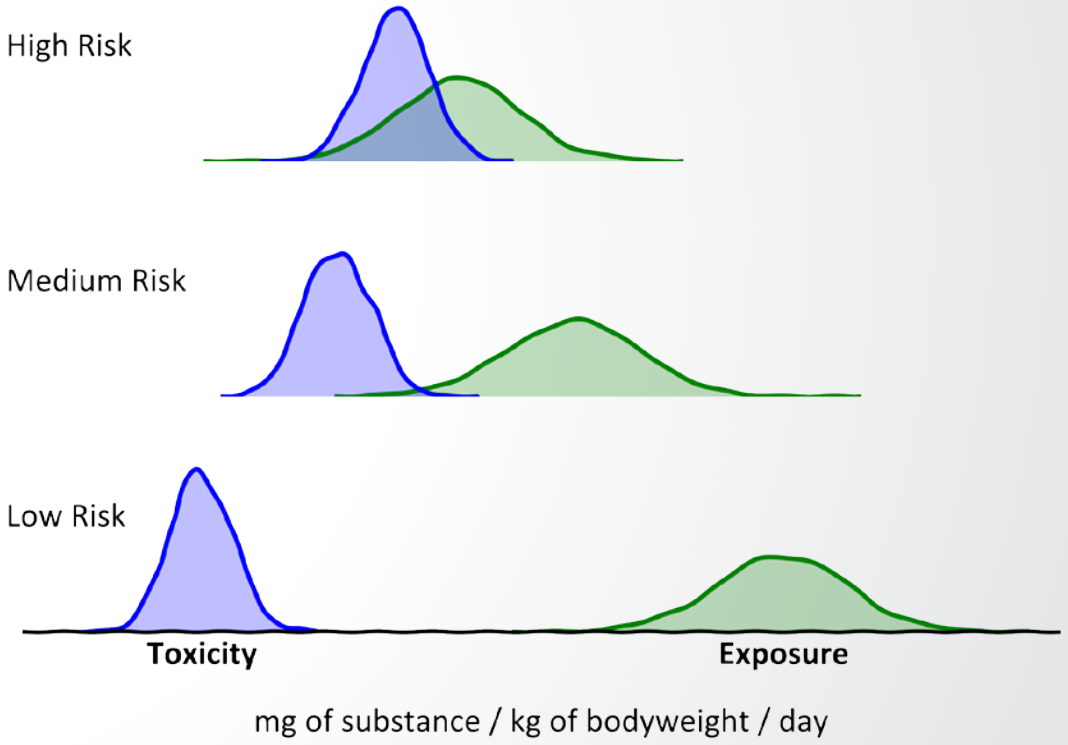
Suspect Screening of Chemicals in Consumer Products

Katherine Phillips, Kristin Isaacs, John Wambaugh

The views expressed in this presentation are those of the authors and do not necessarily represent the views or policies of the U. S. Environmental Protection Agency. Reference to commercial products or services does not constitute endorsement.

Rapid Exposure and Dosimetry

- The timely characterization of the human and ecological risk posed by thousands of existing and emerging commercial chemicals is a critical challenge
- **High throughput risk prioritization** relies on three components:
  1. high throughput **hazard** characterization
  2. high throughput **exposure** forecasts
  3. high throughput **toxicokinetics** (i.e., dosimetry)
- While advances have been made in HT toxicity screening, exposure methods applicable to 1000s of chemicals are needed



Slide from Kristin Isaacs

Available Information

Product Safety Data Sheet

Section 1: Identification of Product and Company

Section 2: Hazards Identification

Section 3: Composition Information on Ingredients

Ingredient	CAS Number	Concentration
Aqua (water)	7732-18-5	30% -- 100%
Glycerin	56-81-5	≤ 1%
Cetyl hyroxyethylcellulose	80455-45-4	≤ 1%

