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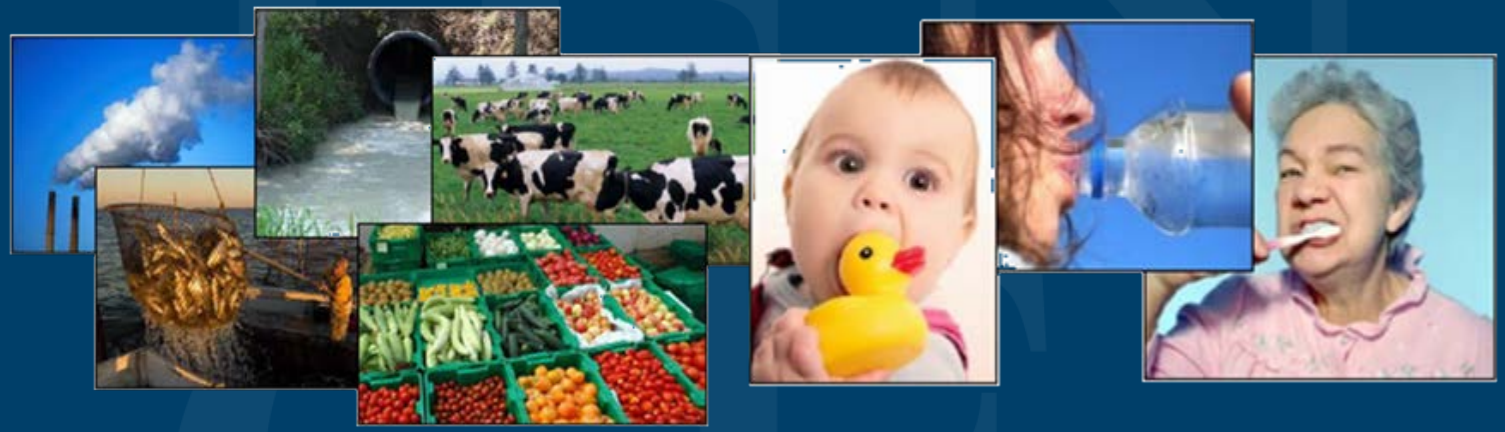
https://orcid.org/0000-0001-9547-1654

EPA United States Environmental Protection Agency

Data and Tools from the Chemical Safety and Sustainability (CSS) Rapid Exposure and Dosimetry (RED) Project

Kristin Isaacs and John Wambaugh
Office of Research and Development



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

Presentation to the Netherlands National Institute for Public Health and the Environment
April 18, 2018

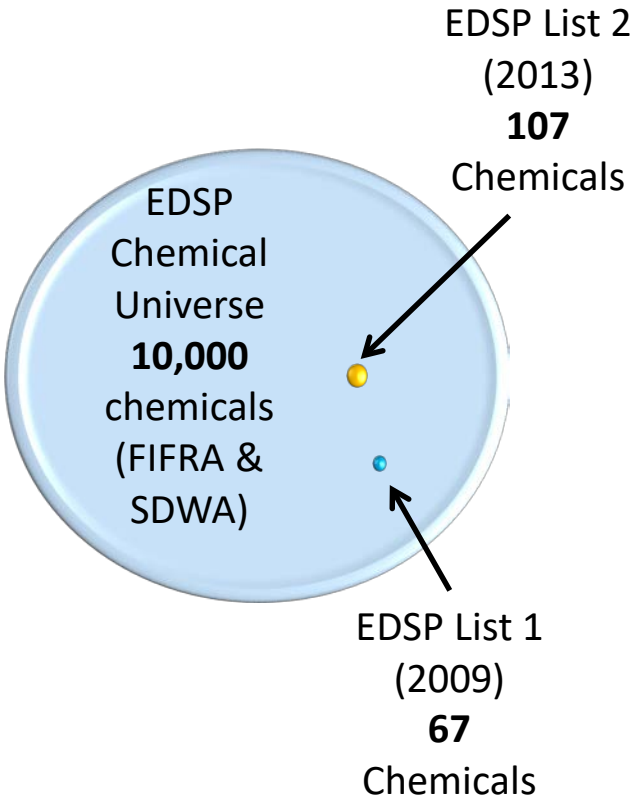
Scale of the Problem

United States Environmental Protection Agency

- Park *et al*. (2012): At least 3221 chemicals in humans, many appear to be exogenous

Endocrine Disruptor Screening Program (EDSP) Chemical List	Number of Compounds
Conventional Active Ingredients	838
Antimicrobial Active Ingredients	324
Biological Pesticide Active Ingredients	287
Non Food Use Inert Ingredients	2,211
Food Use Inert Ingredients	1,536
Fragrances used as Inert Ingredients	1,529
Safe Drinking Water Act Chemicals	3,616
TOTAL	**10,341**

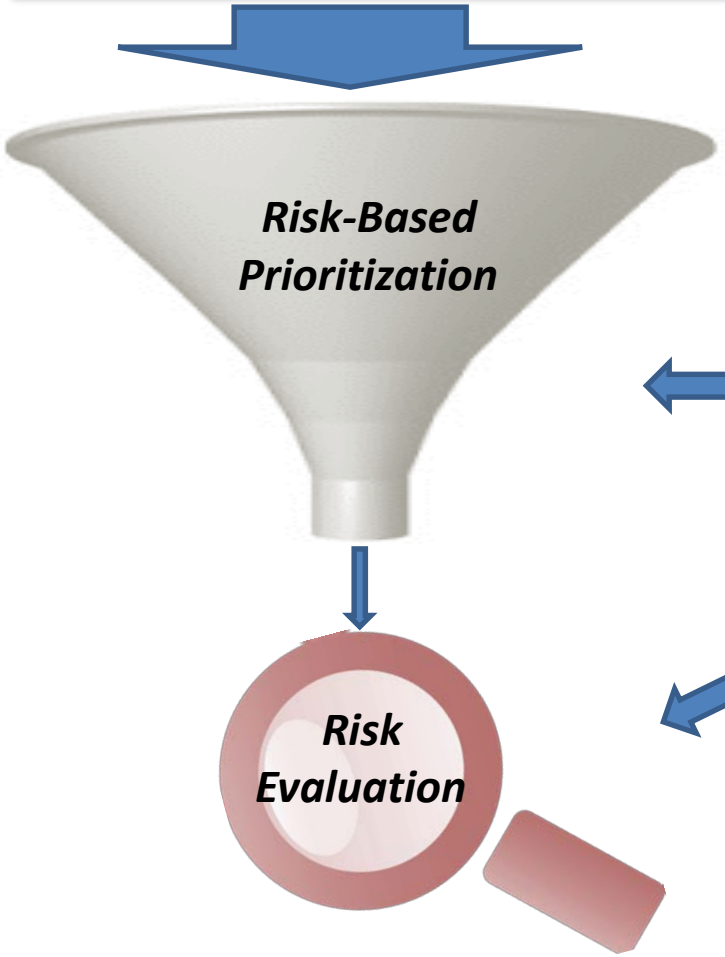
So far 67 chemicals have completed testing and an additional 107 are being tested



Scale of the Problem

United States Environmental Protection Agency

June 2017: **67,709** Chemicals on the TSCA Inventory

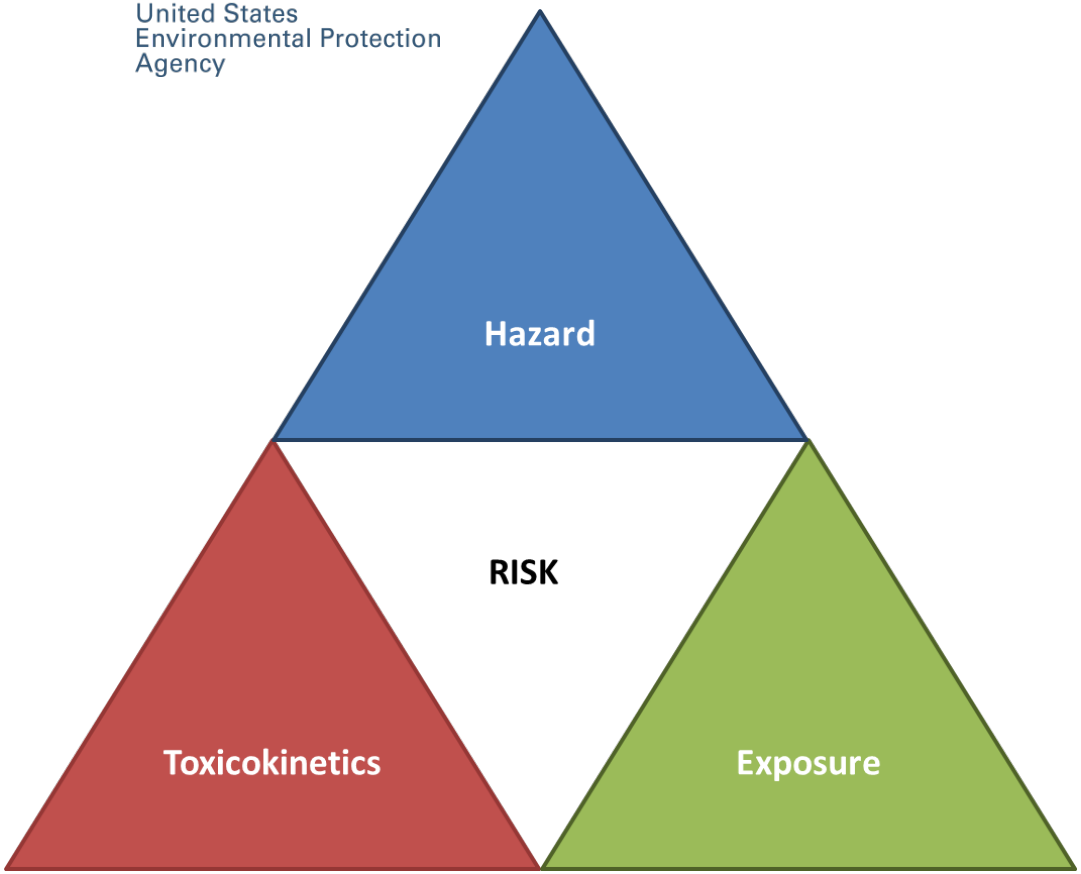


TSCA section 6(b)(1)(A):

