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Agency

Consensus Exposure Predictions with the SEEM Framework

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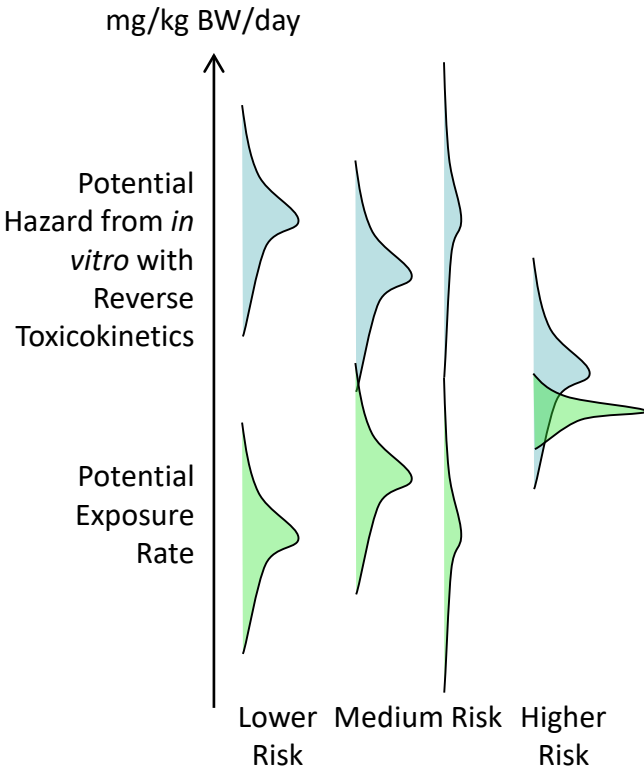
Using 21st Century Science to Improve Risk-Related Evaluations

- **January, 2017 U.S. National Academies of Science report:**

  "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"

- **Tox21/ToxCast**: Examining thousands of chemicals using in vitro assays that test parent chemical in concentration response

- **ExpoCast**: Tentative exposure predictions for daily human exposure rates (mg/kg/day)

