

Advances in Exposure Science

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*Opportunities and Challenges in Using Advanced
21st Century Toxicity Testing and
Risk Assessment Methods in a Modernized TSCA*

February 8, 2016

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

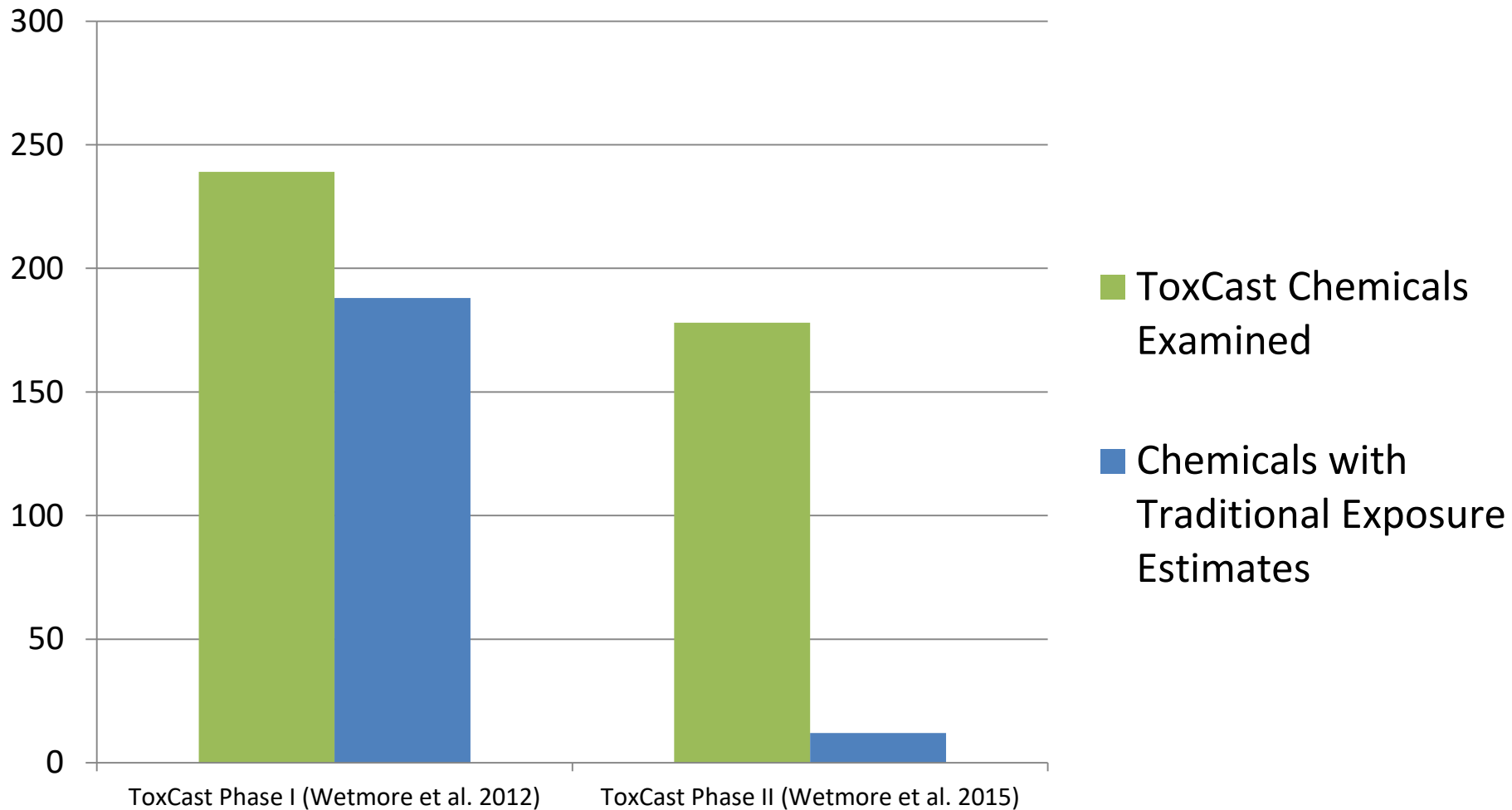
Introduction

