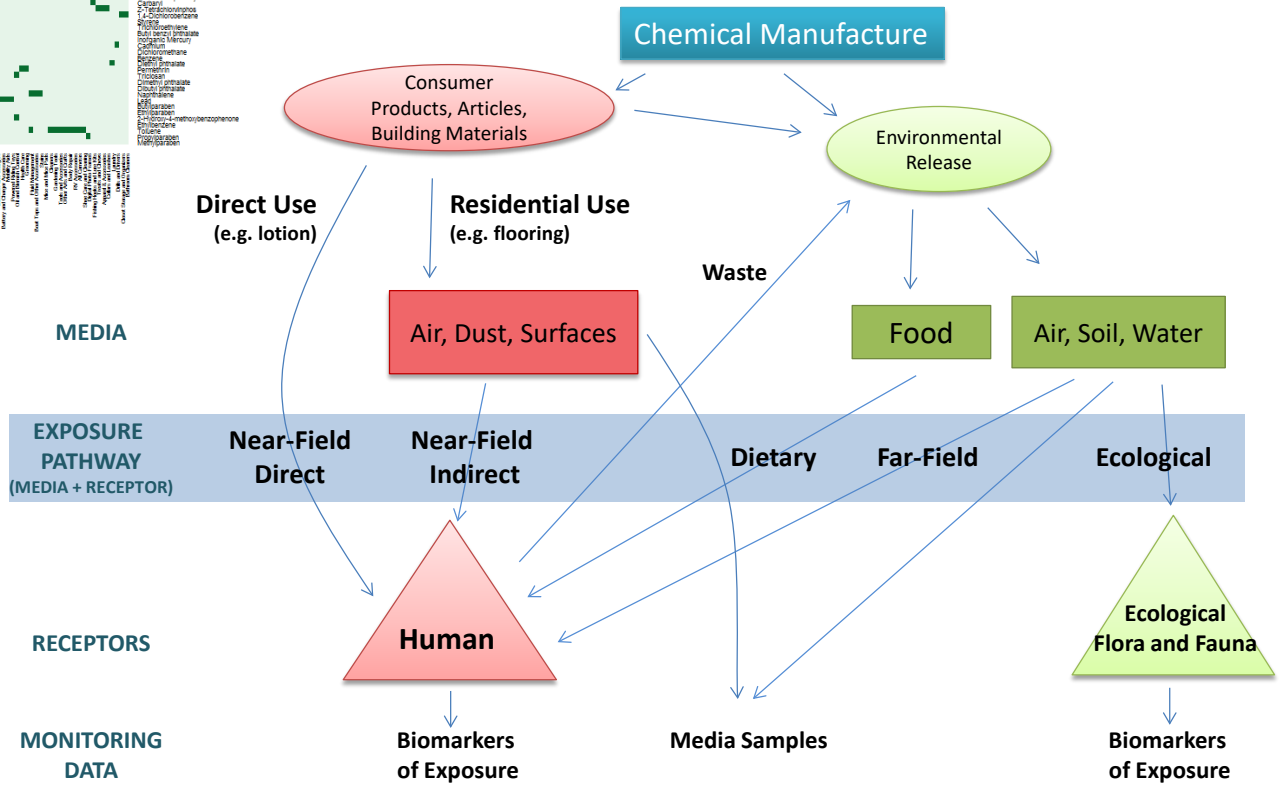
>2000 chemicals with Material Safety Data Sheets (MSDS) in CPCPdb (Goldsmith *et al.*, 2014)