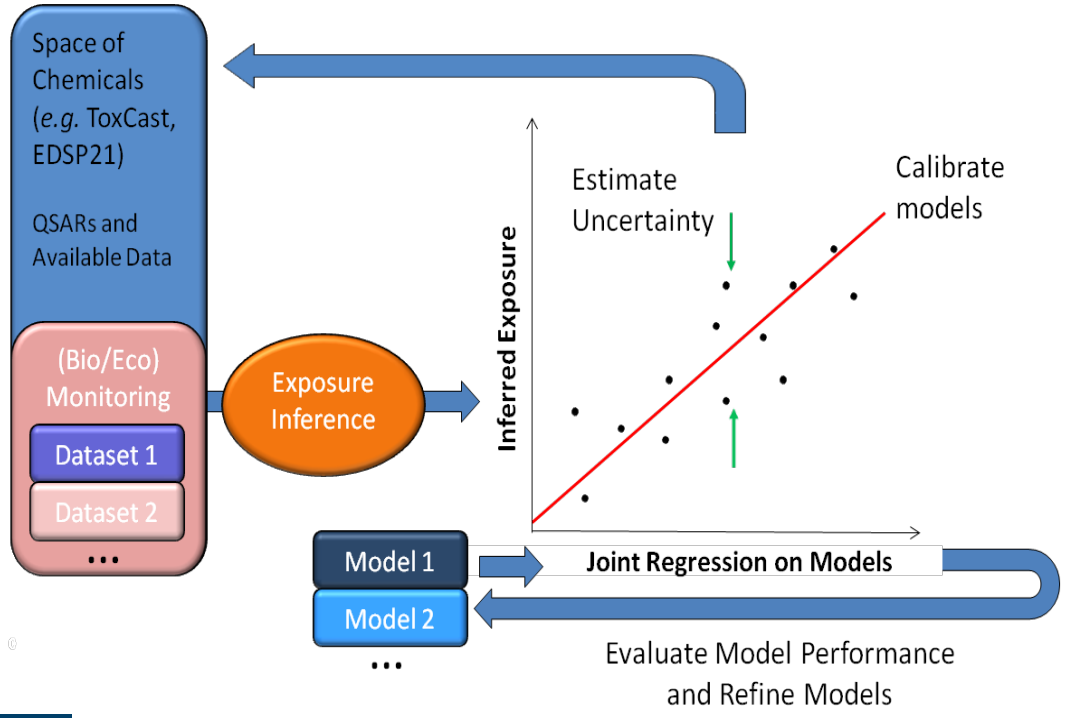


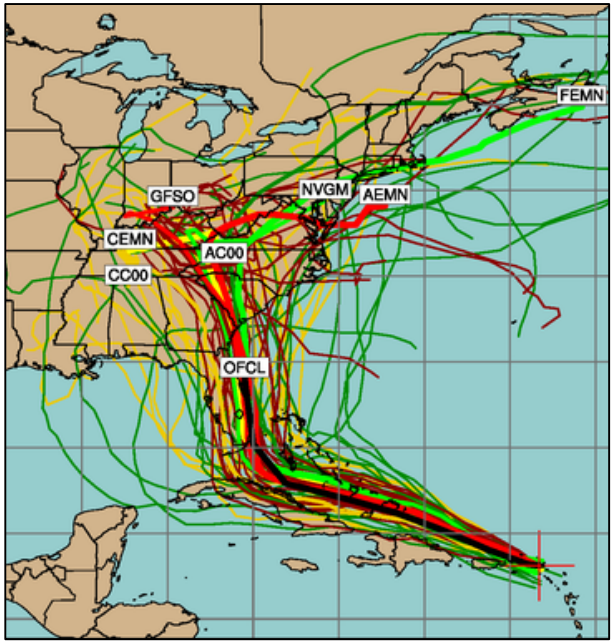
What is acceptable uncertainty?

See Wetmore et al. (2015)

Consensus Exposure Predictions with the SEEM Framework

- Different exposure models incorporate **knowledge**, **assumptions**, and **data** (Macleod, et al., 2010)
- We incorporate multiple models into consensus predictions for 1000s of chemicals within