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



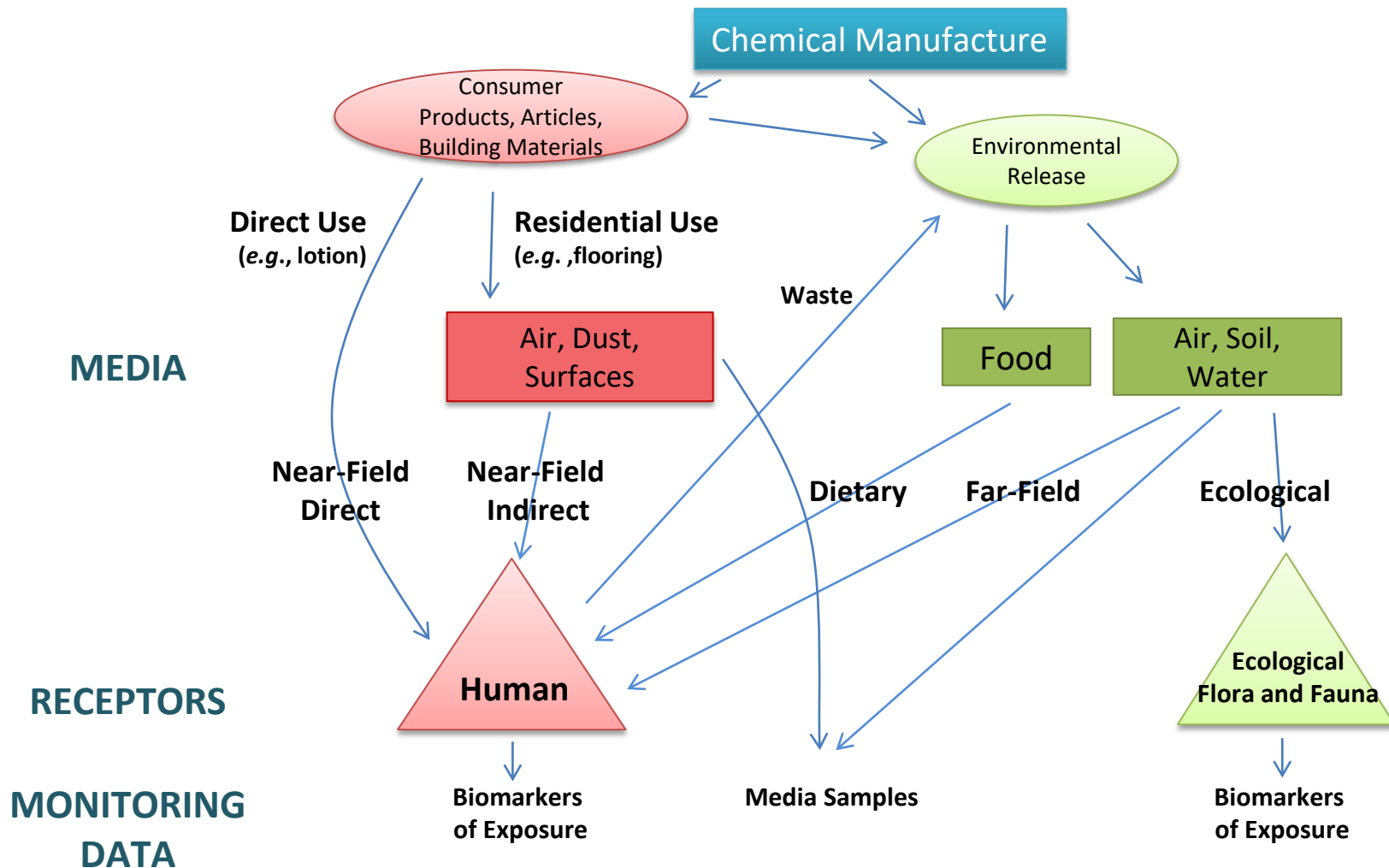
November 29, 2014

Available Data for Exposure Estimations