105 NHANES Chemicals



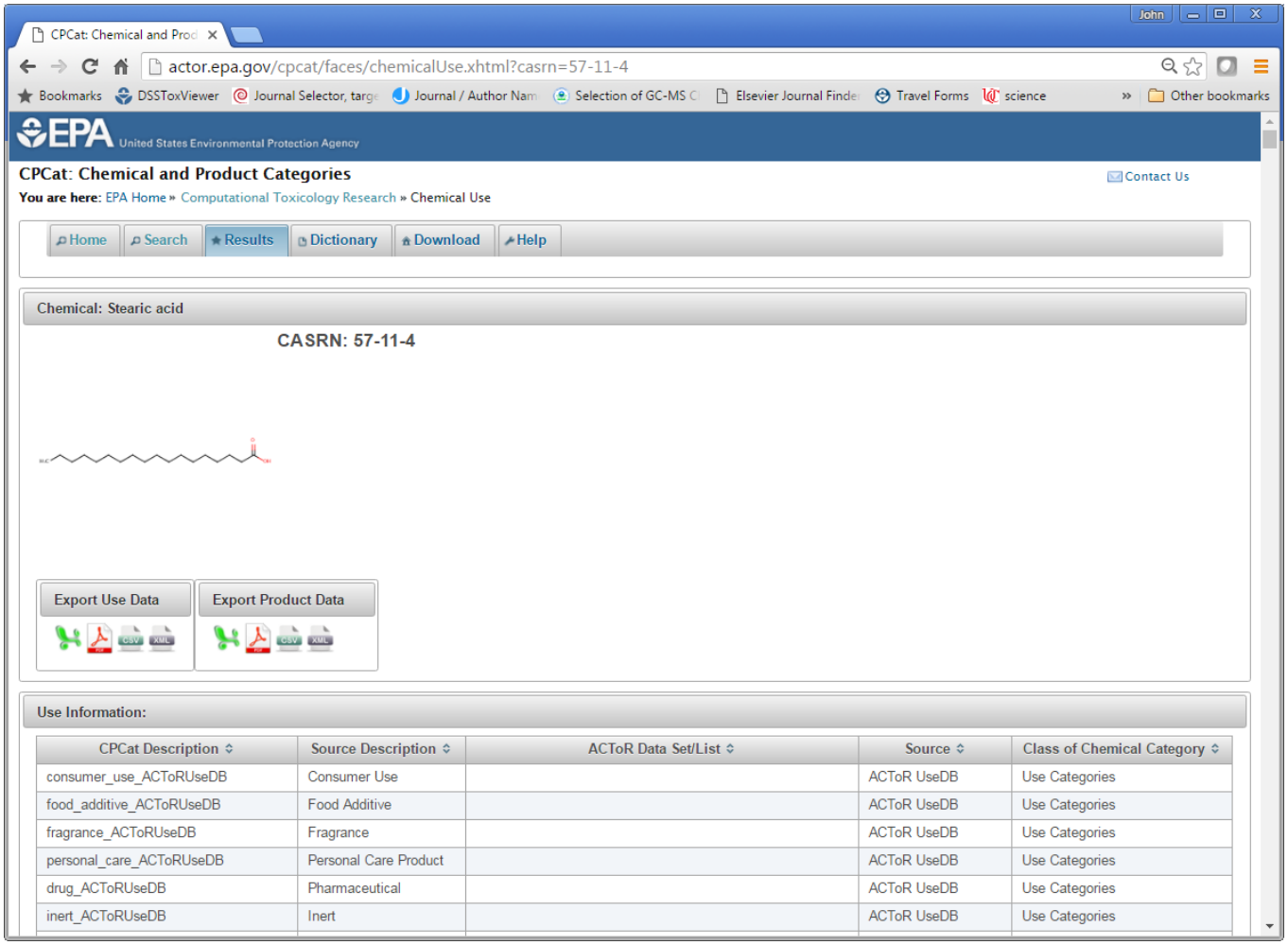
- Apparel
- Auto and Tires
- Baby
- Beauty
- Craft and Party Supply
- Electronics
- Grocery
- Health
- Home
- Home Improvement
- Patio and Garden
- Pets
- Sports and Outdoors
- Toys

…and some pathways have much higher average exposures!



CPdat: Chemical Use Information for ~30,000 Chemicals

- 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
- Largest single database has coarsest information: ACToR UseDB



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

Dionisio et al. *(2015)*

Pilot Projects to Reduce Uncertainty and Expand Validation Domain

Project	Pilot Project Scope
High throughput chemical property measurement (e.g., log P)	200 chemicals
Determine the chemical constituents of products, materials, articles	20 classes of product, 5 samples each
Determine chemical emission rate from specific products, materials, articles	100 materials
Screening for occurrence of large numbers of chemicals in blood samples	500 individuals

- Expands application domain of physical chemical property computational models
- Better understanding of what chemicals are associated with household products
- Better understanding of chemicals in the indoor environment
- Expands validation domain of human biomonitoring chemicals