Section 4: First Aid Measures

Section 5: Fire Fighting Measures

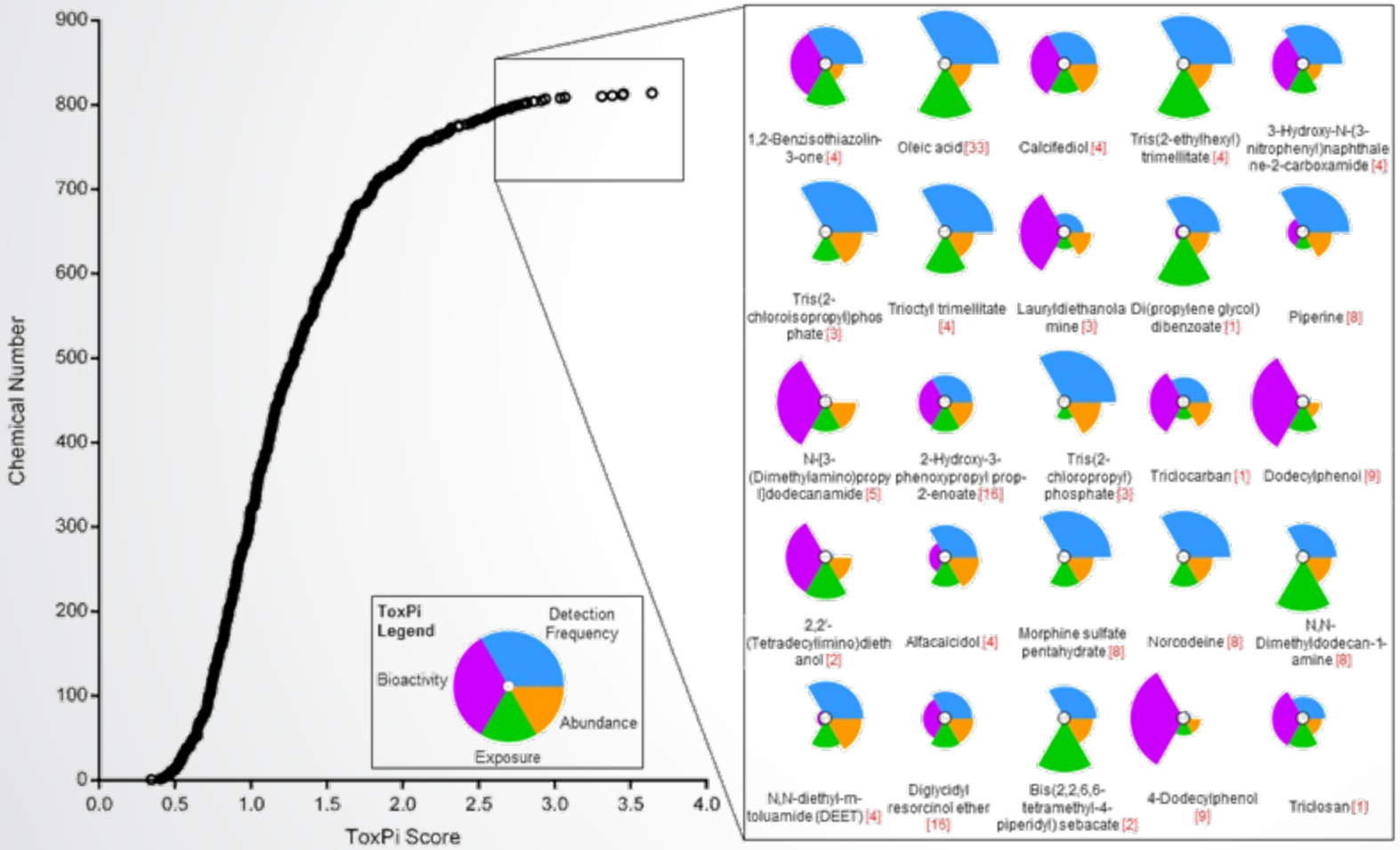
Section 6: Accidental Release Measures

Section 7: Handling and Storage

Section 8: Exposure Controls, Personal Protection

- Many manufacturers of consumer product formulations release a (Material) Safety Data Sheet, or (M)SDS, for products
- This is less common for articles, however some manufacturers release Health Product Declarations (HPDs) which are similar
- Exact concentrations are not known
- Trade secret chemicals are not disclosed
- Fragrances and colorants may not be disclosed with the product

Suspect Screening of House Dust



- 56 dust samples were analyzed using liquid chromatography
- Formulas of potentially identified chemicals were matched against database of chemicals
- Exposure, bioactivity, instrument abundance, and detection frequency were used to rank chemicals for confirmation

Rager, *Environ. Intl.* (2016)

Analytical Analyses

Targeted Analysis

- Uses analytical techniques to look for a predetermined list of 10s to 100s chemicals
- These chemicals make up much less than 1% of the exposome

Suspect Screening Analysis

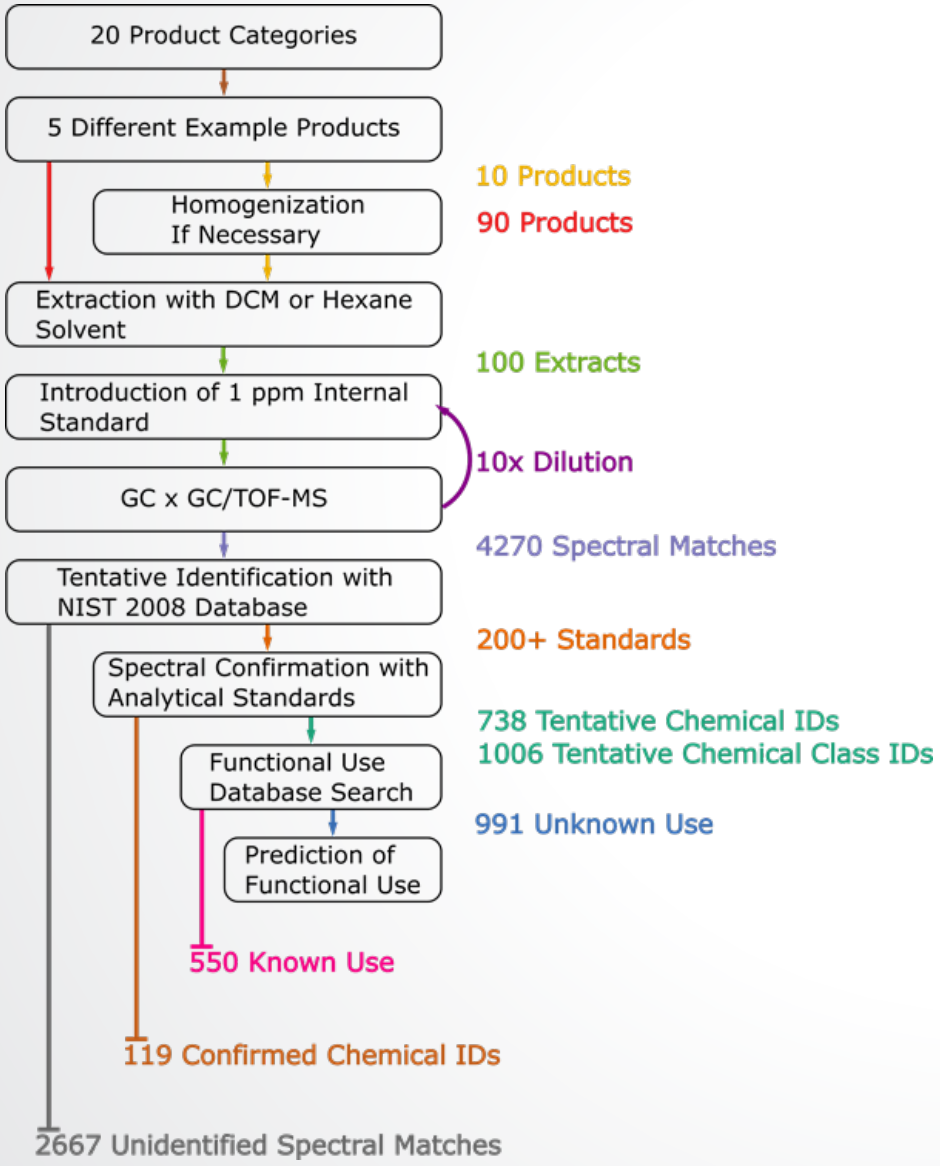
- Uses analytical techniques and spectral databases to compare spectra from a sample to 100s or 1000s of chemicals in the database
- These chemicals make up approximately 5 – 10% of the exposome

Non-targeted Analysis

- Identity of potential chemicals in samples are proposed without the aid of list or database
- These chemicals make up approximately 90 – 95% of the exposome