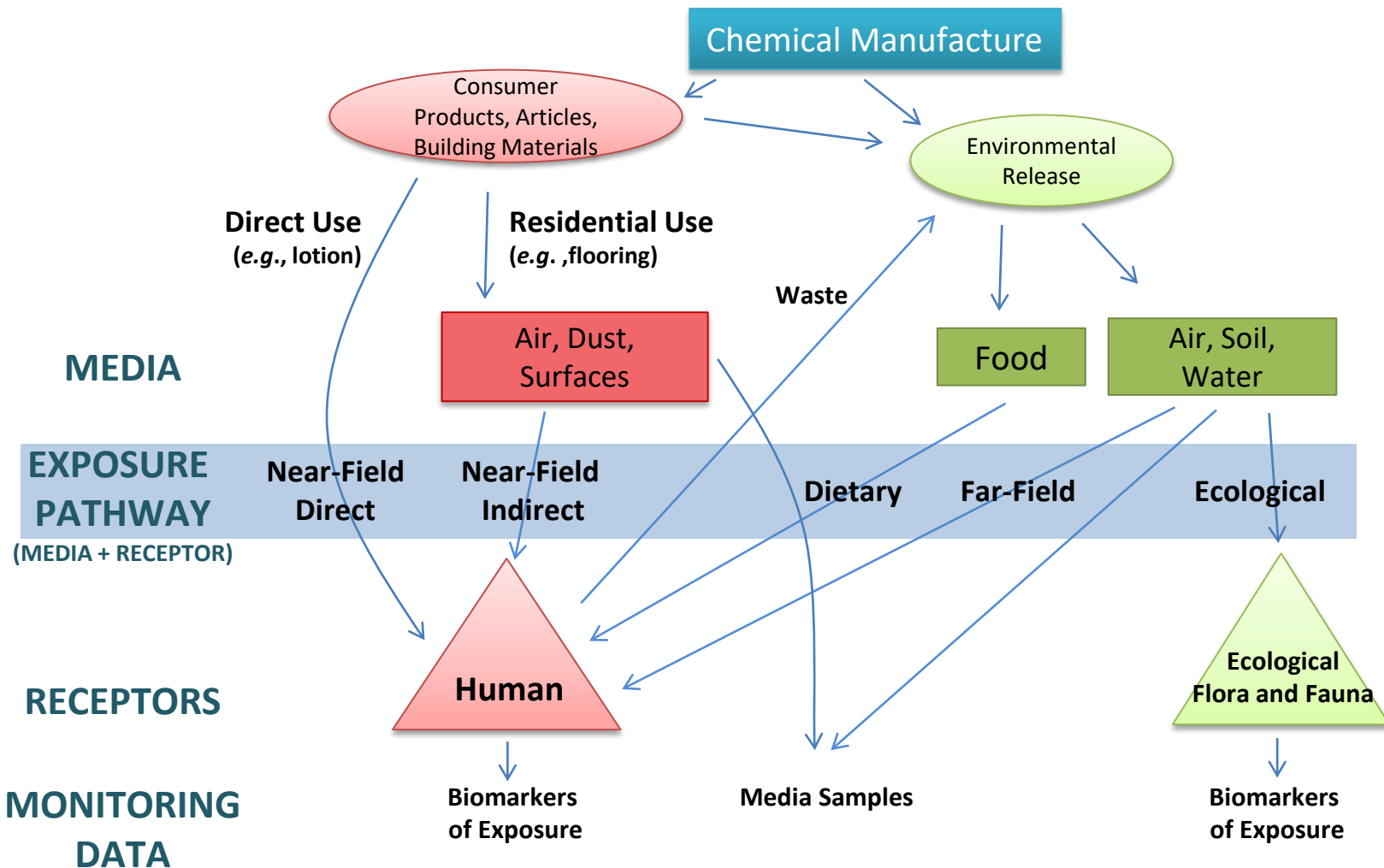


- Egeghy et al. (2012) – Most chemicals lack exposure data

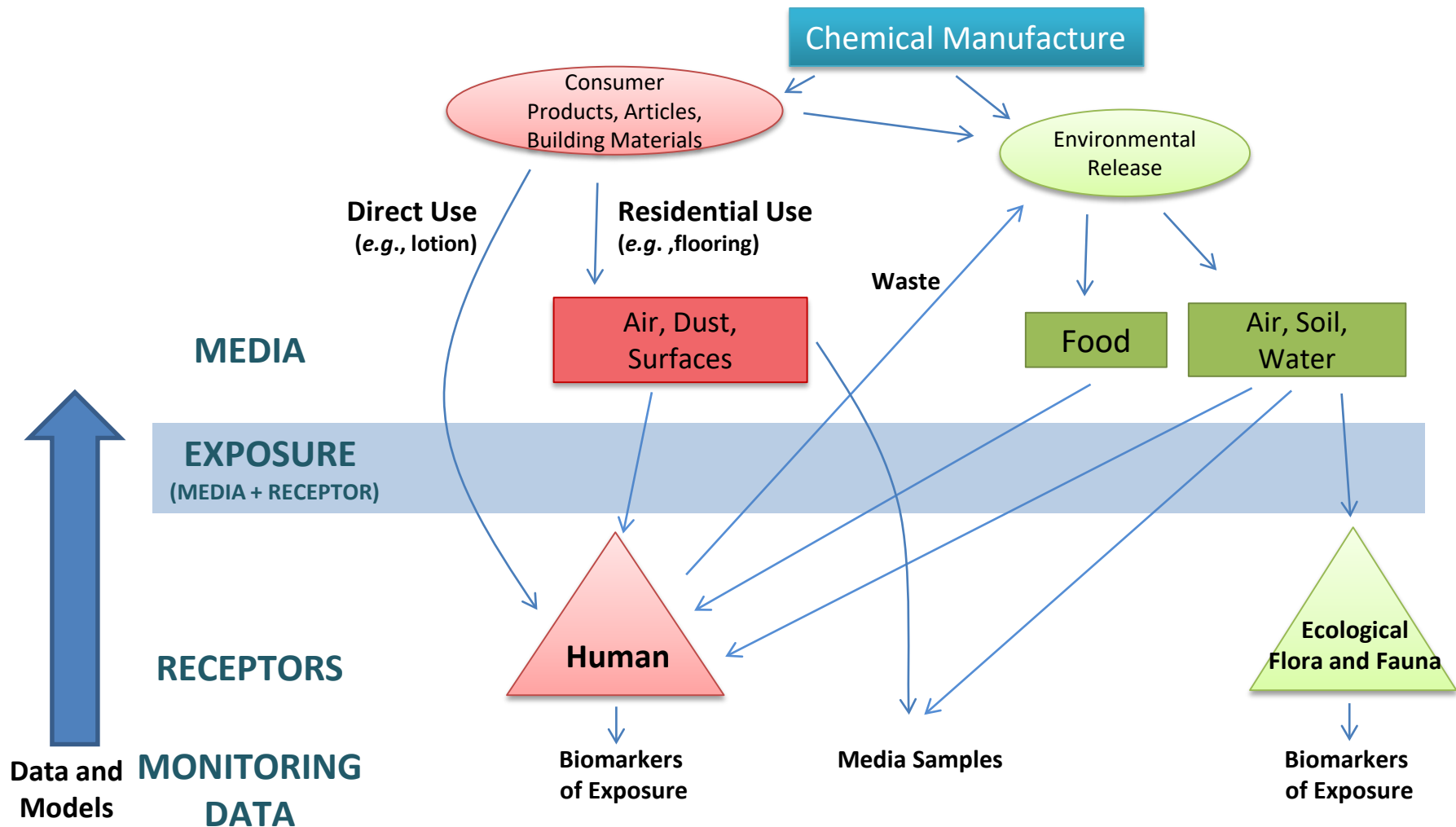
Thinking About Exposure



Exposure Pathways