- Exposure potential of the chemical substance

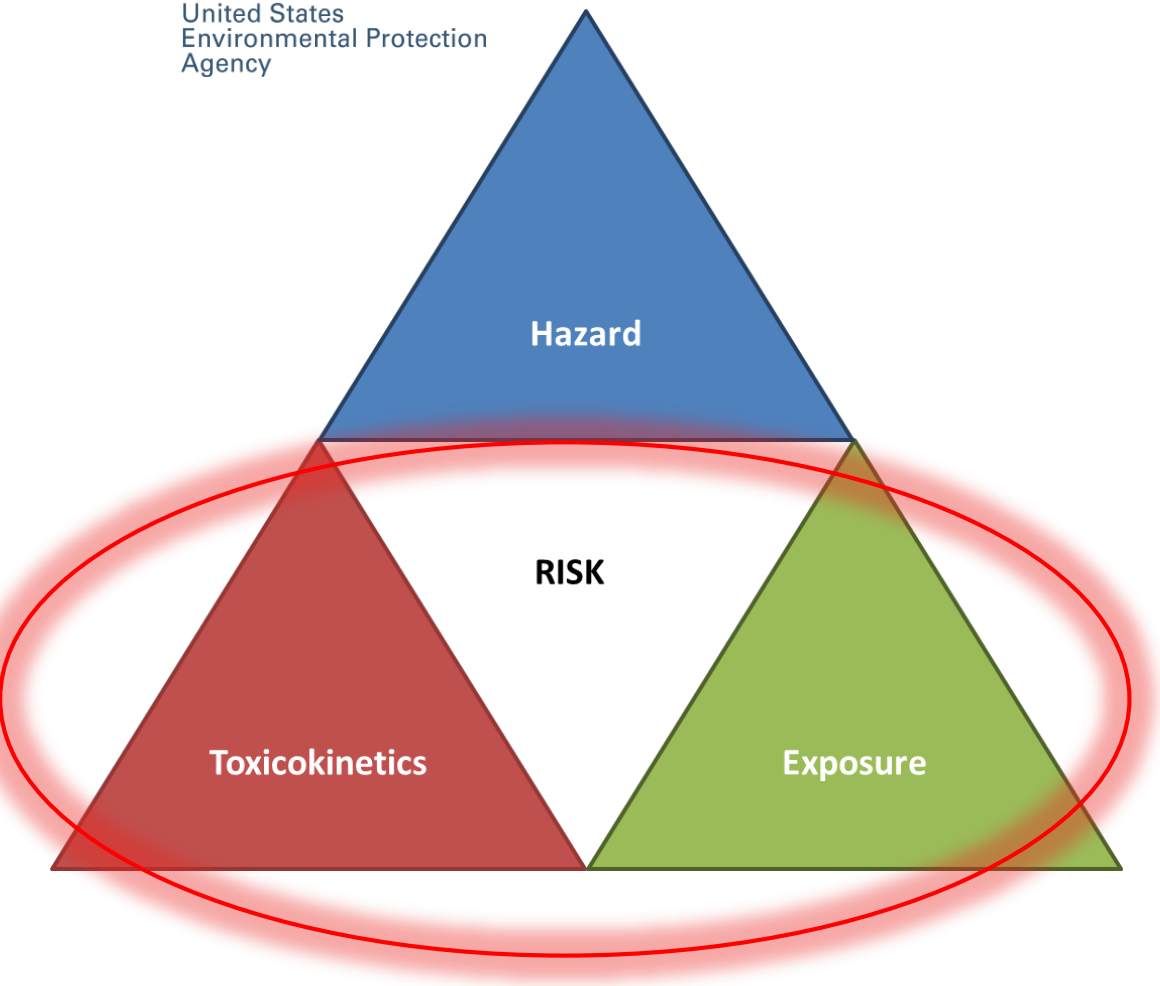
HT Exposure in the RED ("ExpoCast") Project

United States Environmental Protection Agency



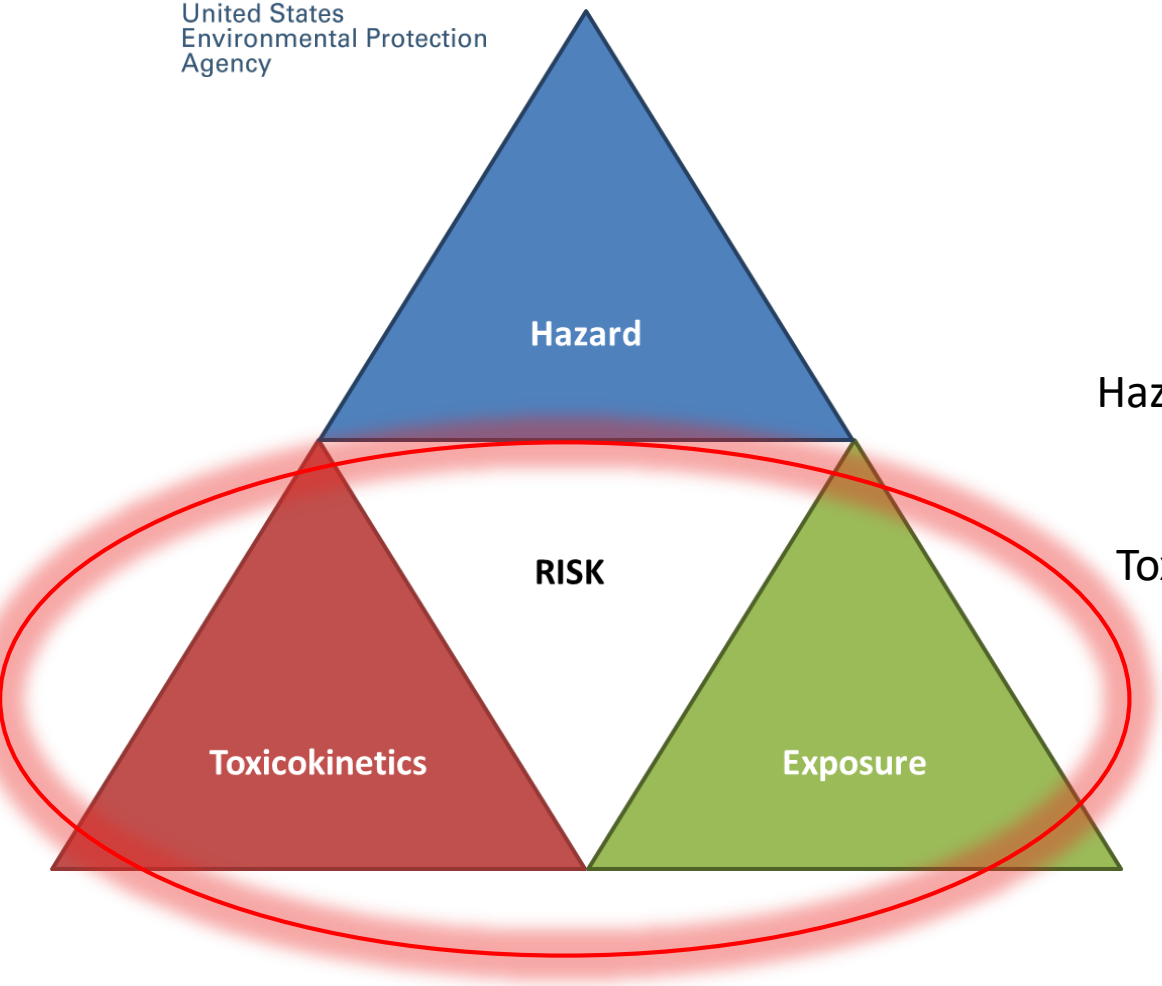
HT Exposure in the RED ("ExpoCast") Project

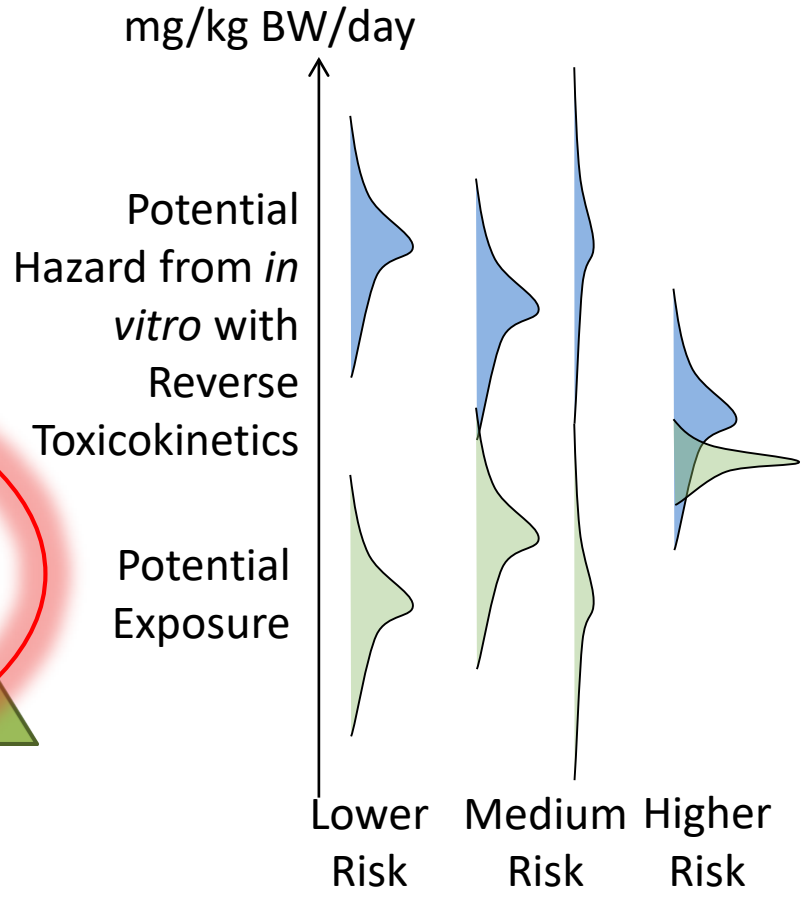
United States Environmental Protection Agency