Targeted vs. Non-Targeted Screening

- Of 106 chemicals with urine biomarkers in CDC NHANES, roughly half were below the limit of detection (Wambaugh et al., 2014)
- Park et al. (2012) found evidence of thousands of exogenous chemicals in blood

  - Differences in sensitivity
  - Differences in screening method – targeted vs. non-targeted screening

Targeted vs. Non-Targeted Screening

- When we do a targeted analysis for a particular analyte, you typically gain accuracy and precision (and quantification) but are deliberately focusing on only part of the story
- Targeting eliminates background to focus on analyte

Targeted vs. Non-Targeted Screening

- Non-targeted approach considers the “background”
- Need to take into account transformation (e.g., metabolism)
- Need to control for background (e.g., endogenous chemicals)

Applying Non-Targeted Screening

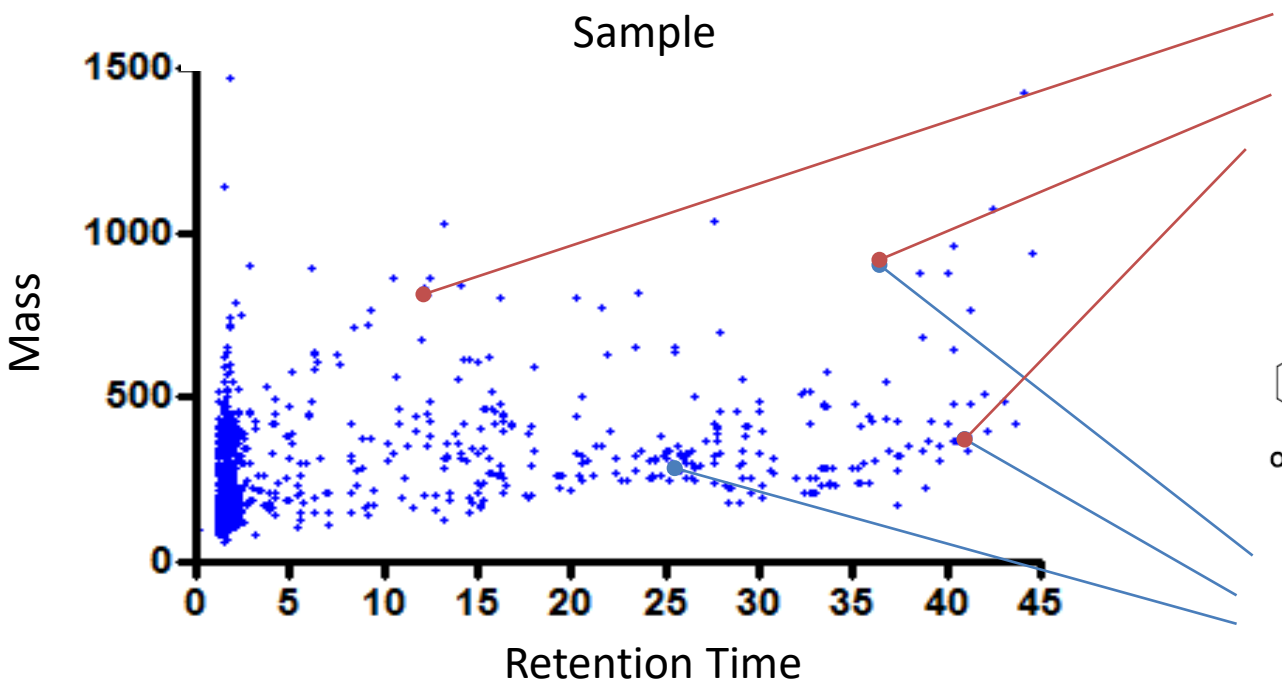
- Ongoing ExpoCast contract consumer product scanning and blood sample monitoring
- EPA has developed significant in house capabilities
  - Published on analysis of house dust from American homes – can identify 50% of the mass but only 2% of the chemicals *Rager et al., Environment International (2016)*

"I'm searching for my keys."