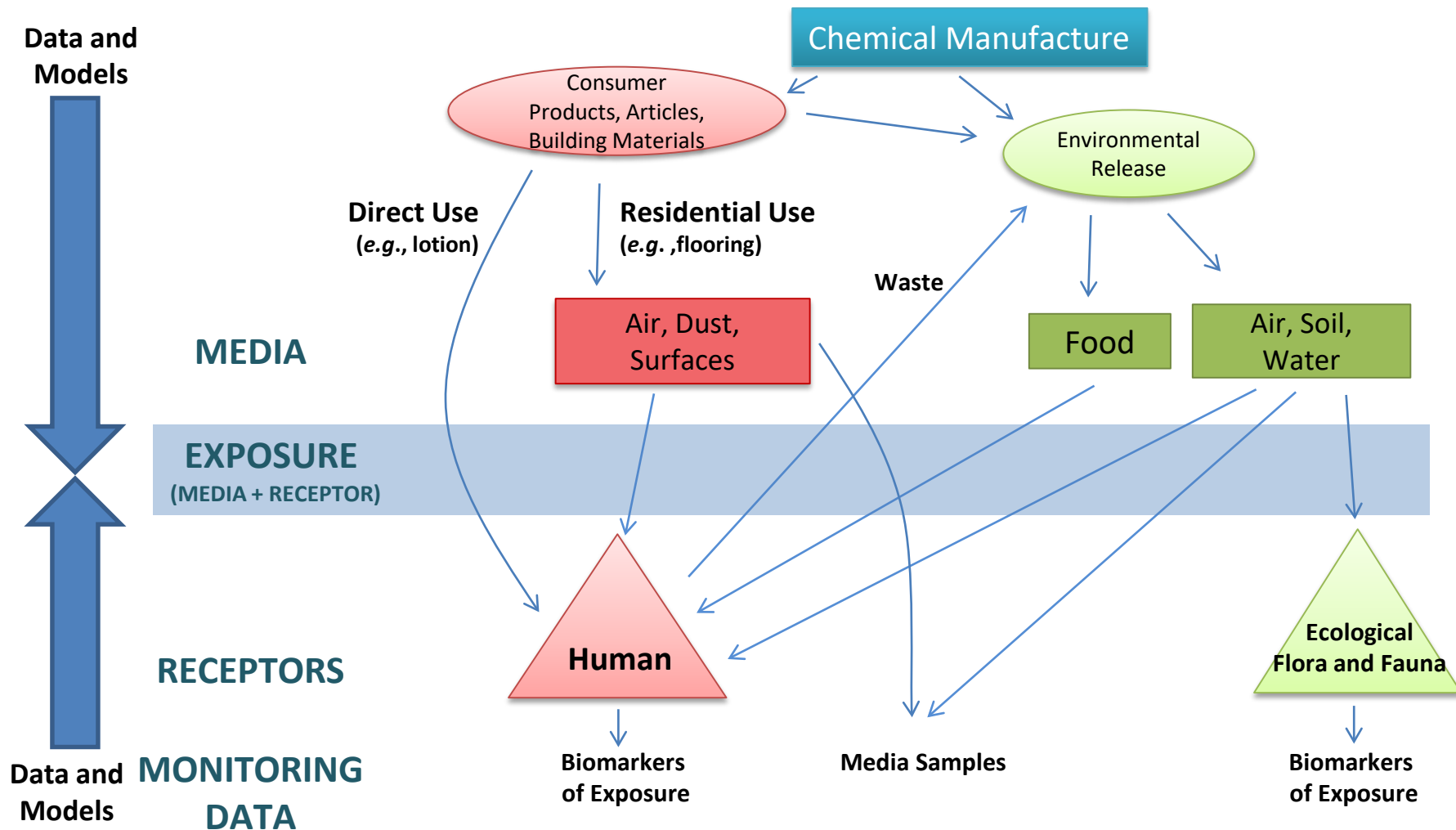


Exposure Monitoring



- Centers for Disease Control monitors a few hundred specific chemicals in urine and blood of U.S. citizens