the **Systematic Empirical Evaluation of Models (SEEM) framework** (Wambaugh et al., 2013, 2014)
- We evaluate/calibrate predictions with available monitoring data
- Error in predictions for chemicals with data is applied as uncertainty to chemicals without data





Integrating Multiple Models

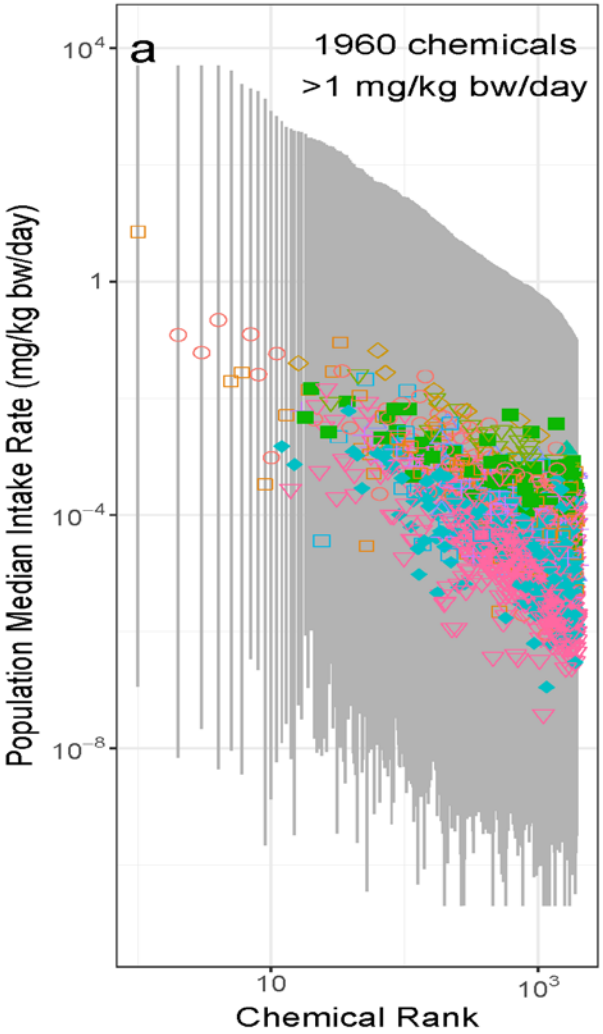
Collaboration on High Throughput Consumer Exposure Predictions