- EPA is coordinating a comparison of non-targeted screening workflows used by leading academic and government groups using known chemical mixtures (ToxCast) and standardized environmental/biological samples (Sobus and Ulrich)

Suspect Screening and Non-Targeted Analytical Chemistry

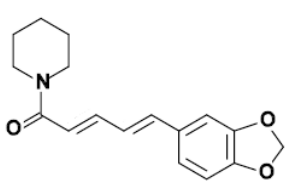
947 Peaks in an American Health Homes Dust Sample

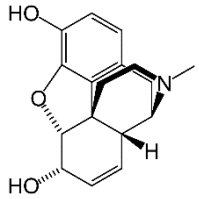


Each peak corresponds to a chemical with an accurate mass and predicted formula:

$C_{17}H_{19}NO_3$

Multiple chemicals can have the same mass and formula:





Is chemical A present, chemical B, both, or some other chemical (neither)?

We are expanding our reference libraries using ToxCast chemicals to enable greater numbers and better accuracy of confirmed chemicals

See Rager et al., Environment International (2016)

Appropriate Skepticism for Non-Targeted Analysis and Suspect Screening

"As chemists we are obliged to accept the assignment of barium to the observed activity, but as nuclear chemists working very closely to the field of physics we cannot yet bring ourselves to take such a drastic step, which goes against all previous experience in nuclear physics. It could be, however, that a series of strange coincidences has misled us."

Hahn and Strassmann (1938)

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Hahn and Strassmann (1938)

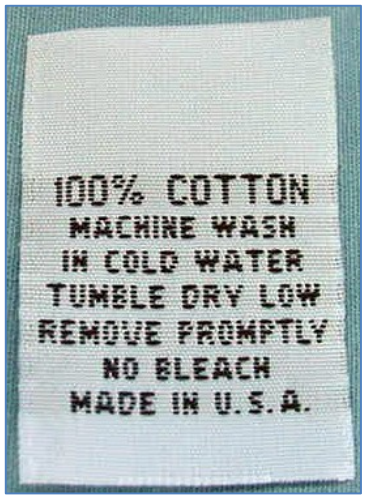
1944 Nobel Prize in Chemistry for "discovery of the fission of heavy nuclei"

ExpoCast Consumer Product Scan

United States Environmental Protection Agency

$Log_{10}(\mu g/g)$

The chemicals found in a cotton shirt



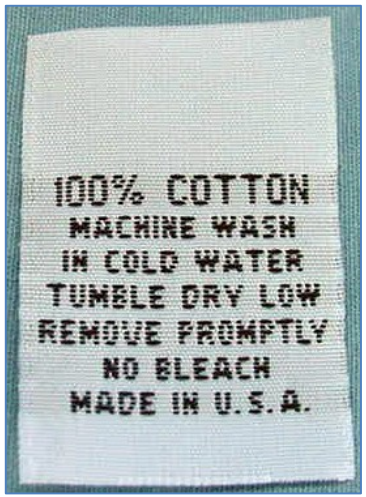
Phillips et al. (in preparation)

ExpoCast Consumer Product Scan

United States Environmental Protection Agency

$Log_{10}(\mu g/g)$

⬅ Chemicals that are present



⬅ Chemicals that are absent (but found in other products)

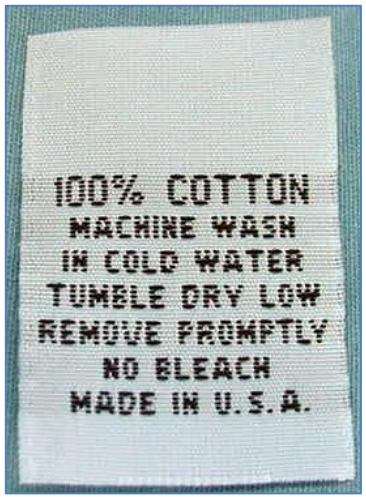
Phillips et al. (in preparation)

ExpoCast Consumer Product Scan

United States Environmental Protection Agency

$Log_{10}(\mu g/g)$

The chemicals found in a cotton shirt



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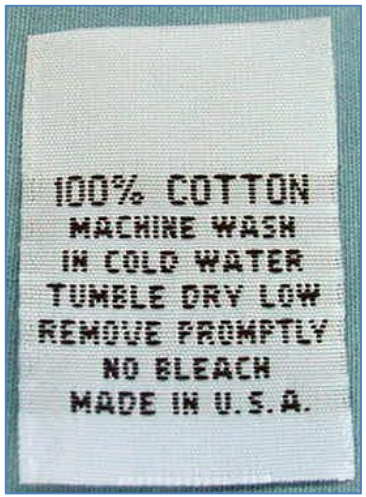