HT Exposure in the RED ("ExpoCast") Project

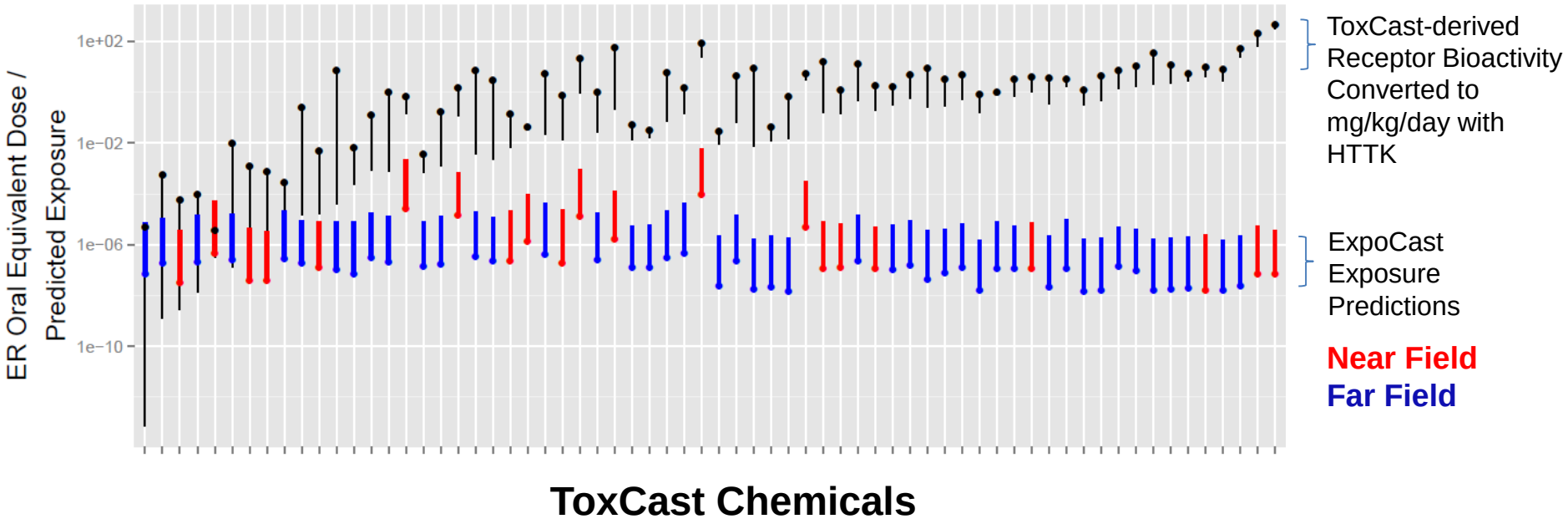
United States Environmental Protection Agency





High-Throughput Risk Prioritization in Practice

United States Environmental Protection Agency

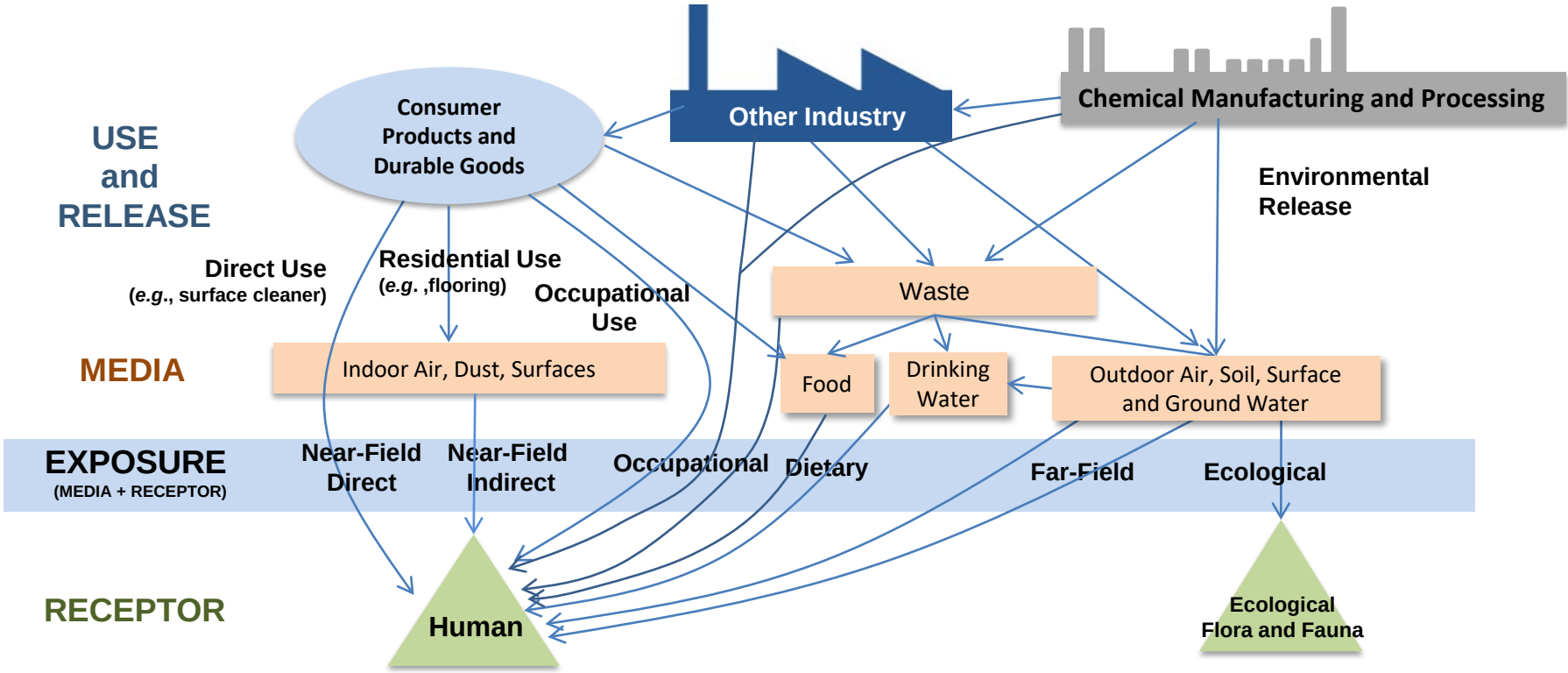


ExpoCast methods were reviewed by a December, 2014 FIFRA SAP "Scientific Issues Associated with Integrated Endocrine Bioactivity and Exposure-Based Prioritization and Screening"

- Prioritization as in Wetmore et al. (2015)

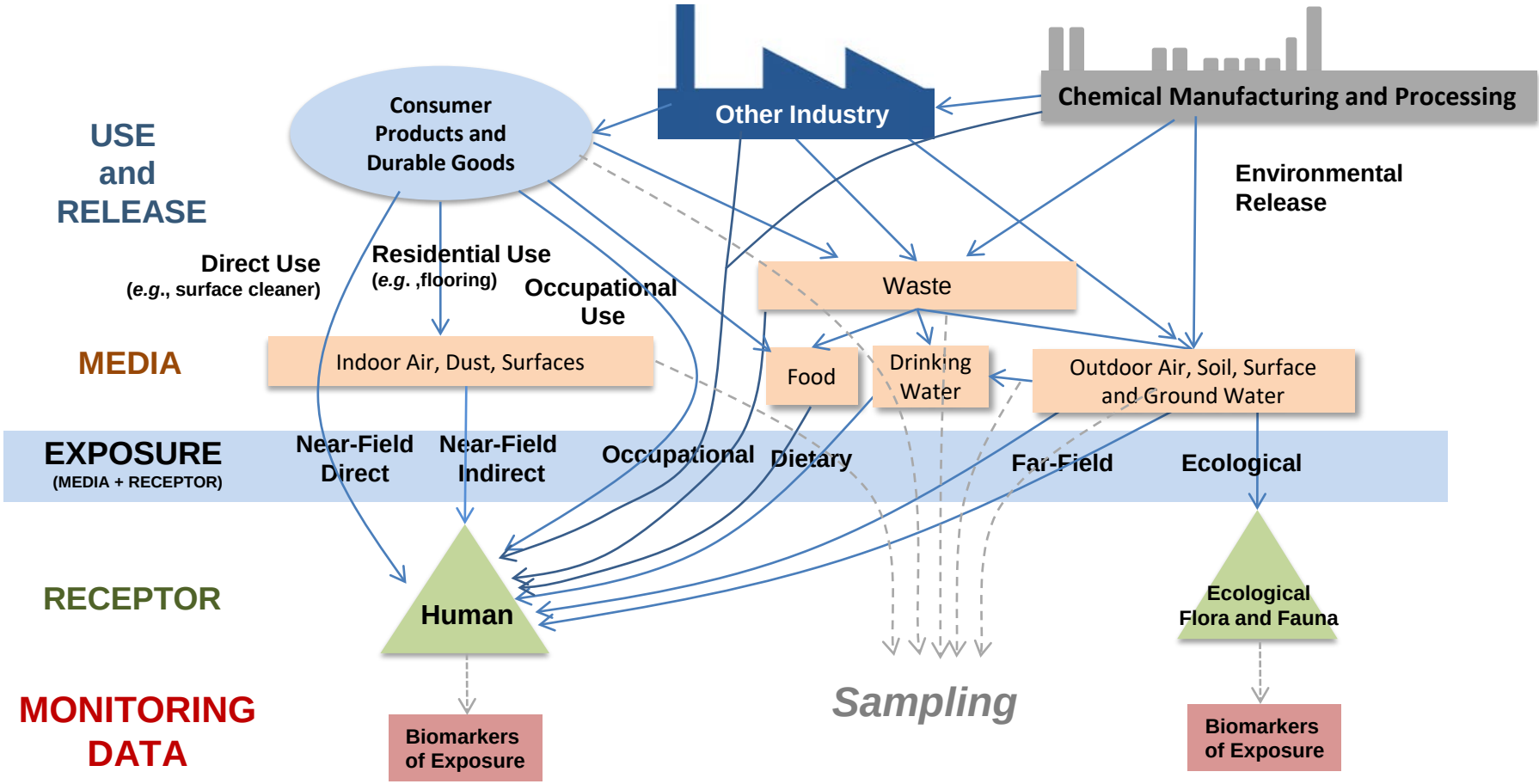
Forecasting Exposure is a Systems Problem