Slide adapted from Jon Sobus

SSA Workflow



- 100 different products were purchased across retail stores
- Products were spread across 20 product categories (5 different products from each category)
- Product Categories covered:
  - **Articles**: long term products in the home (e.g., carpet, upholstery)
  - **Formulations**: short term products that are used up (e.g., shampoo, lotion)
  - **Food**

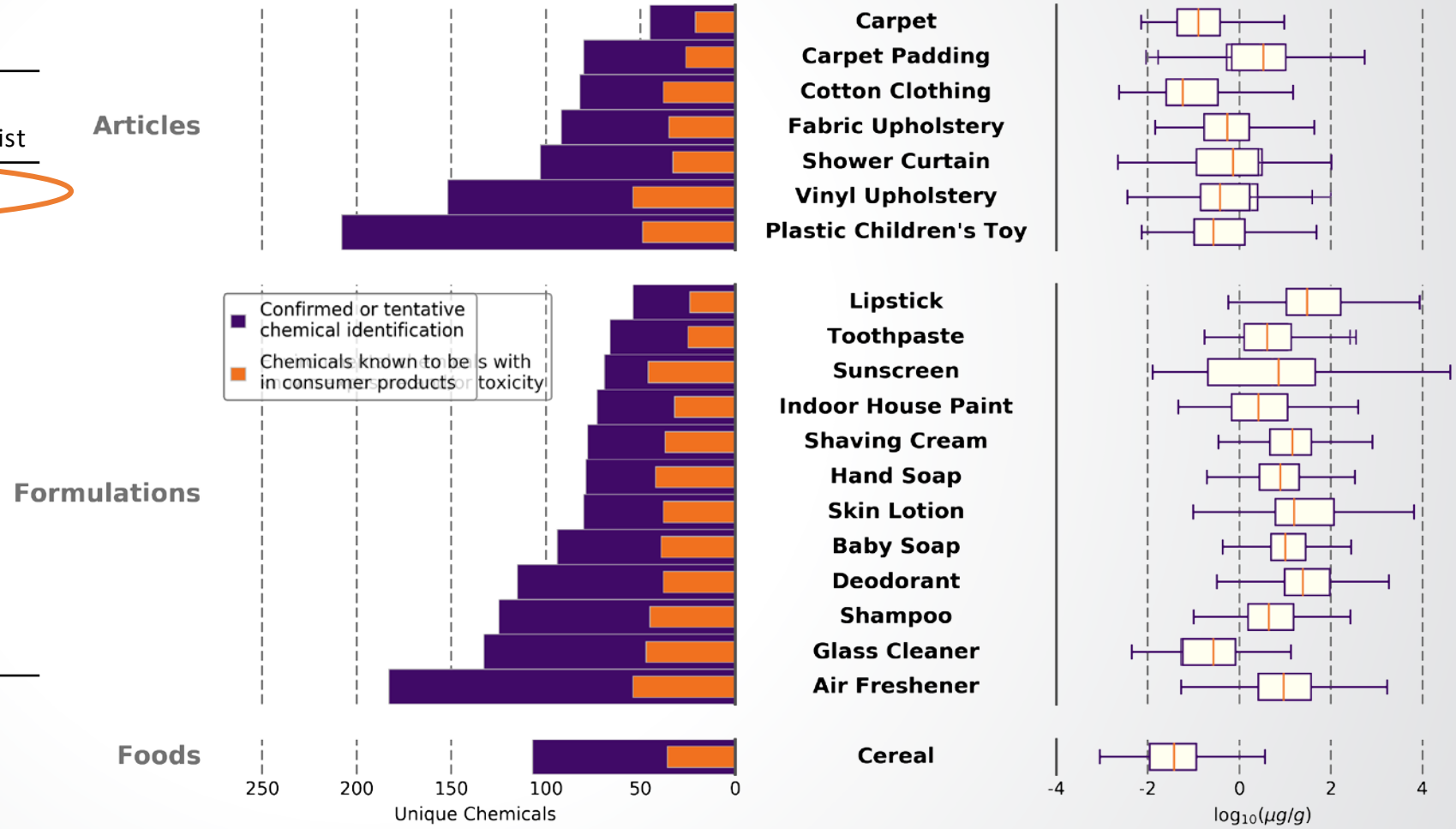
Experimental results provided by Alice Yau and Kristin Favela (Southwest Research Institute)