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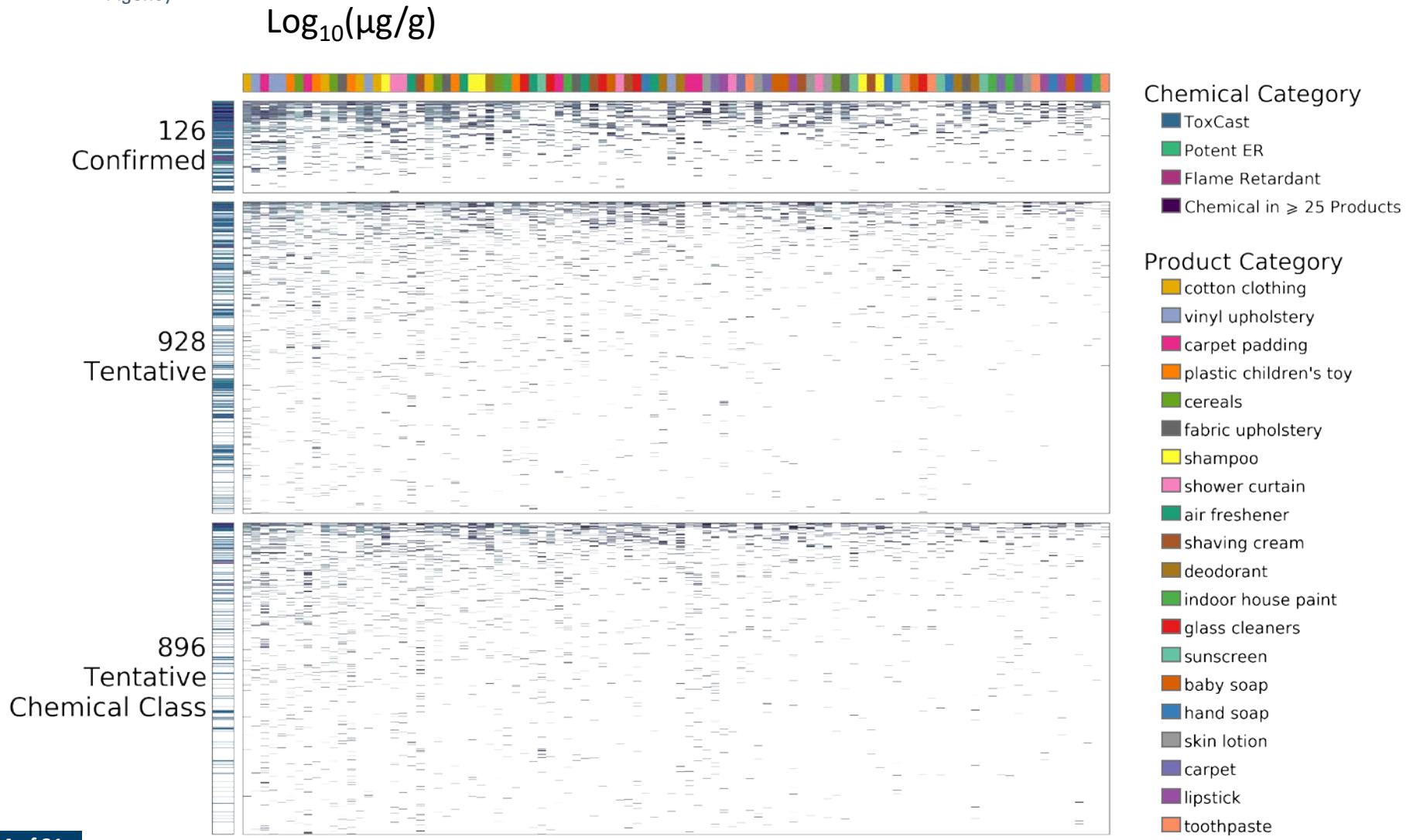
ExpoCast Consumer Product Scan



Of the 1,632 chemicals, 1,445 were not present in CPCPdb

Phillips et al. (in preparation)