Evaluating Exposure Models



Predicting Exposure

Weight of Exposure Predictor

Wambaugh et al. (2014)

Industrial and Consumer Product Use
Pesticide Inert
Production Volume
Pesticide Active
Industrial Use but NOT in Consumer Products

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:

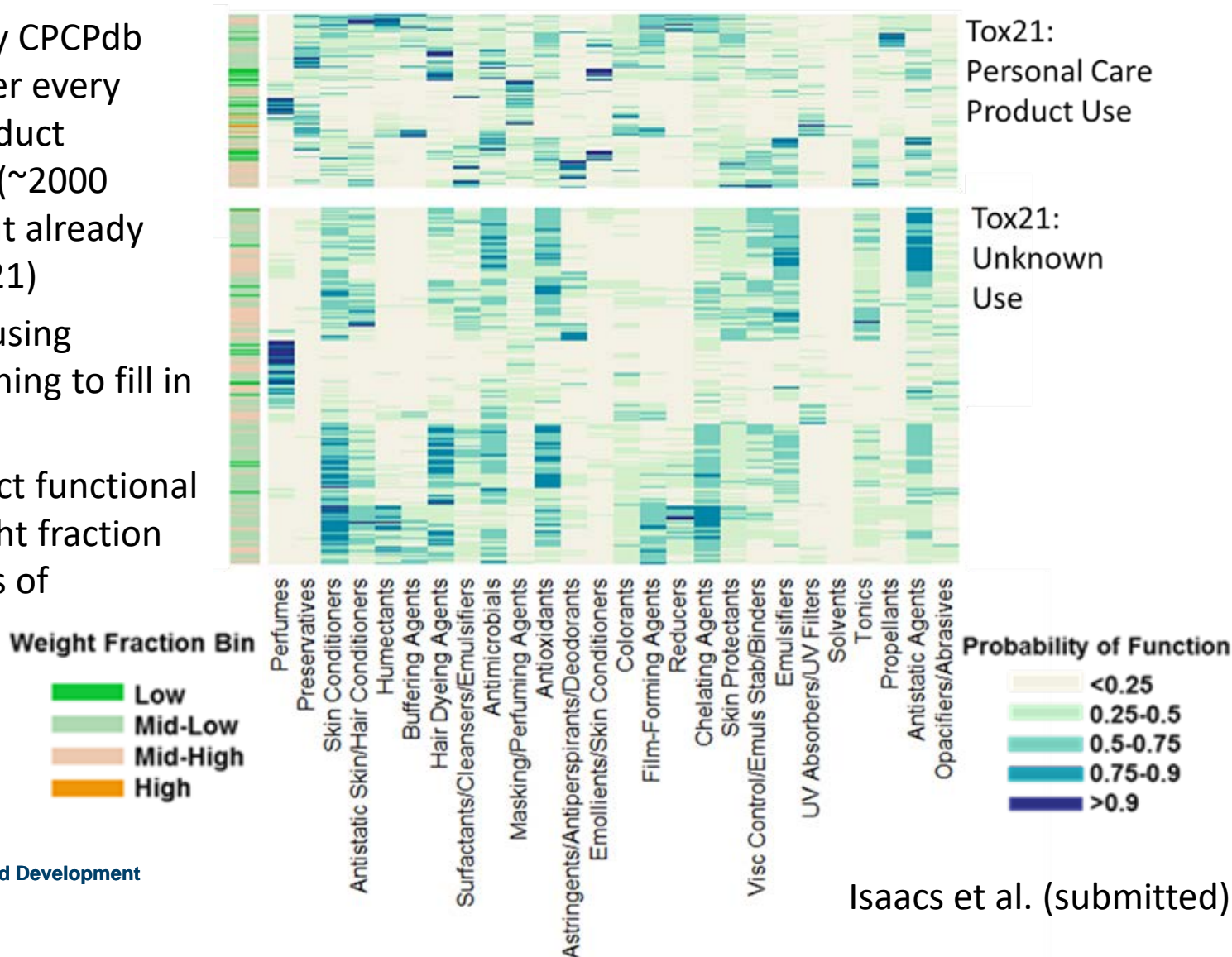
- Industrial and Consumer use
- Pesticide Inert
- Pesticide Active
- Industrial but no Consumer use
- Production Volume