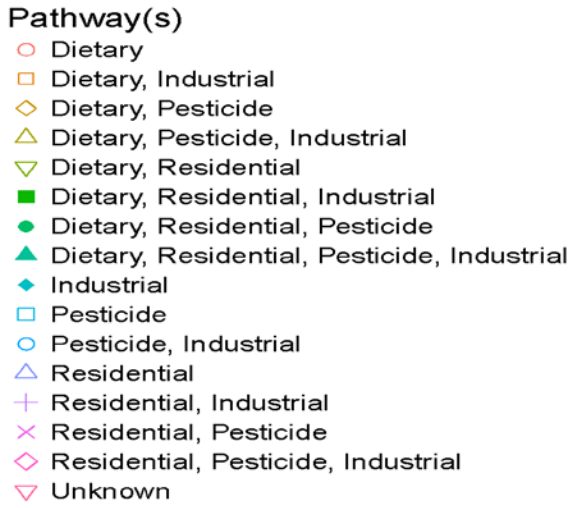
Jon Arnot, Deborah H. Bennett, Peter P. Egeghy, Peter Fantke, Lei Huang, Kristin K. Isaacs, Olivier Jolliet, Hyeong-Moo Shin, Katherine A. Phillips, Caroline Ring, R. Woodrow Setzer, John F. Wambaugh, Johnny Westgate

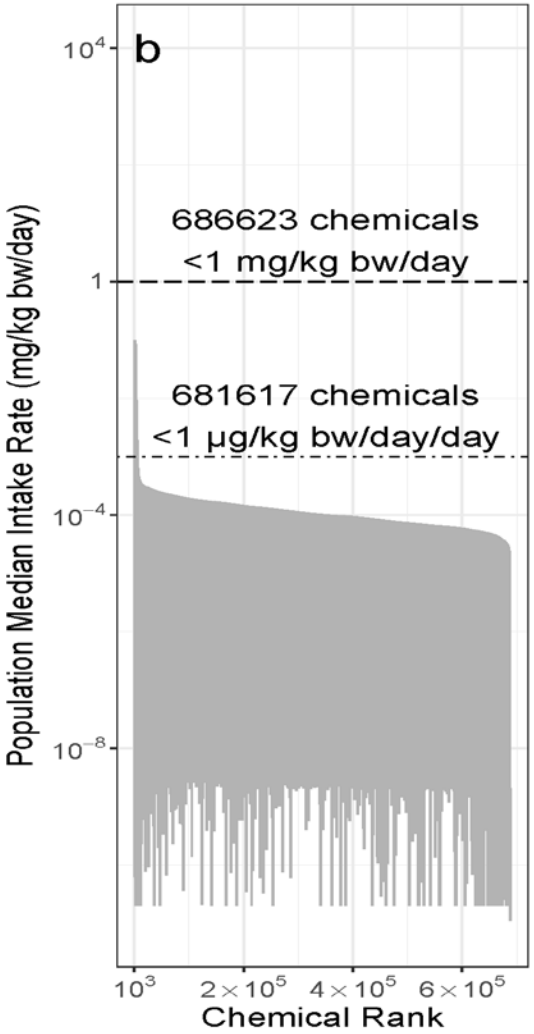
Predictor	Reference(s)	Chemicals Predicted	Pathways
EPA Inventory Update Reporting and Chemical Data Reporting (CDR) (2015)	US EPA (2018)	7856	All
Stockholm Convention of Banned Persistent Organic Pollutants (2017)	Lallas (2001)	248	Far-Field Industrial and Pesticide
EPA Pesticide Reregistration Eligibility Documents (REDs) Exposure Assessments (Through 2015)	Wetmore et al. (2012, 2015)	239	Far-Field Pesticide
United Nations Environment Program and Society for Environmental Toxicology and Chemistry toxicity model (USETox) Industrial Scenario (2.0)	Fantke et al. (2011, 2012, 2016)	940	Dietary
USETox Pesticide Scenario (2.0)	Rosenbaum et al. (2008)	8167	Far-Field Industrial
Risk Assessment IDentification And Ranking (RAIDAR) Far-Field (2.02)	Arnot et al. (2008)	8167	Far-Field Pesticide
EPA Stochastic Human Exposure Dose Simulator High Throughput (SHEDS-HT) Near-Field Direct (2017)	Isaacs (2017)	7511	Far-Field Industrial and Pesticide
SHEDS-HT Near-field Indirect (2017)	Isaacs (2017)	1119	Residential (Near-Field)
Fugacity-based INdoor Exposure (FINE) (2017)	Bennett et al. (2004), Shin et al. (2012)	645	Residential
RAIDAR-ICE Near-Field (0.803)	Arnot et al., (2014), Zhang et al. (2014)	1221	Residential
USETox Residential Scenario (2.0)	Jolliet et al. (2015), Huang et al. (2016,2017)	615	Residential
USETox Dietary Scenario (2.0)	Jolliet et al. (2015), Huang et al. (2016), Ernstoff et al. (2017)	8167	Residential