Product Scan Summary

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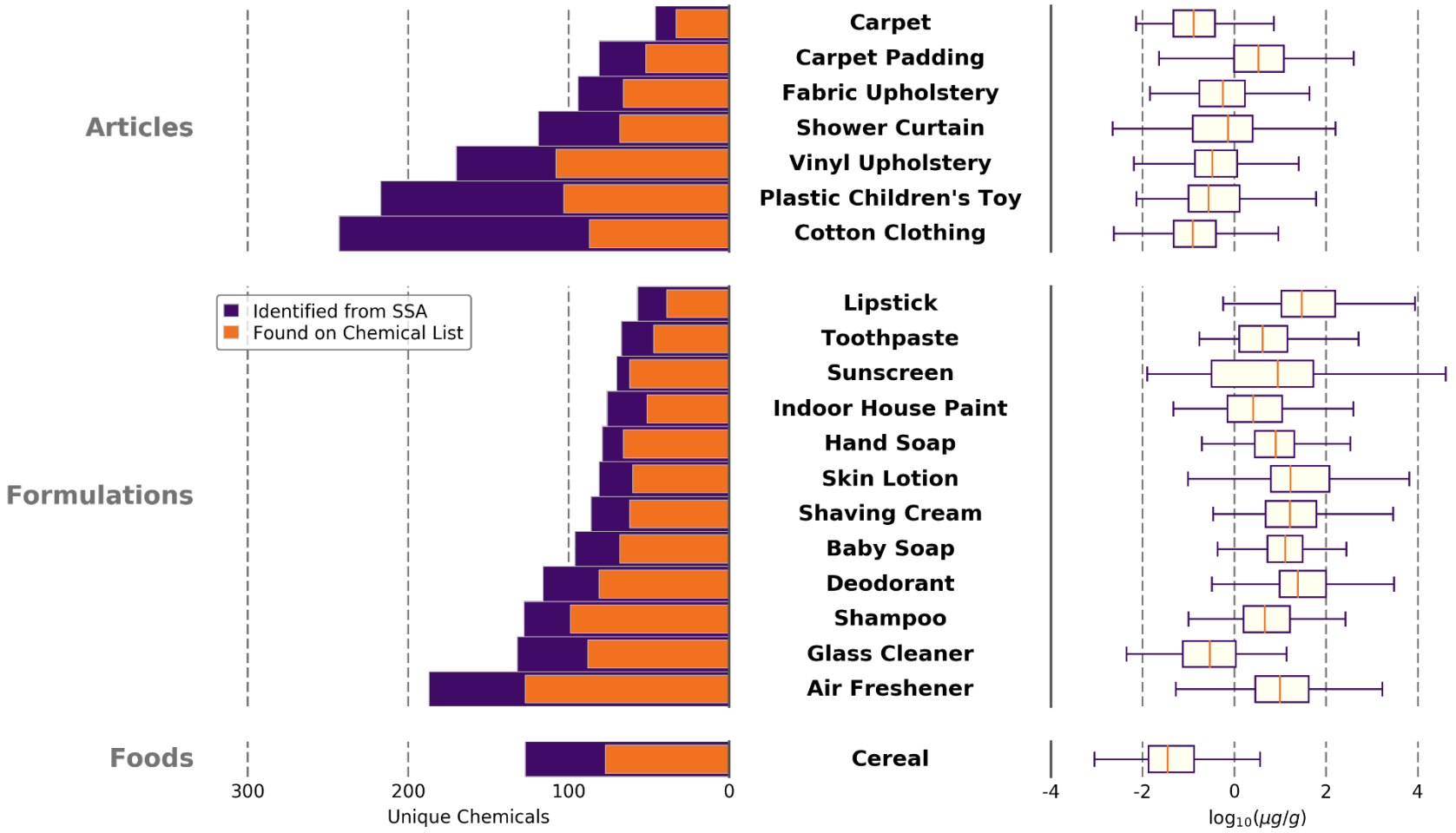
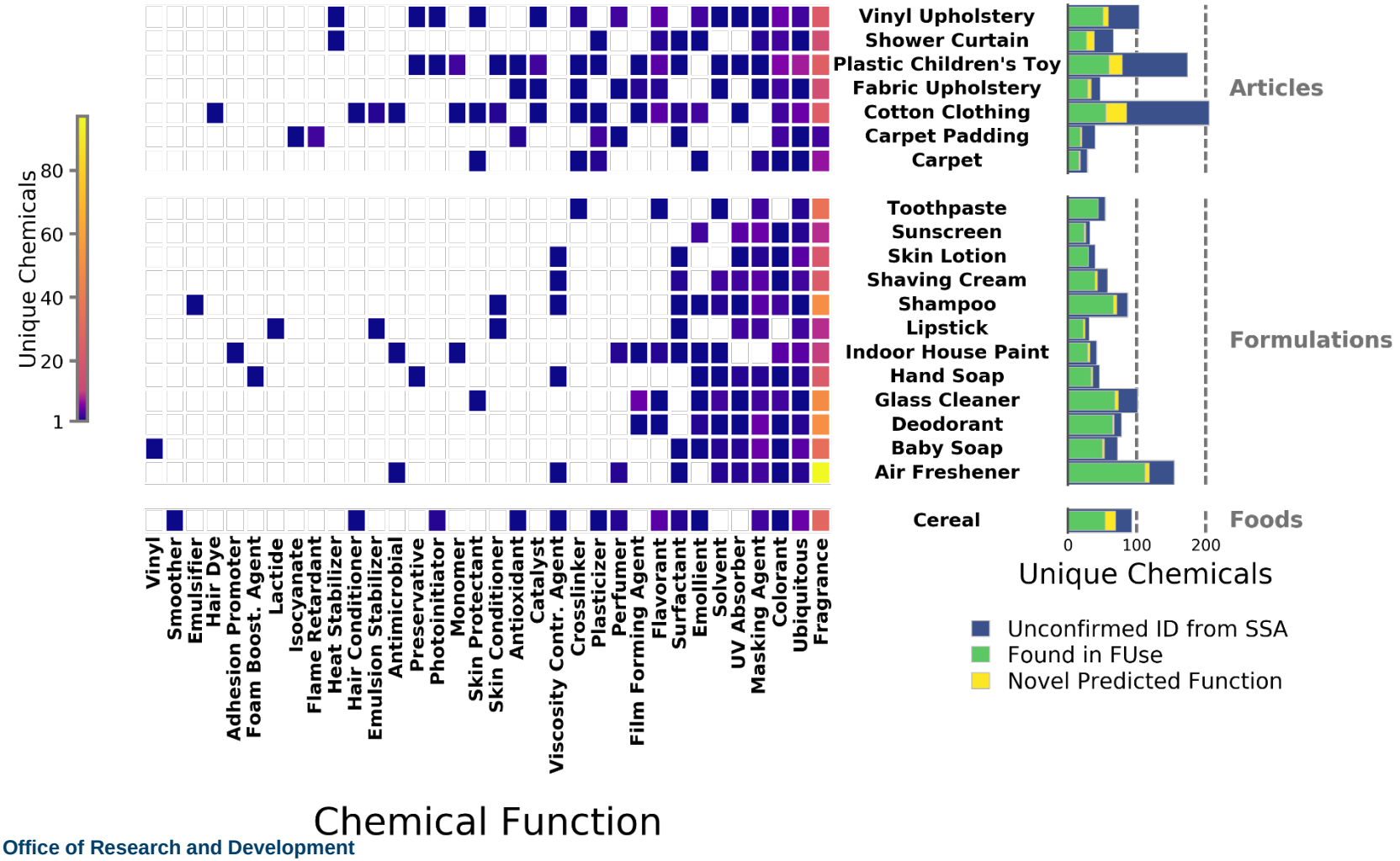