105 NHANES Chemicals



Predicting Chemical Constituents

- Unfortunately CPCPdb does not cover every chemical-product combination (~2000 chemicals, but already >8000 in Tox21)
- We are now using machine learning to fill in the rest
- We can predict functional use and weight fraction for thousands of chemicals



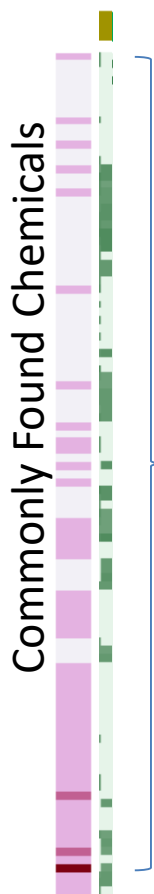
Isaacs et al. (submitted)

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

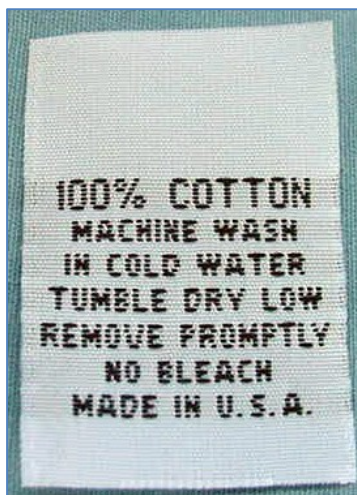
ExpoCast Consumer Product Scan



Scanned 5 examples each of 20 class of consumer products

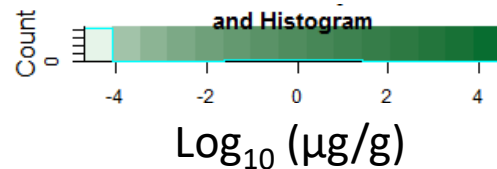
Found >3500 chemicals in total across the 100 products

The chemicals found in a cotton shirt



GC-MS with DCM Extraction

Common Chemical (n>19)
ToxCast
Flame Retardant
Potent ER



- Air freshener
- Baby soap
- Carpet
- Carpet padding
- Cereals
- Cotton clothing
- Deodorant
- Fabric upholstery
- Glass cleaners
- Hand soap
- Indoor house paint
- Lipstick
- Plastic children's toys
- Shampoo
- Shaving cream
- Shower curtain
- Skin lotion
- Sunscreen
- Toothpaste
- Vinyl upholstery

Results from Alice Yau (SWRI)

ExpoCast Consumer Product Scan

Commonly Found Chemicals

Scanned 5 examples each of 20 class of consumer products

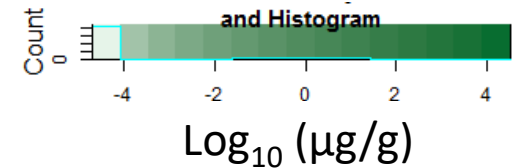
Found >3500 chemicals in total across the 100 products