United States Environmental Protection Agency



Forecasting Exposure is a Systems Problem

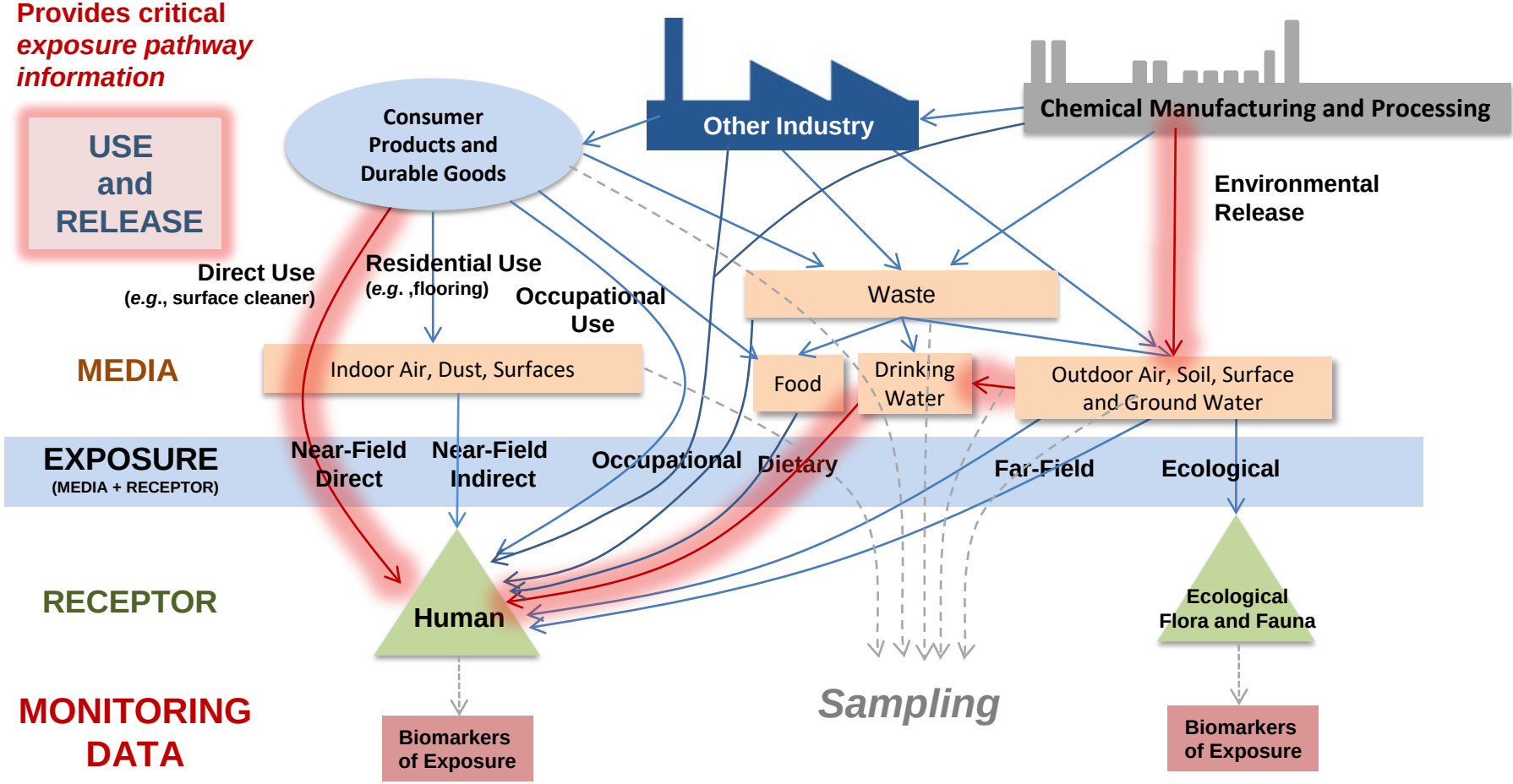
United States Environmental Protection Agency



Forecasting Exposure is a Systems Problem

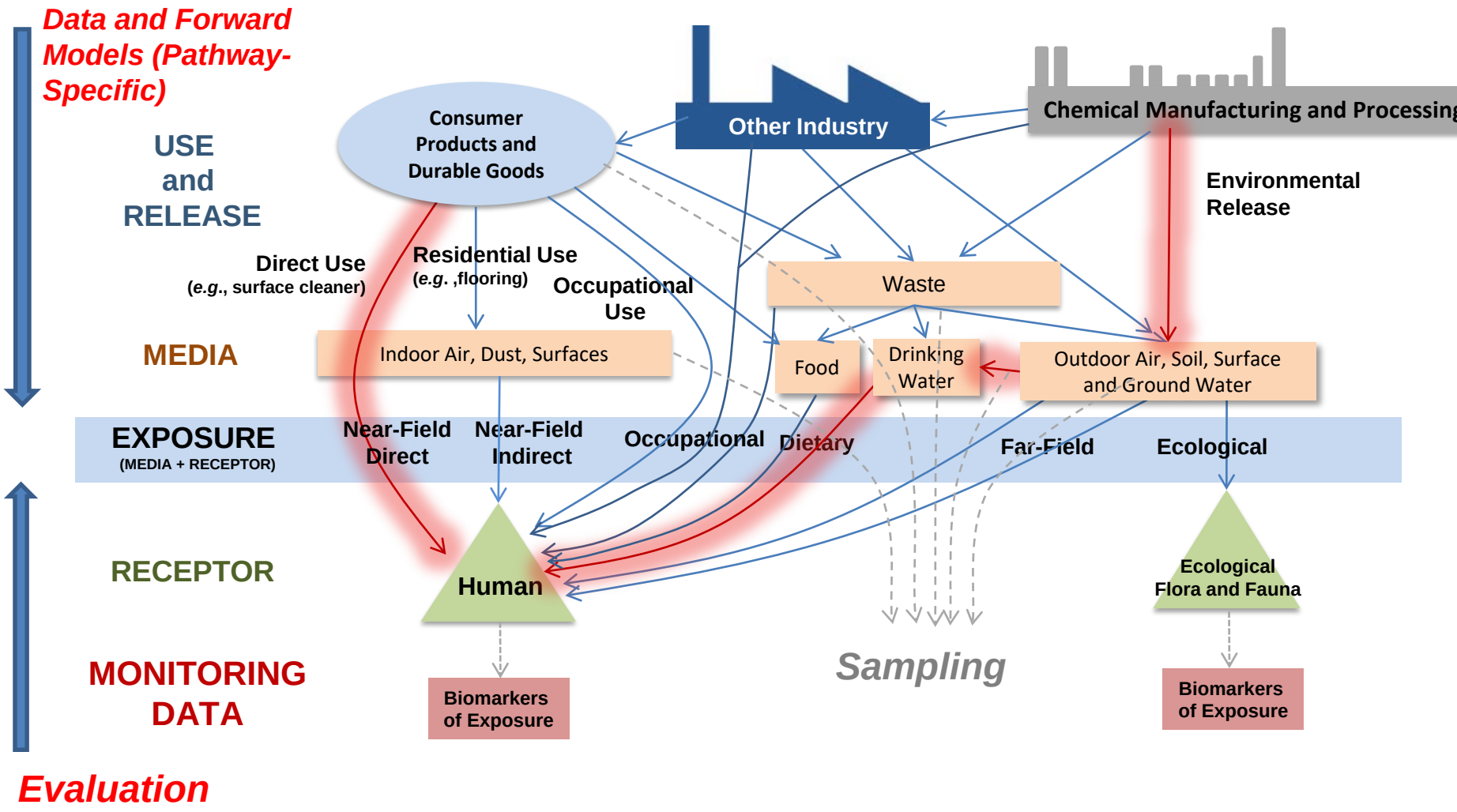
United States Environmental Protection Agency