Phillips et al. (in preparation)

Predicting Chemical Function

Using the methods of Phillips et al., Green Chemistry (2017):



Phillips et al. (in preparation)

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 predictor models as additional evidence
- **Chemical presence in an object does not necessarily mean that it is bioavailable**
  - Can build emission models
- **Small range for quantitation leads to underestimation of concentration**
- **Product de-formulation caveats:**
  - Samples are being homogenized (e.g., grinding) and are extracted with a solvent (dichloro methane, DCM)
  - Only using one solvent (DCM, polar) and one method GCxGC-TOF-MS
  - Varying exposure intimacy, from carpet padding to shampoo to cereal
- **Exposure alone is not risk, need hazard data**

High Throughput Risk Prioritization in Practice

ToxCast-derived Receptor Bioactivity Converted to mg/kg/day with HTTK

ExpoCast Exposure Predictions

Near Field

Far Field

ToxCast Chemicals

Prioritization as in Wetmore *et al*. (2015) Bioactivity, Dosimetry, and Exposure Paper

December, 2014 Panel:
"Scientific Issues Associated with Integrated Endocrine Bioactivity and Exposure-Based Prioritization and Screening"

DOCKET NUMBER:
EPA–HQ–OPP–2014–0614

Conclusion

- We would like to know more about the potential risk posed by thousands of chemicals in the environment – which are most worthy of further study?