High Throughput Consumer Exposure Predictions

United States Environmental Protection Agency







95% confident that median population intake would be <1 µg/kg bw/day for thousands of chemicals

SEEM Analysis for Ecological Exposure

United States Environmental Protection Agency

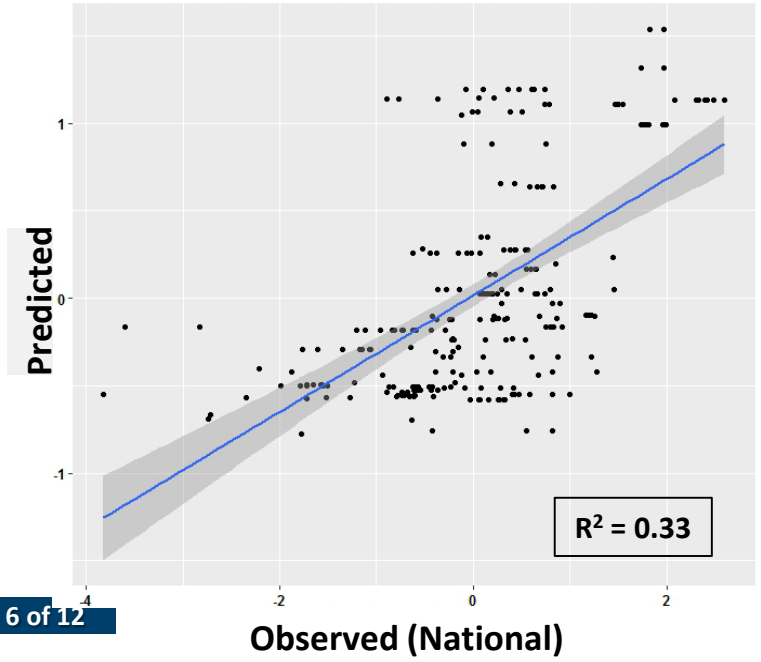
Surface Water Sampling Sites

> 600,000 surface water sites in lower 48

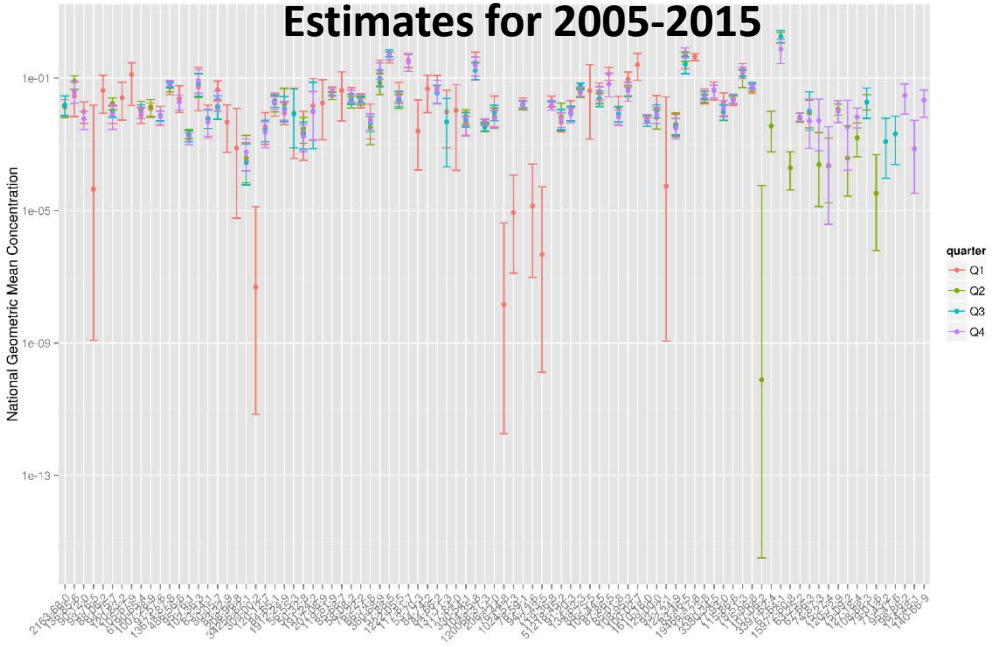
> 700 individual chemicals

GPS, date, and time stamps

LOD indication



Setzer et al. National Geometric Mean Estimates for 2005-2015

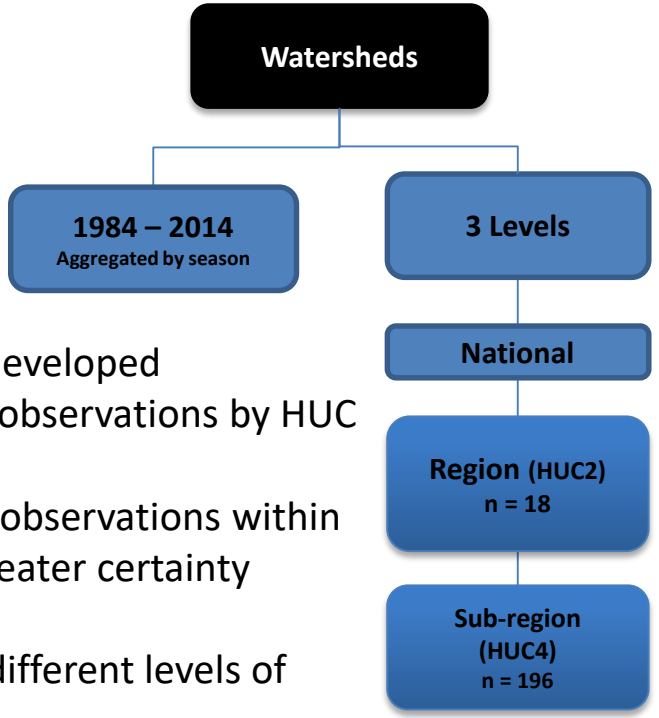


A total of 279 datasets (chemical X decade X quarter) for 86 chemicals.

Analysis by Parichehr Saranjampour

Hydrological Unit Codes

United States Environmental Protection Agency



- Setzer et al., (in prep) developed methodology to group observations by HUC
  - If there are more observations within a HUC, there is greater certainty
- Can infer averages for different levels of hierarchy