Provides critical *exposure pathway information*



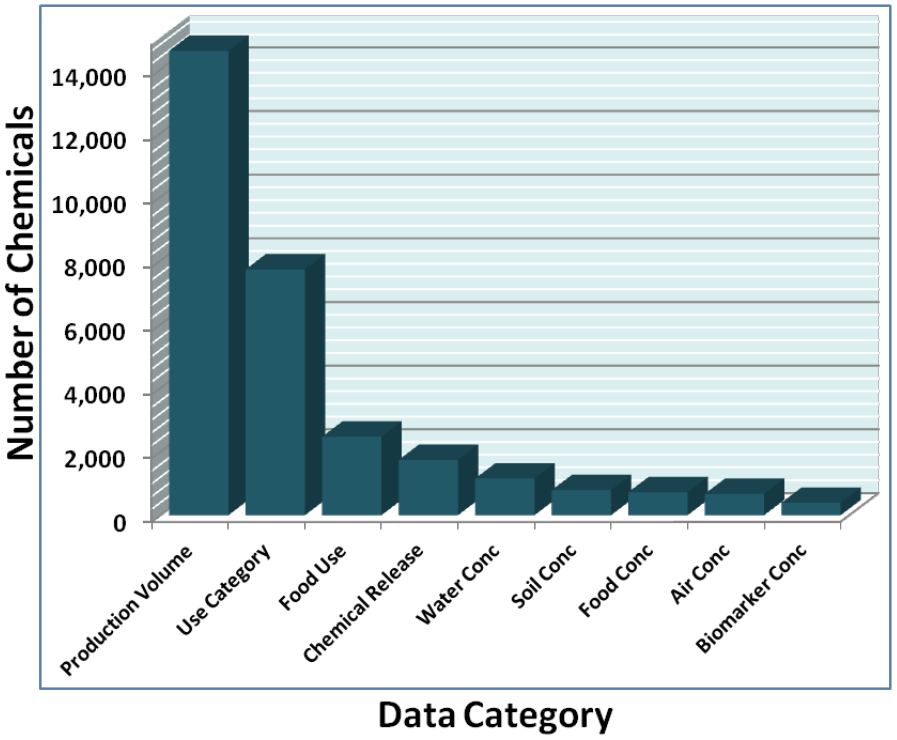
Forecasting Exposure is a Systems Problem

United States Environmental Protection Agency

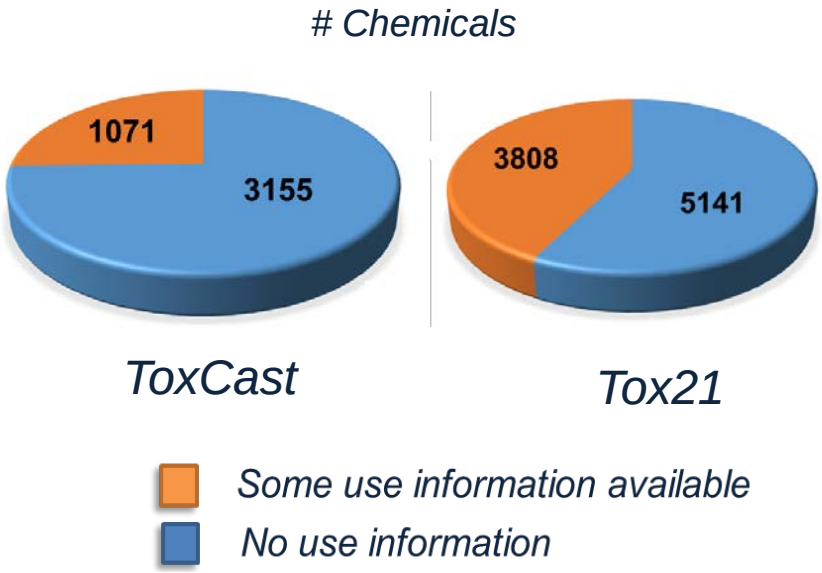


Some Data Critical to Exposure Estimation Are Limited

United States Environmental Protection Agency



Use data for chemicals being tested via high throughput screening at EPA



Egeghy et al. (2012)

The Chemicals and Products Database (CPDat)

United States Environmental Protection Agency

Broad index of chemical use


Contents lists available at ScienceDirect

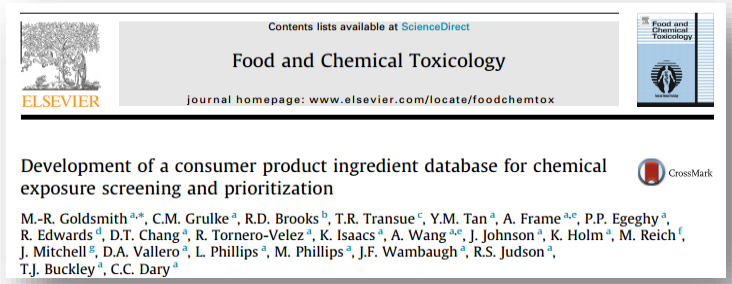
Toxicology Reports

journal homepage: www.elsevier.com/locate/toxrep

Exploring consumer exposure pathways and patterns of use for chemicals in the environment

Kathie L. Dionisio[a], Alicia M. Frame[b,1], Michael-Rock Goldsmith[a,2], John F. Wambaugh[b], Alan Liddell[c,3], Tommy Cathey[d], Doris Smith[b], James Vail[b], Alexi S. Ernstoff[e], Peter Fantke[e], Olivier Jolliet[f],

Retail product category based categorization of chemical use


Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Development of a consumer product ingredient database for chemical exposure screening and prioritization

M.-R. Goldsmith[a,*], C.M. Grulke[a], R.D. Brooks[b], T.R. Transue[c], Y.M. Tan[a], A. Frame[a,e], P.P. Egeghy[a], R. Edwards[d], D.T. Chang[a], R. Tornero-Velez[a], K. Isaacs[a], A. Wang[a,e], J. Johnson[a], K. Holm[a], M. Reich[f], J. Mitchell[g], D.A. Vallero[a], L. Phillips[a], M. Phillips[a], J.F. Wambaugh[a], R.S. Judson[a], T.J. Buckley[a], C.C. Dary[a]

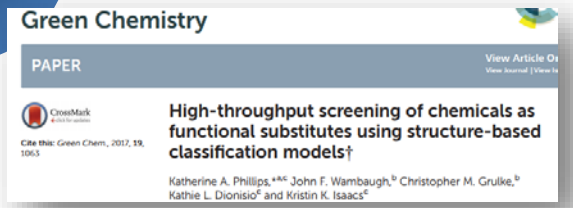
CPCPdb

CPCat

CPDat

FUse

Categorization by functional use


Green Chemistry

PAPER

High-throughput screening of chemicals as functional substitutes using structure-based classification models†

Katherine A. Phillips,*[a,c] John F. Wambaugh,[b] Christopher M. Grulke,[b] Kathie L. Dionisio[c] and Kristin K. Isaacs[c]

New product composition data

Chemical composition of consumer products


Journal of Exposure Science and Environmental Epidemiology (2017) 00, 1–7

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www.nature.com/jes

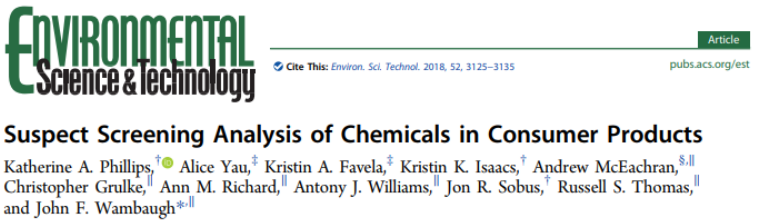
ORIGINAL ARTICLE

Consumer product chemical weight fractions from ingredient lists

Kristin K. Isaacs[1], Katherine A. Phillips[1], Derya Biryol[1,2], Kathie L. Dionisio[1] and Paul S. Price[1]