Caveats of this Study

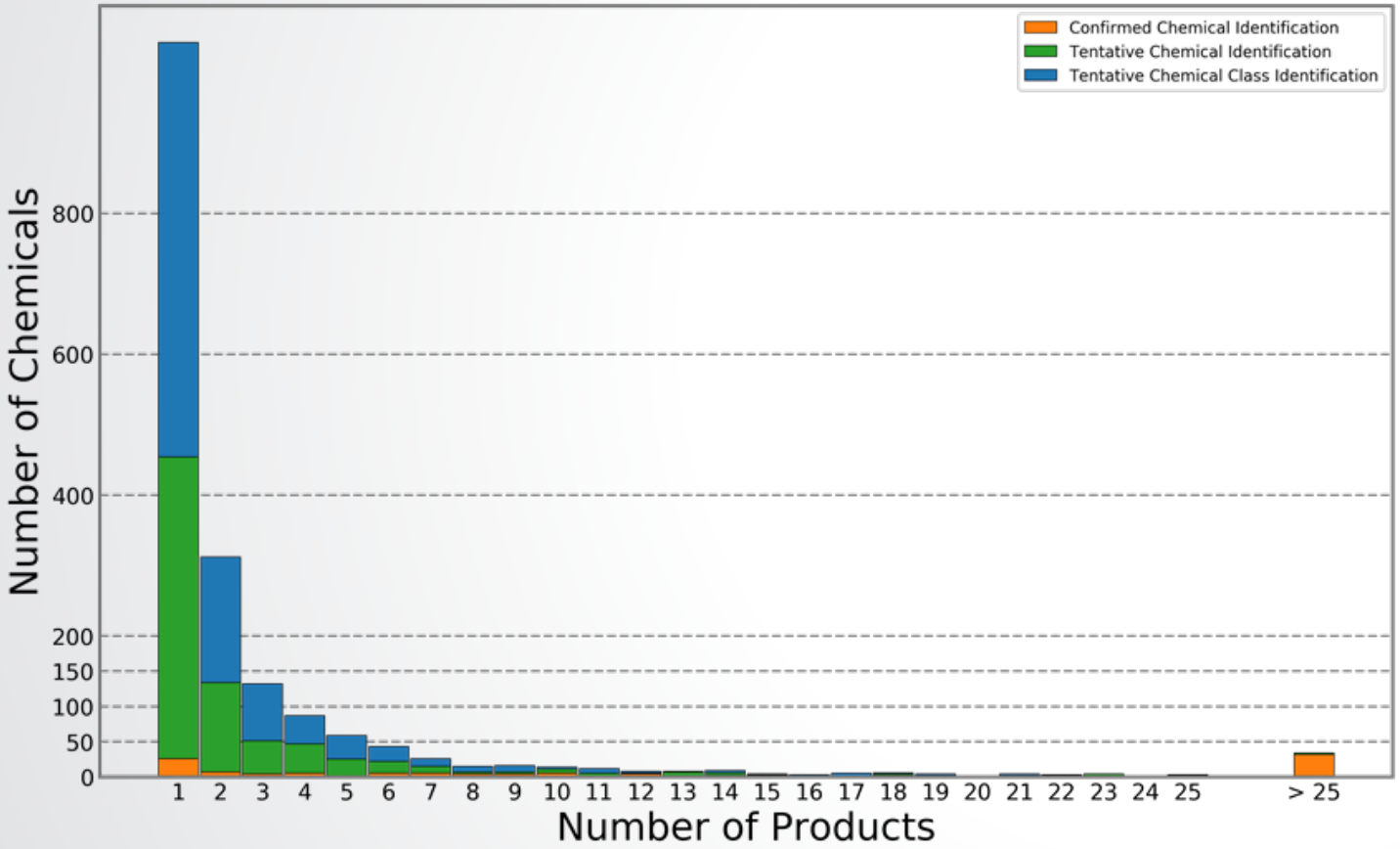
- Presence of a chemical does not imply exposure
- Presence of a chemical does not imply bioavailability
- Homogenized samples are created from products for SSA
- Chemicals in samples are extracted with organic solvents
- Different exposure pathways exist for different products
- Toxicity of chemical exposure is not evaluated here (i.e., exposure alone is not risk)

Chemicals Tentatively Identified

Chemical List	Number of Chemicals in List	Number of Ident. Spect. Matches in List
CPCPdb	1797	199
EDSP	177	19
ToxCast ER Agonist	64	10
Flame Retardant	67	9
NHANES	452	36
Pharmaceuticals	670	1
Tox21	8948	522
ToxCast	4745	443
ToxRef	1172	105