Dark green is a high concentration

Light green is not detected

GC-MS with DCM Extraction

Common Chemical (n>19)
ToxCast
Flame Retardant
Potent ER



Air freshener
Baby soap
Carpet
Carpet padding
Cereals
Cotton clothing
Deodorant
Fabric upholstery
Glass cleaners
Hand soap
Indoor house paint
Lipstick
Plastic children's toys
Shampoo
Shaving cream
Shower curtain
Skin lotion
Sunscreen
Toothpaste
Vinyl upholstery

Results from Alice Yau (SWRI)

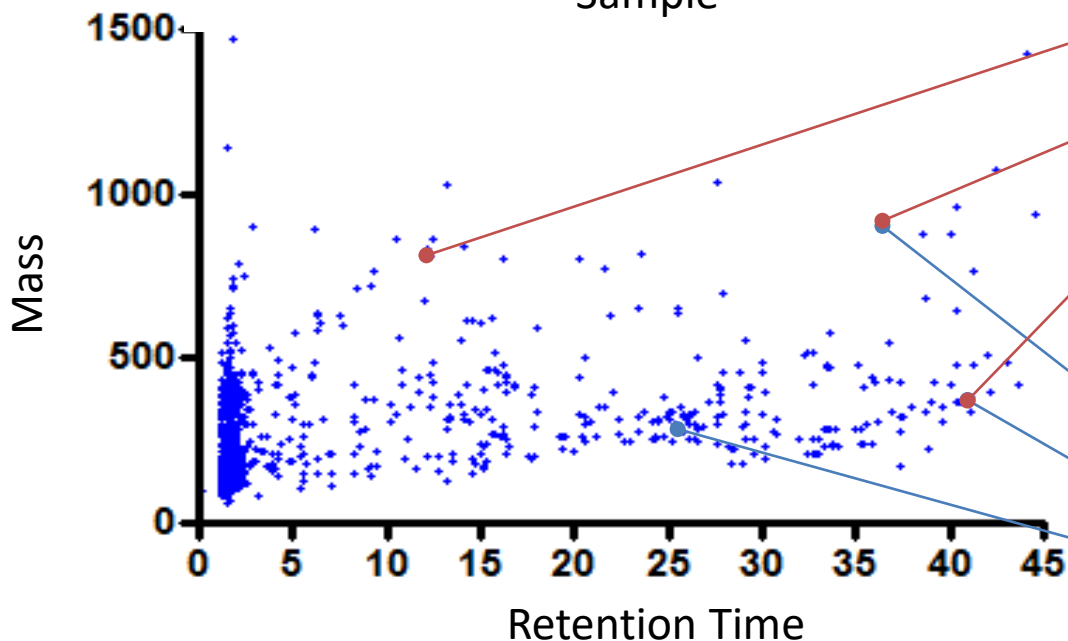
ExpoCast Consumer Product Scan



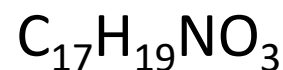
Results from Alice Yau (SWRI)

Suspect Screening and Non-Targeted Analytical Chemistry

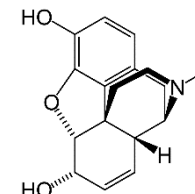
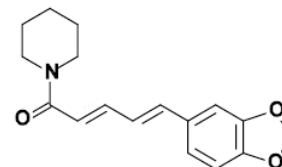
947 Peaks in an American Health Homes Dust
Sample



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



Multiple chemicals can have the
same mass and formula:



Is chemical A present,
chemical B, or both?

We are now expanding our identity libraries using reference samples of ToxCast chemicals

Applying Non-Targeted Screening

- ExpoCast consumer product scanning and blood sample monitoring
- EPA is also analyzing house dust from American homes – can identify 50% of the mass but only 2% of the chemicals Rager et al., Environment International (In Press)
- EPA is coordinating a comparison of the abilities of leading academic, government, and industry non-targeted screening groups to assess strengths and weaknesses



High Throughput Risk Prioritization in Practice

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

} 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 risk posed by thousands of chemicals in the environment – which are most worthy of further study?
 - Exposure provides real world context to hazards indicated by high-throughput bioactivity screening
- 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

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

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