Measured data

Targeted and non-targeted measurement of chemicals in consumer products


Environmental Science & Technology

Article

Cite This: Environ. Sci. Technol. 2018, 52, 3125−3135

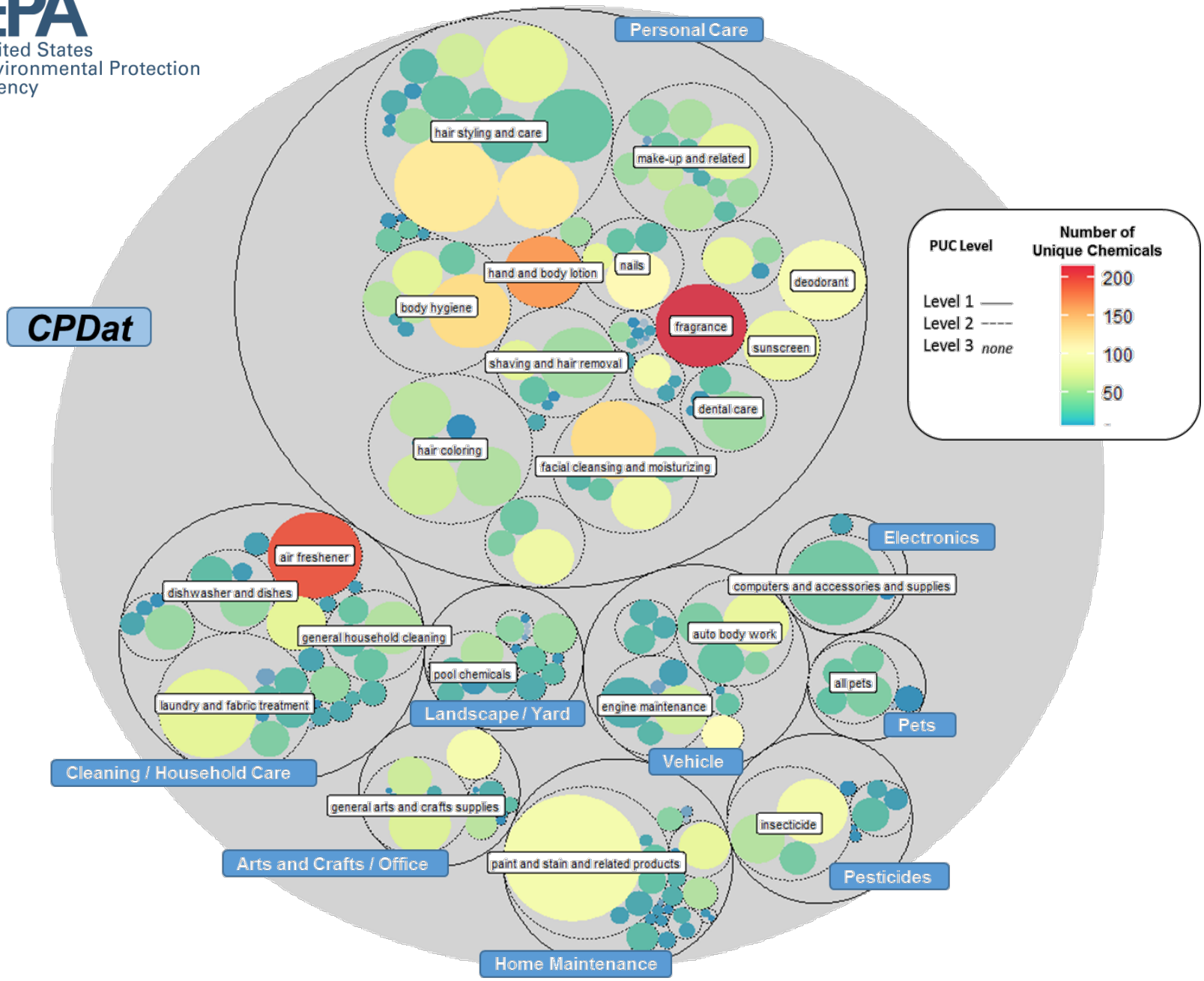
pubs.acs.org/est

Suspect Screening Analysis of Chemicals in Consumer Products

Katherine A. Phillips,[†] Alice Yau,[‡] Kristin A. Favela,[‡] Kristin K. Isaacs,[†] Andrew McEachran,[§,∥] Christopher Grulke,[∥] Ann M. Richard,[∥] Antony J. Williams,[∥] Jon R. Sobus,[†] Russell S. Thomas,[∥] and John F. Wambaugh[*,∥]

Chemicals and Product Use Categories (PUCs) in CPDat

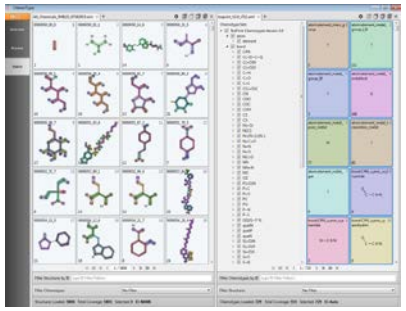
EPA United States Environmental Protection Agency

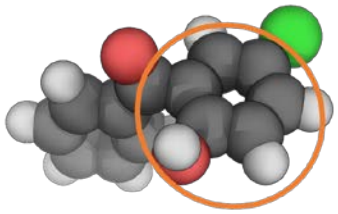


Predictive Models for Functional Use

United States Environmental Protection Agency

Chemical Structure and Property Descriptors





EPI-Suite™

Chemical Function Information

FUSE

Prediction of Potential Functions for Unclassified Chemicals

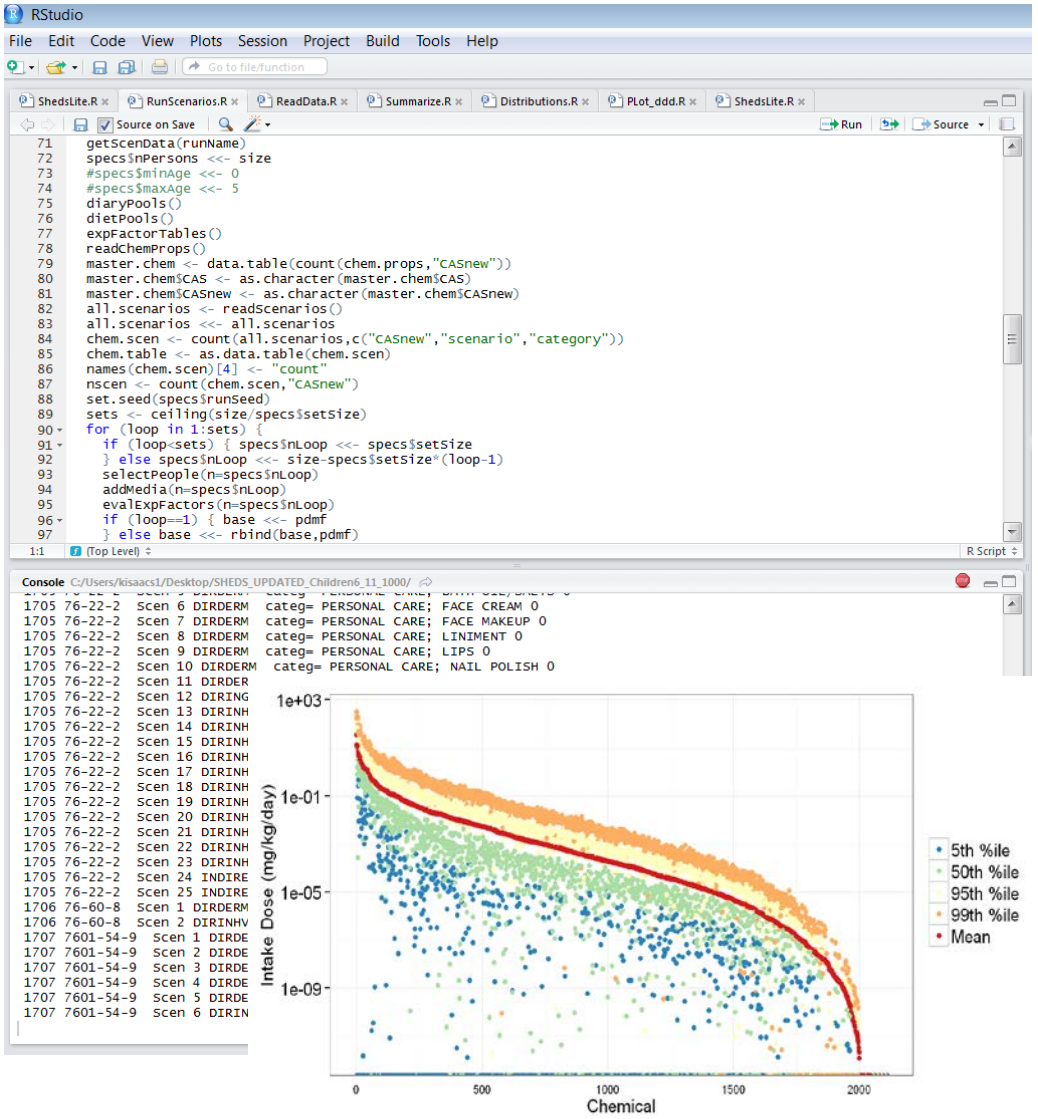
Machine-Learning Based Classification Models

Phillips et al., Green Chemistry., 2017, 19, 1063.

High-Throughput Stochastic Human Exposure Model (SHEDS-HT)

United States Environmental Protection Agency

- *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***
- *Design Purpose: development of HT near-field exposure predictions for use in **chemical prioritization***



SHEDS-HT Exposure Scenarios

EPA United States Environmental Protection Agency

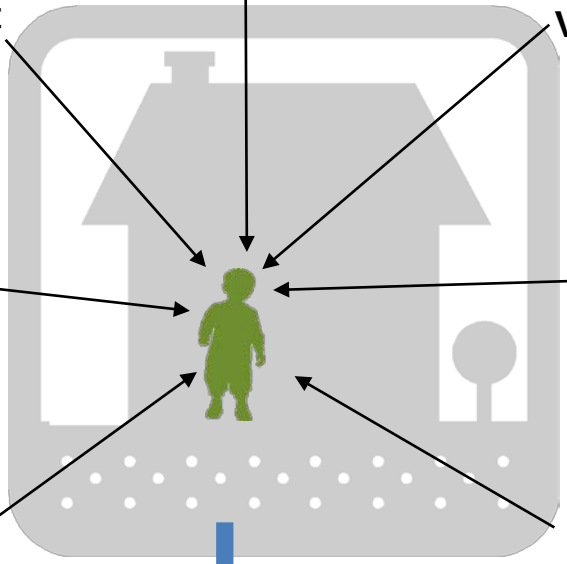
Incidental Direct Ingestion of Product

Dietary Ingestion

Direct Inhalation of Vapor from Product

Direct Inhalation of Aerosol From Product

Direct Dermal Application Of Product



Indirect Exposure to Bolus Applied Product

Indirect Exposure to Constant Emission of Chemical

Down the Drain Release of Chemical

R Package 'ShedsHT"

United States Environmental Protection Agency

Package 'ShedsHT'

September 9, 2016

Title To run the SHEDS-HT screening model for estimating human exposure to chemicals.

Version 0.1.1

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.