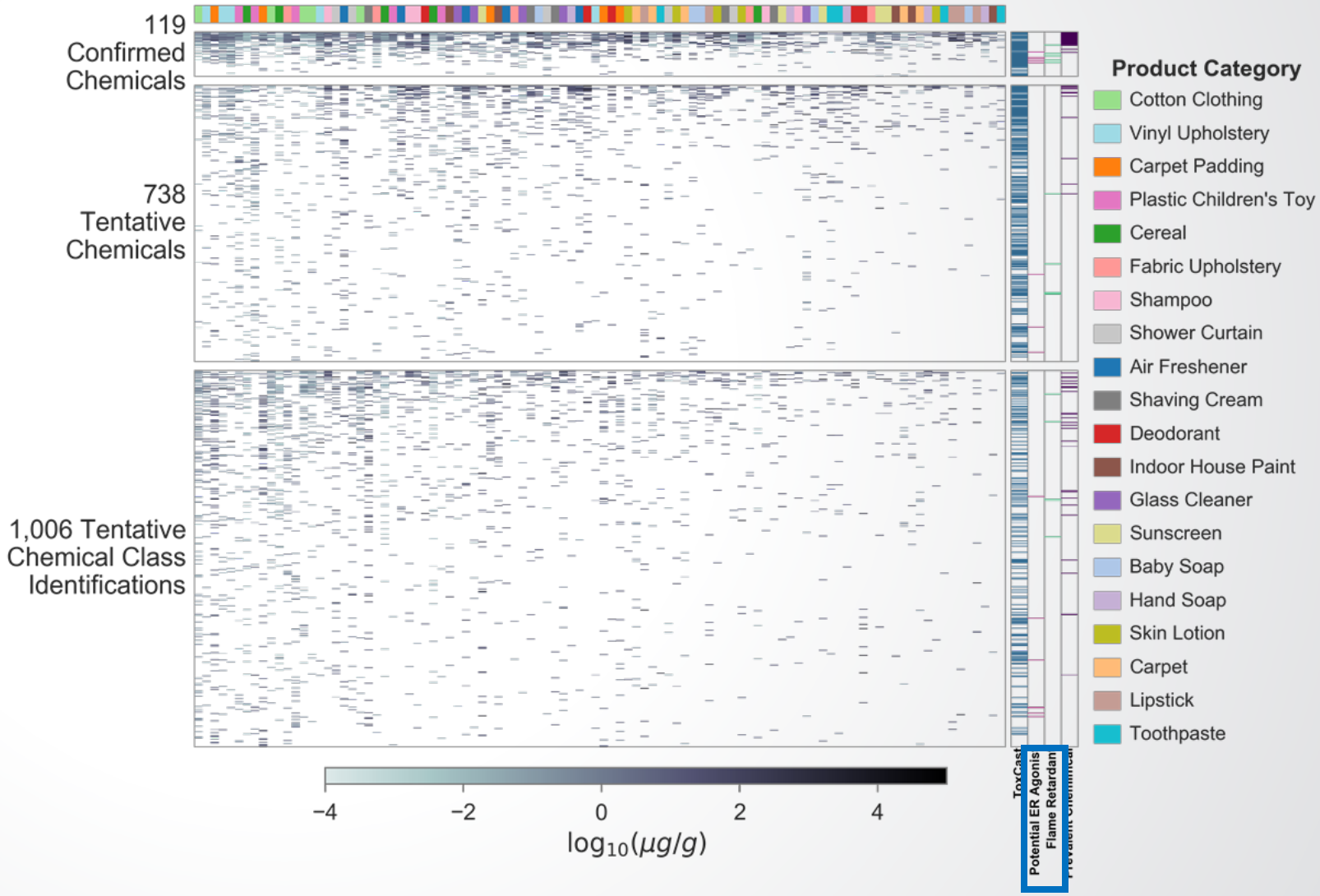
Prevalence of Chemicals



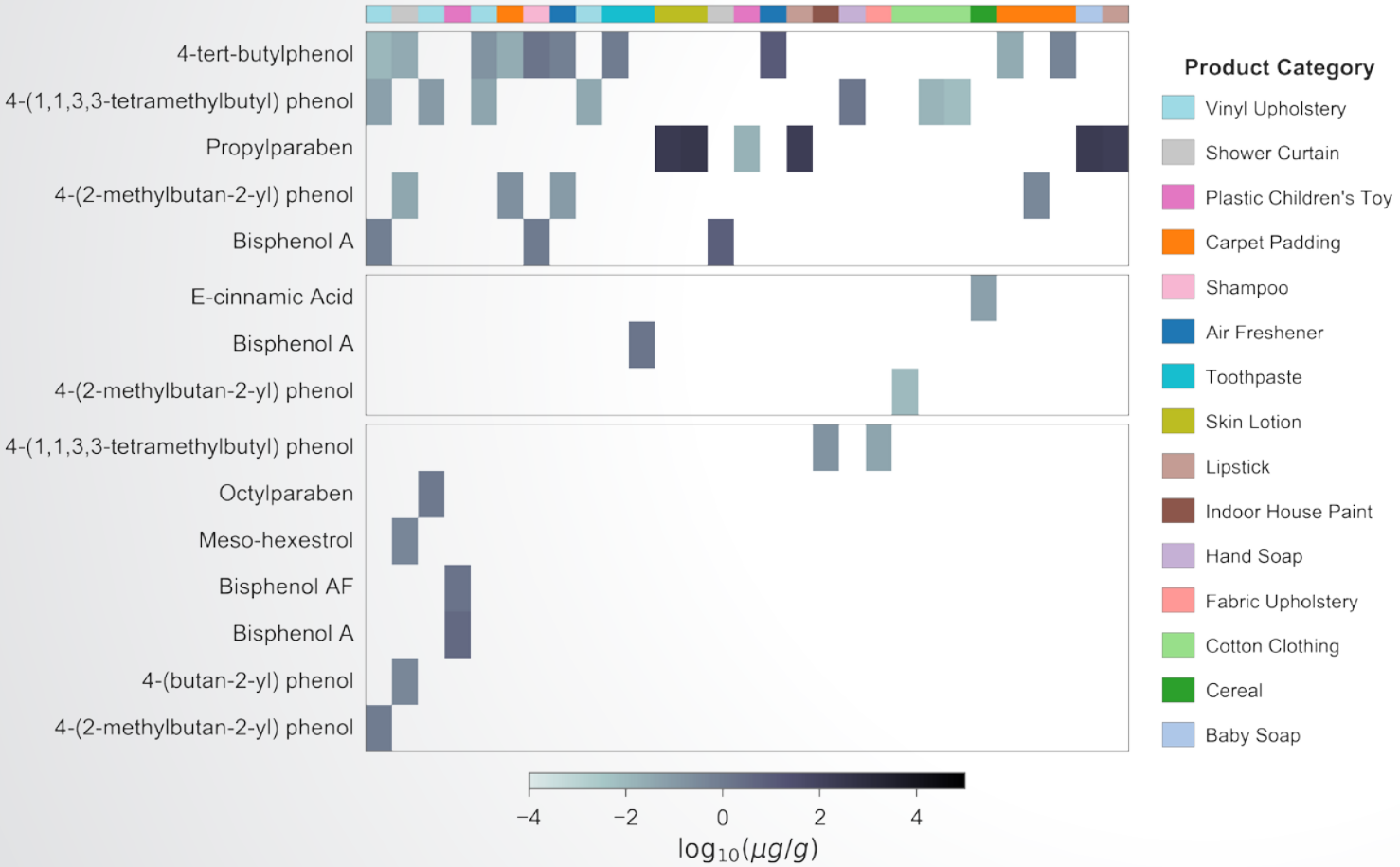
- The majority of tentative hits were found in only 1 or 2 products
- Many confirmed hits were found in larger number of products

Prevalence of Chemicals

- 1603 spectra from samples were mapped to spectra in NIST 08
- 119 were confirmed with 200+ internal standards
- 119 + 738 + 1006 ≠ 1603 some chemicals are in more than one identification category