- Using **high throughput exposure** approaches we can make *coarse* predictions of exposure
  - We are actively refining and better validating these predictions with new models and data
  - In some cases, upper confidence limit on current predictions is already many times lower than predicted hazard

- Monitoring is tricky, and there are trade offs between the precision of targeted monitoring for specific chemicals and non-targeted screening for all exogenous chemicals

- Expanded monitoring data (exposure surveillance) allows evaluation of model predictions
  - Are chemicals missing that we predicted would be there?
  - Are there unexpected chemicals?

"Measurement and Prediction of Chemicals in Consumer Products"

Society of Toxicology Annual Meeting

- What is the potential for new rapid forensic measurement techniques for characterizing substances in consumer products (formulations, articles, building materials, food contact materials)?
- How can modeling approaches that consider chemical structure and/or chemical use information add value to rapid forensic measurement data?
- How should consumer product chemicals be categorized in terms of their use or properties for informing read-across in terms of exposure pathways and sources?
- What efforts exist or are being initiated to manage, inventory, or quantify chemicals used in products from manufacturing source through supply chain to finished product?
- How can consumer product chemical inventories (both ingredients and contaminants) inform aggregate or cumulative exposure-based risk assessments?
- Ultimately, how can improved exposure estimates for chemicals in consumer products be integrated with different types of toxicological information to support frameworks for risk-based chemical evaluation and decision-making?

"Measurement and Prediction of Chemicals in Consumer Products"

Society of Toxicology Annual Meeting

Panel discussion at the end of the session (Noon – 12:15 pm)

- Deborah Bennett, University of California, Davis,
- Cian O'Mahony, Creme Global
- Kristin Isaacs, US EPA
- Treye Thomas, US Consumer Product Safety Commission
- John Wambaugh, US EPA

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

NCCT
Chris Grulke
Greg Honda*
Richard Judson
Andrew McEachran*
Robert Pearce*
Ann Richard
Parichehr Saranjampour*
Risa Sayre*
Woody Setzer
Rusty Thomas
John Wambaugh
Antony Williams

NRMRL
Yirui Liang*
Xiaoyu Liu

NHEERL
Linda Adams
Christopher Ecklund
Marina Evans
Mike Hughes
Jane Ellen Simmons

*Trainees

NERL
Craig Barber
Namdi Brandon*
Peter Egeghy
Jarod Grossman*
Hongtai Huang*
Brandall Ingle*
Kristin Isaacs
Sarah Laughlin-Toth*
Aurelie Marcotte*
Seth Newton
Katherine Phillips
Paul Price
Jeanette Reyes*
Jon Sobus
John Streicher*
Mark Strynar
Mike Tornero-Velez
Elin Ulrich
Dan Vallero
Barbara Wetmore

Lead CSS Matrix Interface:
John Kenneke (NERL)

Collaborators

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Battelle Memorial Institute
Anne Louise Sumner
Anne Gregg
Chemical Computing Group
Rocky Goldsmith
National Institute for Environmental Health Sciences (NIEHS) National Toxicology Program
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Netherlands Organisation for Applied Scientifi Research (TNO)
Sieto Bosgra
Research Triangle Institute
Timothy Fennell
ScitoVation
Harvey Clewell
Chantel Nicolas
Silent Spring Institute
Robin Dodson
Southwest Research Institute
Alice Yau
Kristin Favela
Summit Toxicology
Lesa Aylward
Tox Strategies
Caroline Ring
University of California, Davis
Deborah Bennett
Hyeong-Moo Shin
University of Michigan
Olivier Jolliet
University of North Carolina, Chapel Hill
Alex Tropsha

References

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Demos by Our Scientists

- ECOTOX
- SeqAPASS
- HTTK Package
- CPDat
- AOP Wiki
- CompTox Chemistry Dashboard
- ToxCast Dashboard and Data Downloads
- GenRA

Meet the Directors Sessions

- EPA Lab, Center and Office Directors
- Informal- 1 Hour Sessions

epa.gov/research/2017-sot

For full list of events and materials