License MIT

Encoding UTF-8

LazyData true

RoxygenNote 5.0.1

Imports data.table, ggplot2, stringr, plyr

Suggests knitr, rmarkdown

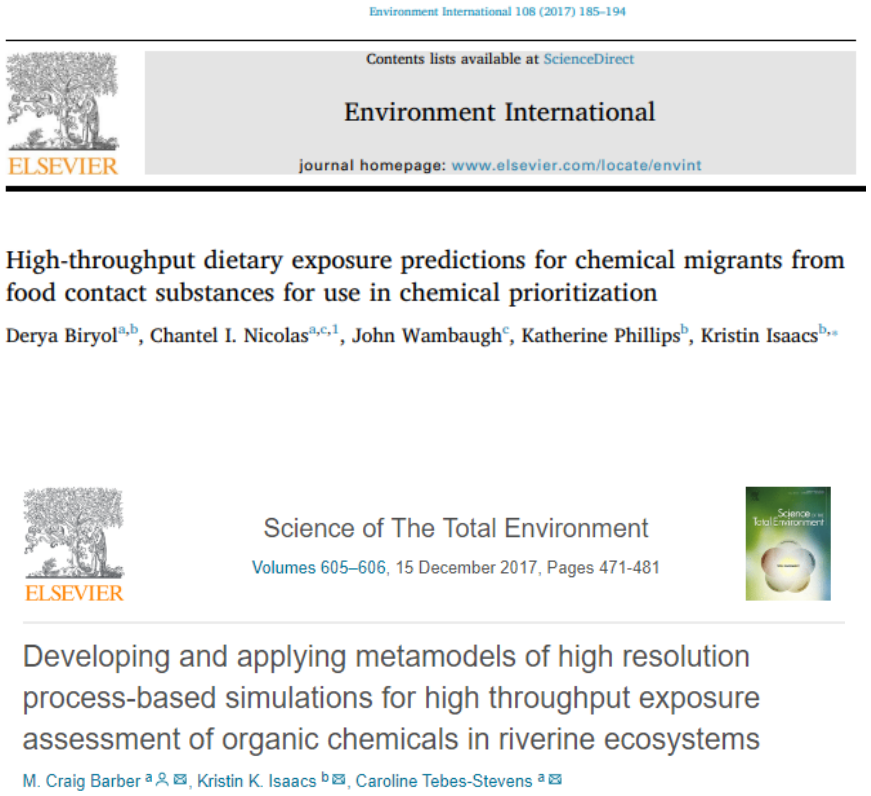
VignetteBuilder knitr

- R Package with help documentation and User's Guide
- Current model release
- Default input files (e.g. population, food diaries, CPDat data in correct form)
- Example run-specific input files
- Training materials

https://github.com/HumanExposure/SHEDSHTRPackage

Other Pathway-Specific Exposure Models

- Have developed HT models for exposure to chemicals in food contact materials
- Are currently exploring approaches for occupational pathways
- Ecological receptors are also of interest; ORD is implementing or developing models for water and biota concentrations associated with down-the-drain consumer and industrial releases



Environment International 108 (2017) 185–194

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

ELSEVIER

High-throughput dietary exposure predictions for chemical migrants from food contact substances for use in chemical prioritization

Derya Biryol[a,b], Chantel I. Nicolas[a,c,1], John Wambaugh[c], Katherine Phillips[b], Kristin Isaacs[b,*]

ELSEVIER

Science of The Total Environment

Volumes 605–606, 15 December 2017, Pages 471-481

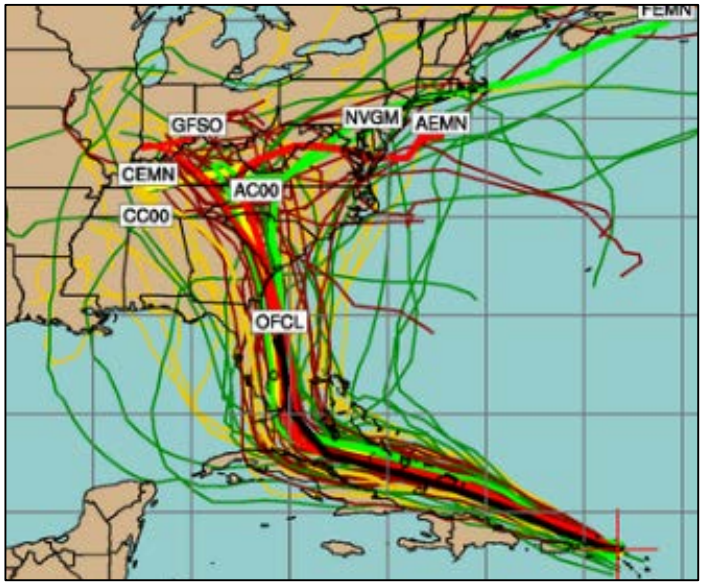
Developing and applying metamodels of high resolution process-based simulations for high throughput exposure assessment of organic chemicals in riverine ecosystems

M. Craig Barber [a], Kristin K. Isaacs [b], Caroline Tebes-Stevens [a]

Consensus Exposure Forecasts

United States Environmental Protection Agency

Incorporate data from many models; those that perform best are weighted more heavily in forecasts



Consensus Exposure Forecasts

United States Environmental Protection Agency

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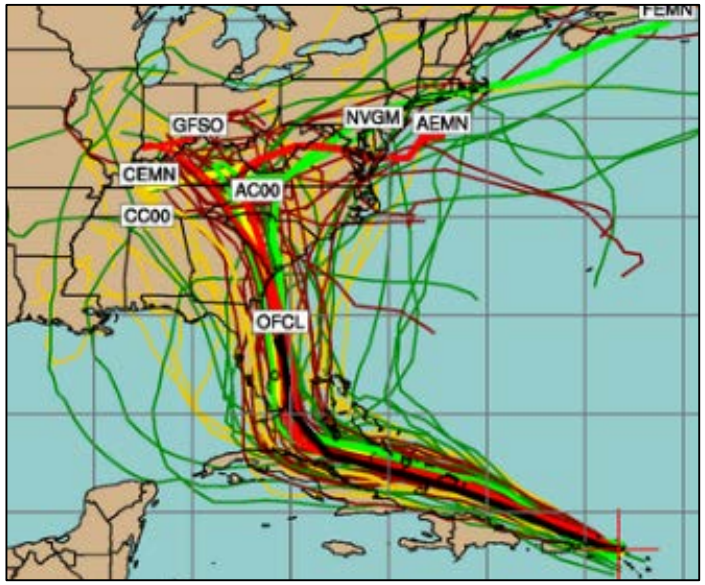
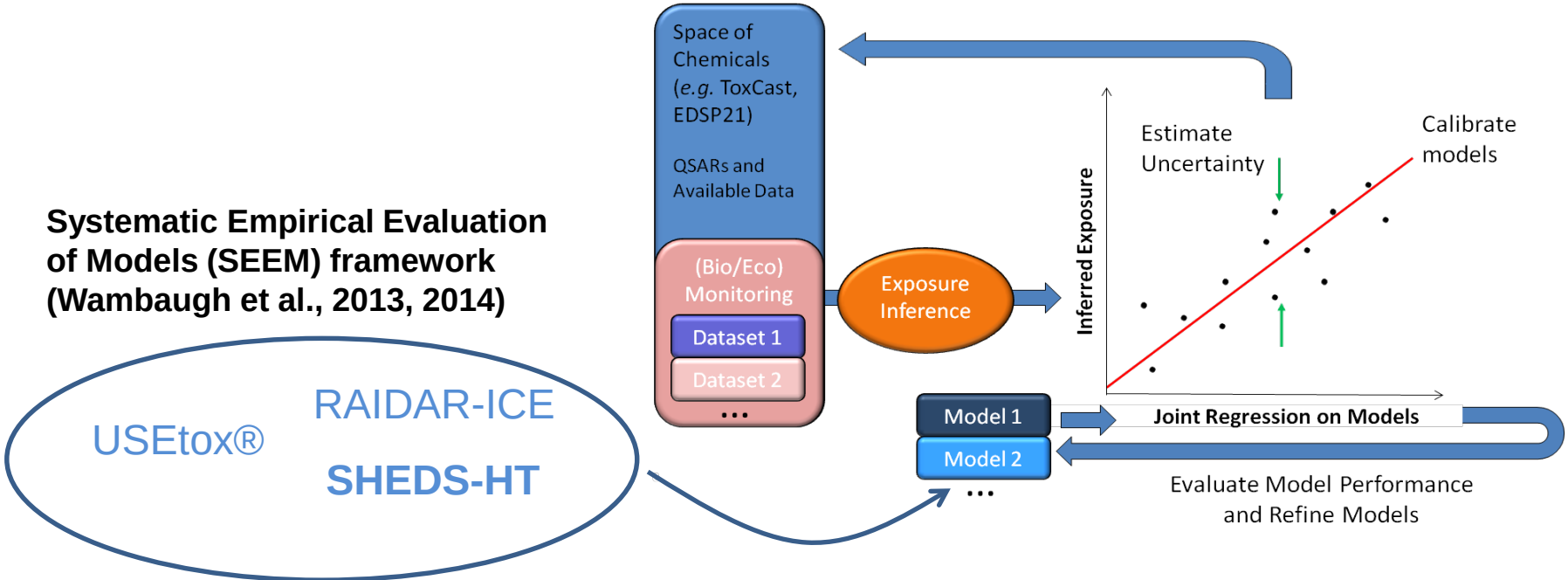


Systematic Empirical Evaluation of Models (SEEM) framework (Wambaugh et al., 2013, 2014)