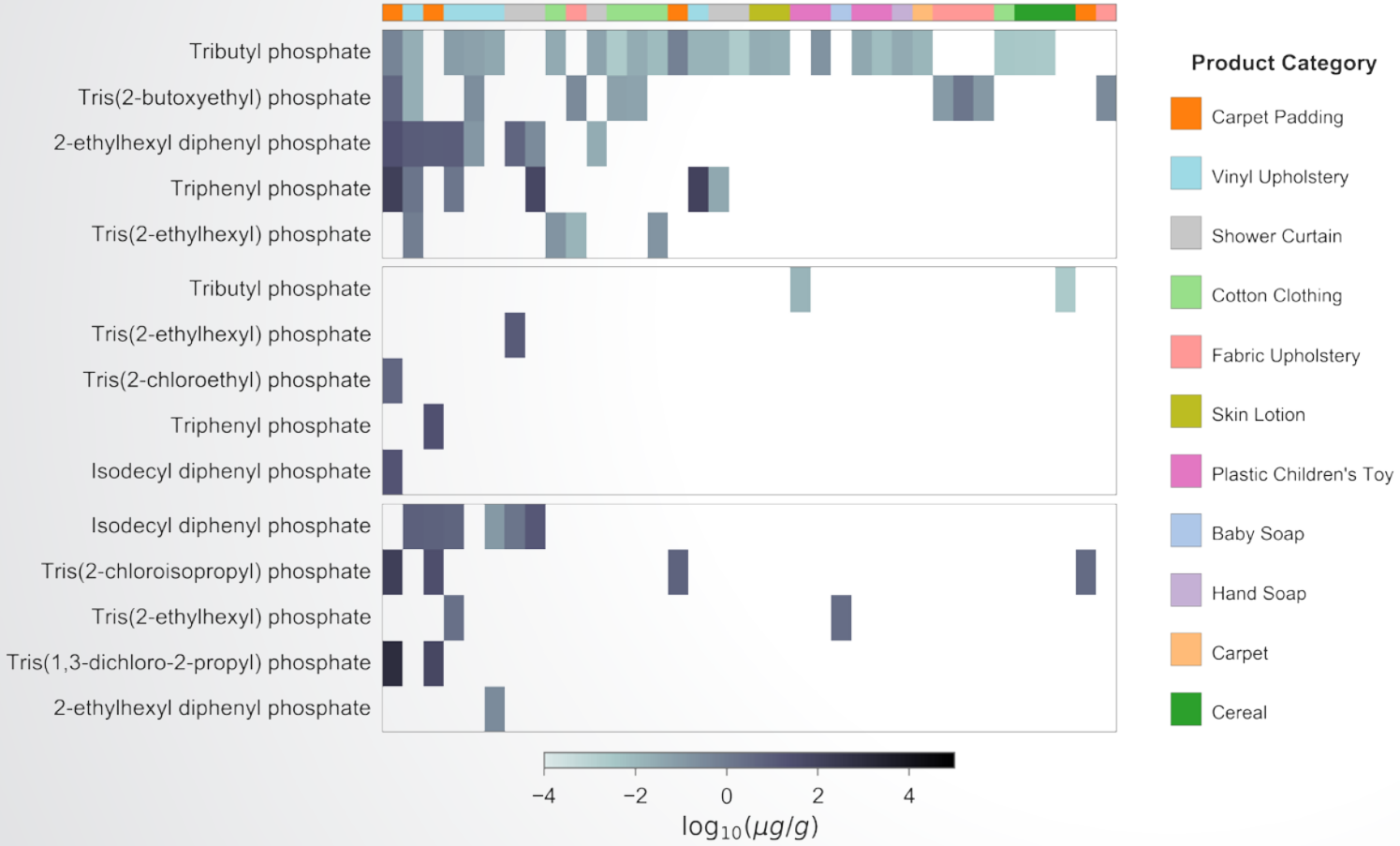


ER Agonists



- Propylparaben is commonly used in personal care products typically used as a preservative
- Bisphenol A was confirmed in vinyl upholstery, shampoo, and a shower curtain with tentative identifications in one toothpaste and one plastic children's toy
- 4-tert-butylphenol is typically used in adhesive/sealant and coating applications

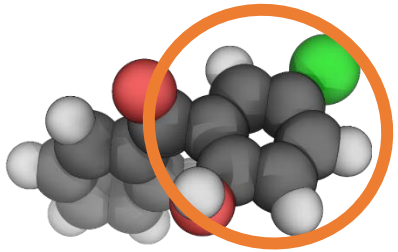
Flame Retardants



- ToxCast chemical annotations and public information were used to generate a list of chemicals used as flame retardants
- Chemicals with flame retardant applications were indicated most in carpet padding, vinyl materials, and cotton clothing
- Tributyl phosphate has multiple uses and was likely in cereals serving some other functional role or is an unintentionally added chemical

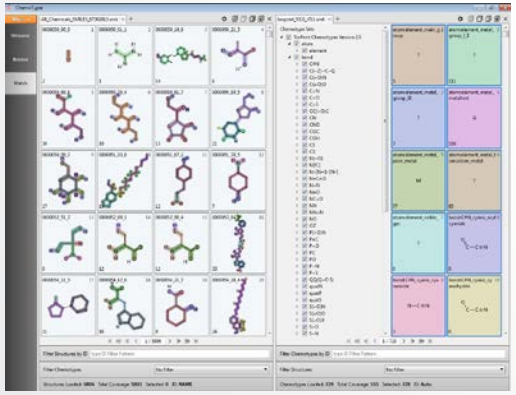
Functional Use

Identify functional use of chemicals in commerce



FUse DB has ~14000 chemicals with reported uses

Obtain structural features of chemicals

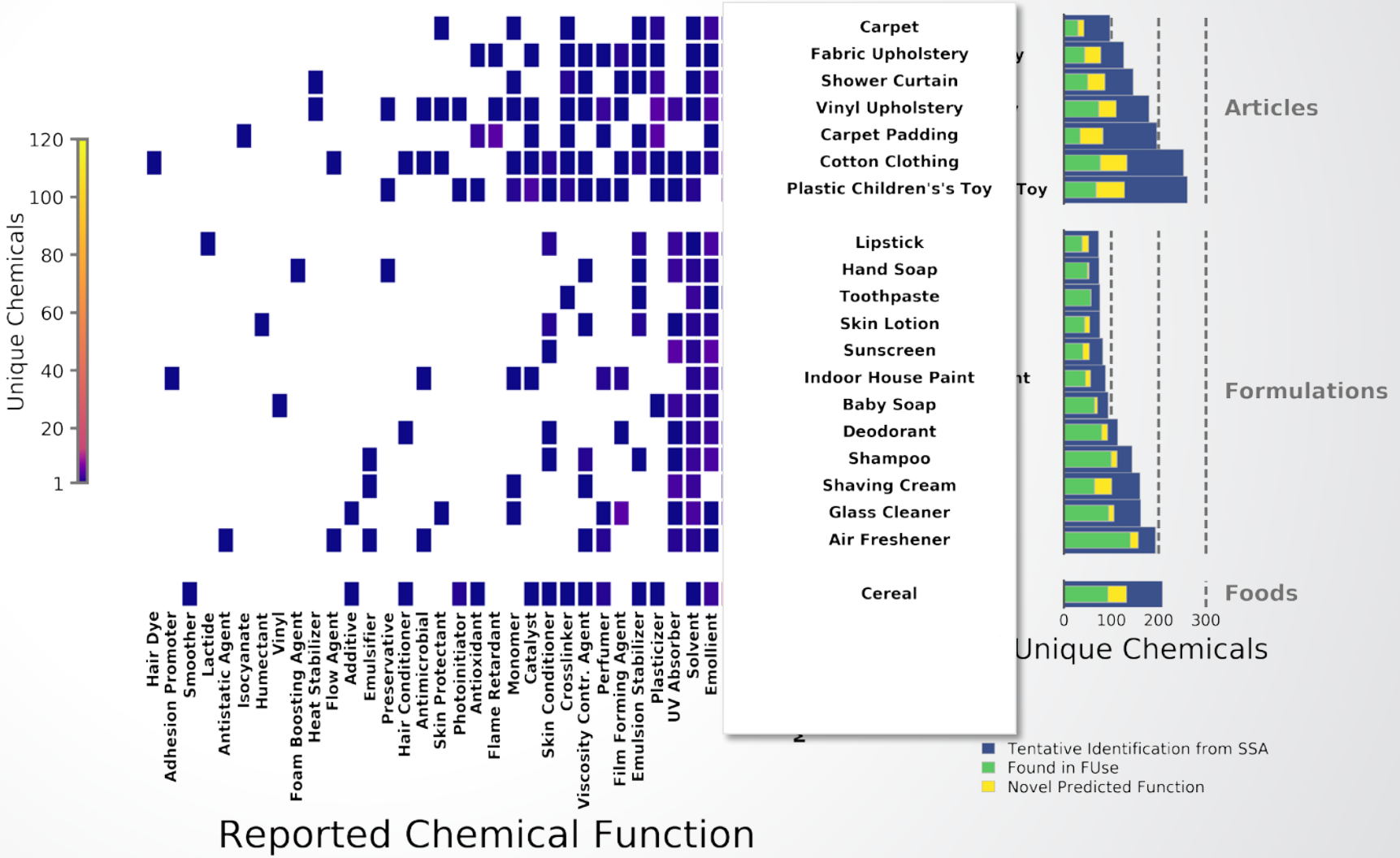


Build models that predict functional use from chemical structure

Phillips et al., Green Chemistry, 2017

ID Bolstering with Functional Use

- Only looked at tentatively identified (1541) chemicals
- 550 IDs had at least one reported use in FUse
- An additions 317 IDs had validated predicted functional uses from QSURs
- Can prioritize chemicals for confirmation by first looking at those with reported uses, and then those with predicted uses



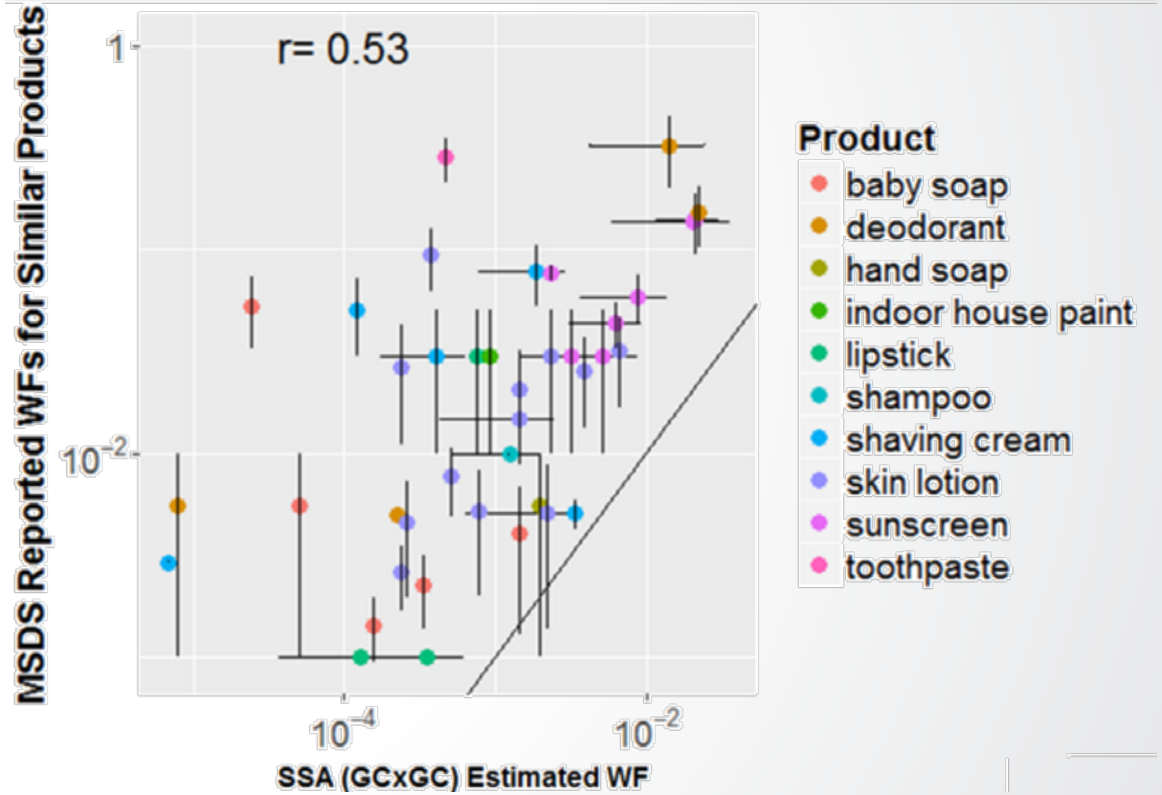
Comparison with Ingredient Lists

- Only 931 ingredients were reported in total for all 100 products (either on packaging or manufacturer's website)
- Only 65 products (formulations and food) should have reported ingredients
- Only 821 could be mapped back to chemical identifiers
- 95 of 821 ingredients were actually identified in the SSA

	Number of Chemicals Identified	
Product Category	Ingredient List	Tentative SSA Hits
air freshener	4	183
baby soap	9	94
deodorant	6	115
glass cleaner	4	133
hand soap	10	79
lipstick	14	54
shampoo	10	125
shaving cream	9	78
skin lotion	10	80
sunscreen	7	69
toothpaste	6	66