Collaboration on High Throughput Exposure Predictions

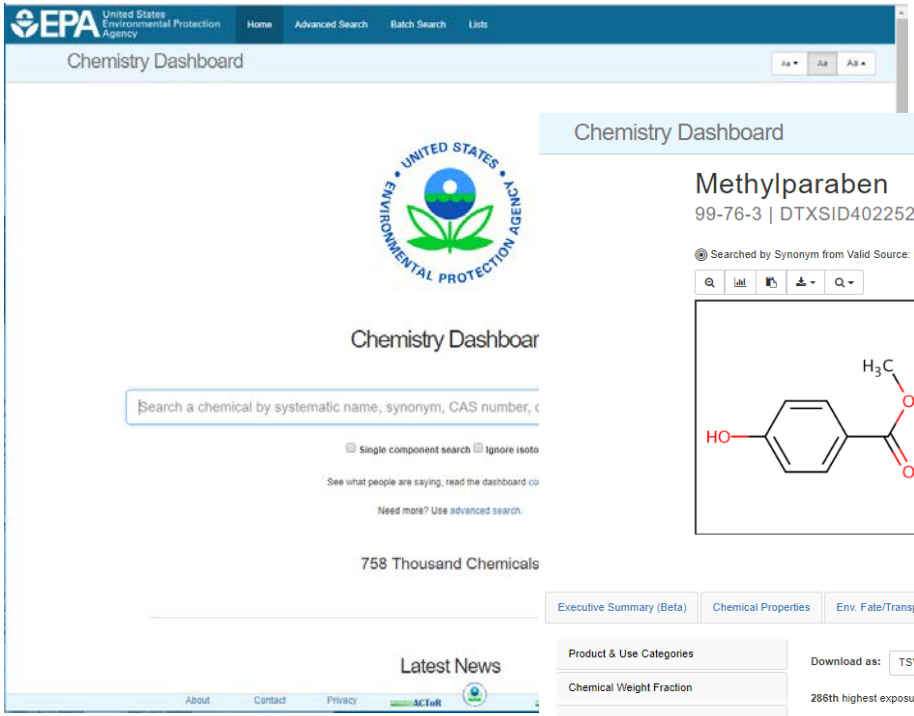
Jon Arnot, Deborah H. Bennett, Peter P. Egeghy, Peter Fantke, Lei Huang, Kristin K. Isaacs, Olivier Jolliet, Hyeong-Moo Shin, Katherine A. Phillips, Caroline Ring, R. Woodrow Setzer, John F. Wambaugh, Johnny Westgate

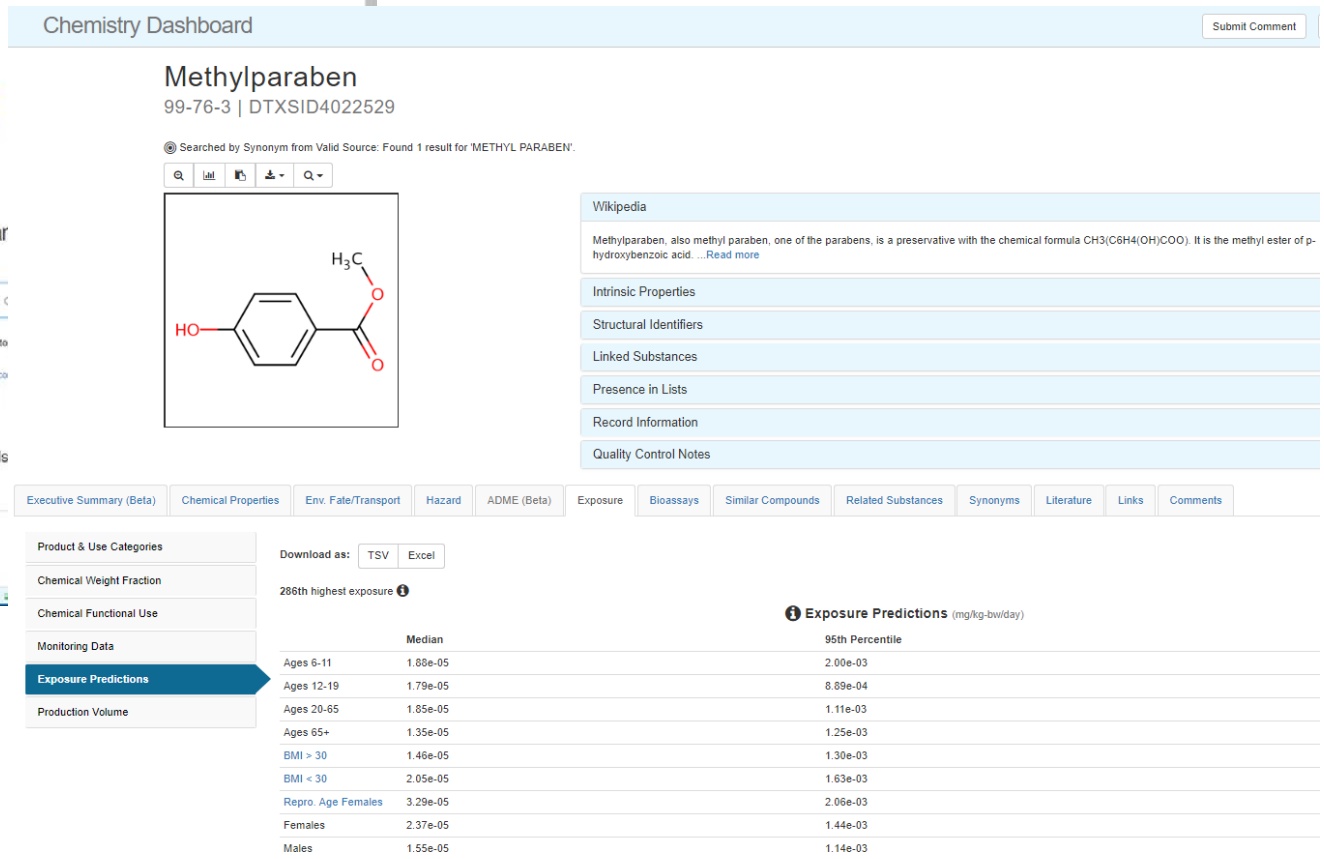
Predictor	Chemicals Predicted	Pathways
EPA Inventory Update Reporting and Chemical Data Reporting (CDR) (2015)	7856	All
Stockholm Convention of Banned Persistent Organic Pollutants (2017)	248	Far-Field Industrial and Pesticide
EPA Pesticide Reregistration Eligibility Documents (REDs) Exposure Assessments (Through 2015)	239	Far-Field Pesticide
FDA Cumulative Estimated Daily Intake (CEDI)	748	Dietary
Food Contact Substance Migration Model (2017)	940	Dietary
United Nations Environment Program and Society for Environmental Toxicology and Chemistry toxicity model (USETox) Industrial Scenario (2.0)	8167	Far-Field Industrial
USETox Pesticide Scenario (2.0)	8167	Far-Field Pesticide
Risk Assessment IDentification And Ranking (RAIDAR) Far-Field (2.02)	7511	Far-Field Industrial and Pesticide
EPA Stochastic Human Exposure Dose Simulator High Throughput (SHEDS-HT) Near-Field Direct (2017)	1119	Residential
SHEDS-HT Near-field Indirect (2017)	645	Residential
Fugacity-based INdoor Exposure (FINE) (2017)	1221	Residential
RAIDAR-ICE Near-Field (0.803)	615	Residential
USEtox Residential Scenario (2.0)	8167	Residential
USEtox Dietary Scenario (2.0)	8167	Dietary

Exposure Data in the CompTox Chemistry Dashboard

United States Environmental Protection Agency

https://comptox.epa.gov/dashboard





	Median	95th Percentile
Ages 6-11	1.88e-05	2.00e-03
Ages 12-19	1.79e-05	8.89e-04
Ages 20-65	1.85e-05	1.11e-03
Ages 65+	1.35e-05	1.25e-03
BMI > 30	1.46e-05	1.30e-03
BMI < 30	2.05e-05	1.63e-03
Repro. Age Females	3.29e-05	2.06e-03
Females	2.37e-05	1.44e-03
Males	1.55e-05	1.14e-03

Improving Exposure Pathway Characterization and Model Evaluation: Non-Targeted Analyses of Monitoring Data

United States Environmental Protection Agency

- Targeted Analysis:
  - We know exactly what we're looking for
  - 10s – 100s of chemicals
- Non-Targeted Analysis (NTA):
  - We have no preconceived lists
  - 1,000s – 10,000s of chemical
- Ongoing consumer product scanning and blood sample monitoring
- Development of significant in-house capabilities

- 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
- Goal is to develop tools, databases, and workflows for rapid analysis of any sample for chemicals of interest, i.e. ***exposure forensics***

Chemical Safety for Sustainability (CSS) Research Program

EPA United States Environmental Protection Agency

Rapid Exposure and Dosimetry (RED) Project

NCCT
Chris Grulke
Greg Honda*
Richard Judson
Andrew McEachran*
Robert Pearce*
Ann Richard
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
Jarod Grossman*
Hongtai Huang*
Brandall Ingle*
Kristin Isaacs
Sarah Laughlin-Toth*
Seth Newton
Katherine Phillips
Paul Price
Jeanette Reyes*
Jon Sobus
John Streicher*
Mark Strynar
Mike Tornero-Velez
Elin Ulrich
Dan Vallero
Barbara Wetmore

Human Exposure Model Project

Cody Addington*
Namdi Brandon*
Nicholas Coco*
Kathie Dionisio
Peter Egeghy
Kristin Isaacs
Dave Lyons
Katherine Phillips
Paul Price
Steve Prince
Dan Vallero

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

*Trainees

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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
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Tox Strategies
Caroline Ring
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Deborah Bennett
Hyeong-Moo Shin
University of Michigan
Olivier Jolliet
University of North Carolina, Chapel Hill
Alex Tropsha