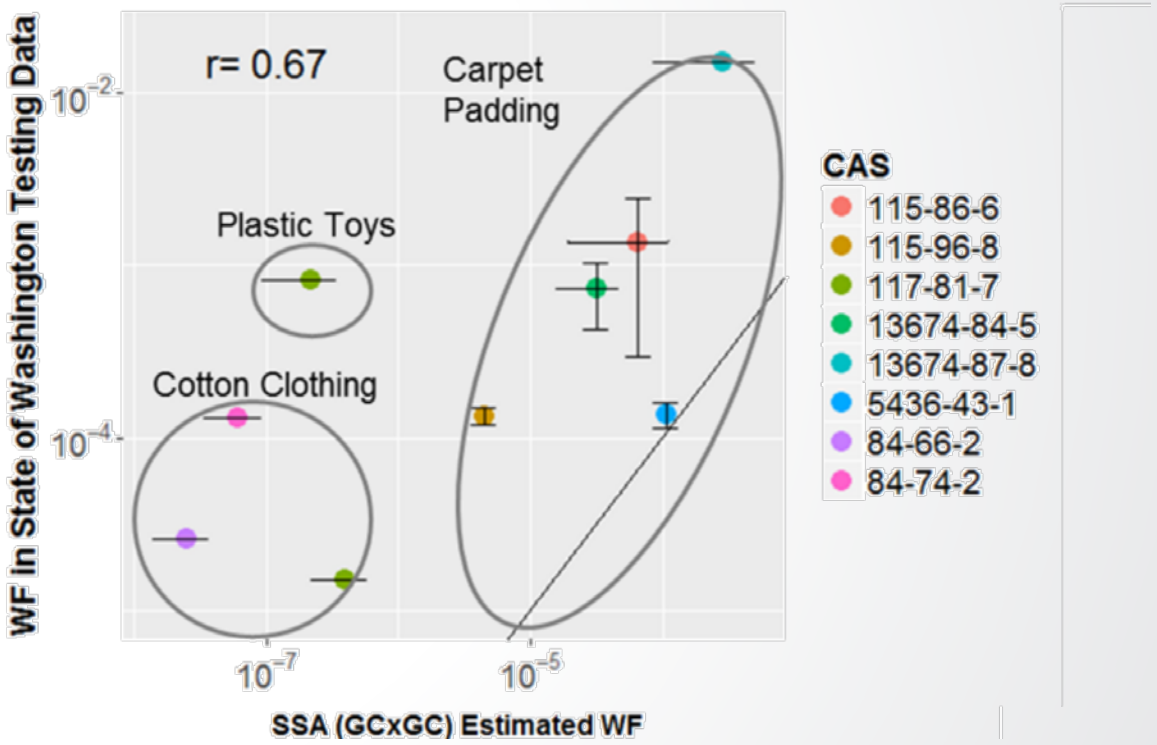
Comparison with CPDat

- 37 CASRN-product pairs were found from MSDS data in CPDat among the 1603 identified spectral matches
- Mean values of MSDS reported weight fractions were compared to estimated concentration from SSA
- SSA values tend to be an underestimate of reported values



Comparison with Product Testing Data

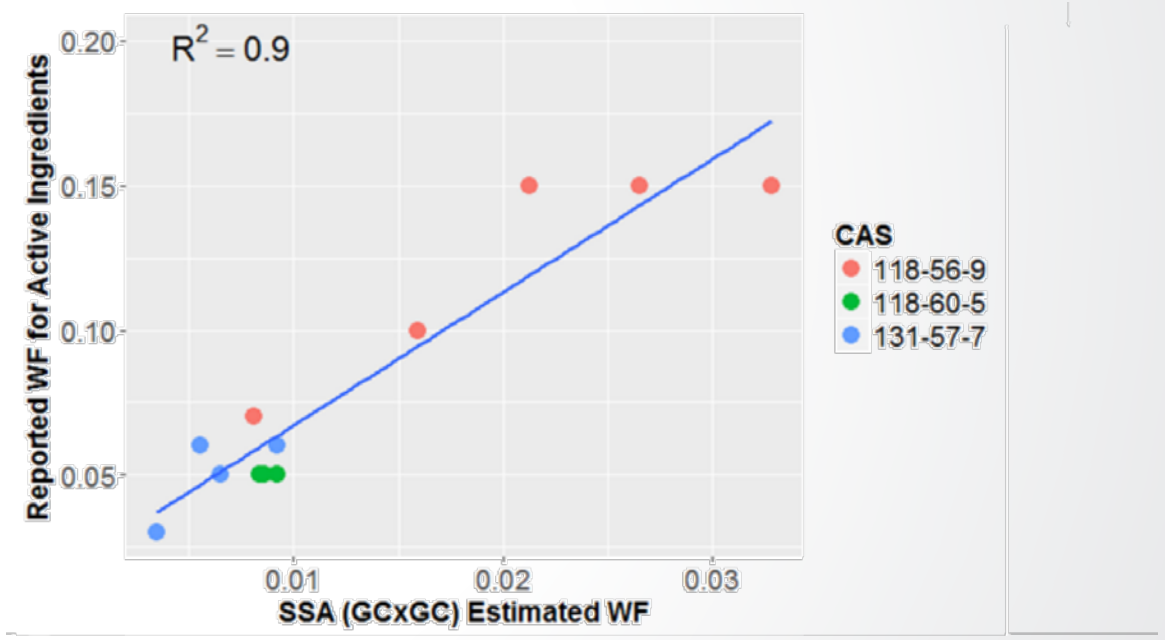
- MSDS is only provided for formulations
- Information on article concentration were found through State of Washington's reporting data
- Reporting data results from targeted analysis of products
- SSA values were still underestimated



Reported data obtained from State of Washington Department of Ecology's Product Testing Data (https://fortress.wa.gov/ecy/ptdbpublicreporting/)

Comparison with Active Ingredients

- Actual weight fractions are required to be reported for active ingredients in a personal care products
- Only sunscreens had active ingredients in the SSA
- Much better comparison here than with the ranges of MSDS concentration or reported concentrations of articles



Summary

- Limited information for the tens of thousands of chemicals in commerce
- 100 different products across 20 product categories were analyzed via SSA
- 1603 of the 4270 spectral matches were tentatively identified (119 confirmed)
- 652 chemicals were tentatively identified in formulations that were not previously known to be in formulations
- 867chemicals could be prioritized for confirmation using functional use
- Estimated concentrations from SSA was typically lower than either manufacturer or state reported values of ingredients

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

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

Lead CSS Matrix Interface:
John Kenneke (NERL)
John Cowden (NCCT)

*Trainees
Project Leads

Collaborators

Arnot Research and Consulting
Jon Arnot
Battelle Memorial Institute
Anne Louise Sumner
Anne Gregg
Chemical Computing Group
Rocky Goldsmith
National Institute for Environmental Health Sciences (NIEHS) National Toxicology Program
Mike Devito
Steve Ferguson
Nisha Sipes
Netherlands Organisation for Applied Scientific 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