HUC = hydrological unit code

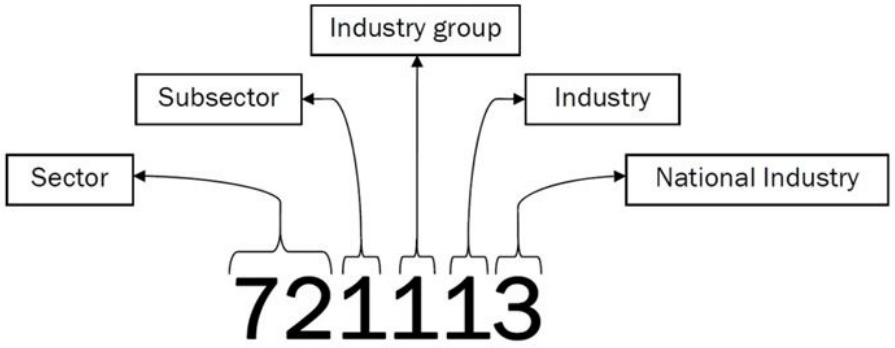
Name	Level	Digits	Average size (square miles)	Number of HUs (approximate)	Example name	Example code (HUC)
Region	1	2	177,560	21	Pacific Northwest	17
Subregion	2	4	16,800	222	Lower Snake	1706
Basin	3	6	10,596	370	Lower Snake	170601
Subbasin	4	8	700	2,200	Imnaha River	17060102
Watershed	5	10	227 (40,000–250,000 acres)	22,000	Upper Imnaha River	1706010201
Subwatershed	6	12	40 (10,000–40,000 acres)	160,000	South Fork Imnaha River	170601020101

Occupational Exposure Database

- EPA has built a database of occupational chemical monitoring data from Occupational Safety and Health Administration (OSHA) and the EPA's Chemical Data Reporting (CDR)

- Samples are coded according to the North American Industry Classification System (NAICS) developed by Office of Management and Budget (OMB)

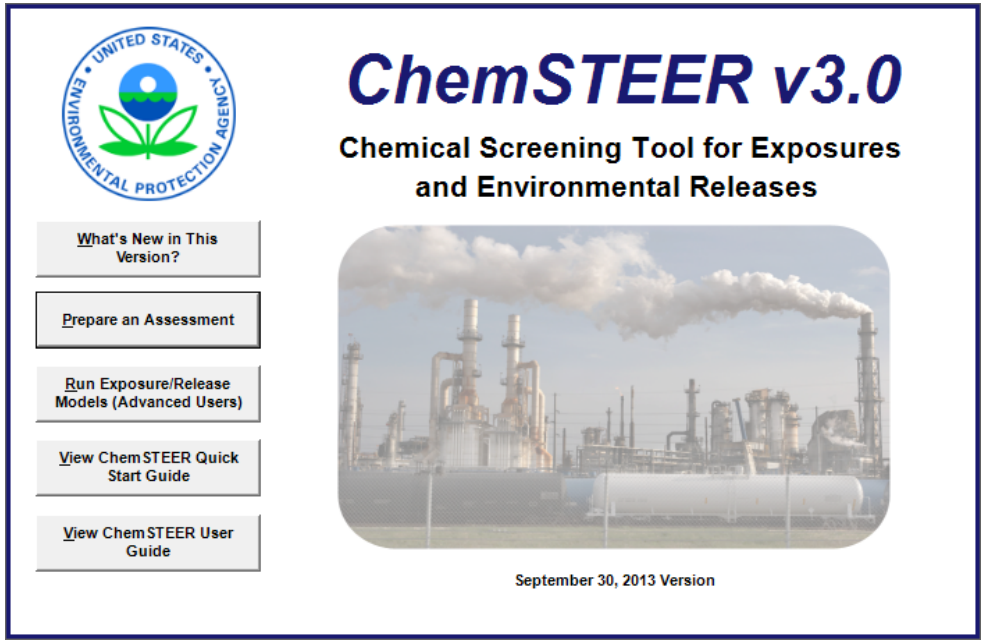
- 2,303,043 observations from OSHA
  - 1984-present
  - They include data on personal, area, and bulk samples for various airborne contaminants
  - 1140 different substances
  - 1040 different NAICS



NAICS Level	NAICS Code	Description
Sector	31–33	Manufacturing
Subsector	334	Computer and electronic product manufacturing
Industry group	3346	Manufacturing and reproduction of magnetic and optical media
Industry	33461	Manufacturing and reproduction of magnetic and optical media
U.S. Industry	334611	Reproduction of software

ChemSTEER:
Chemical Screening Tool for Exposures and Environmental Releases

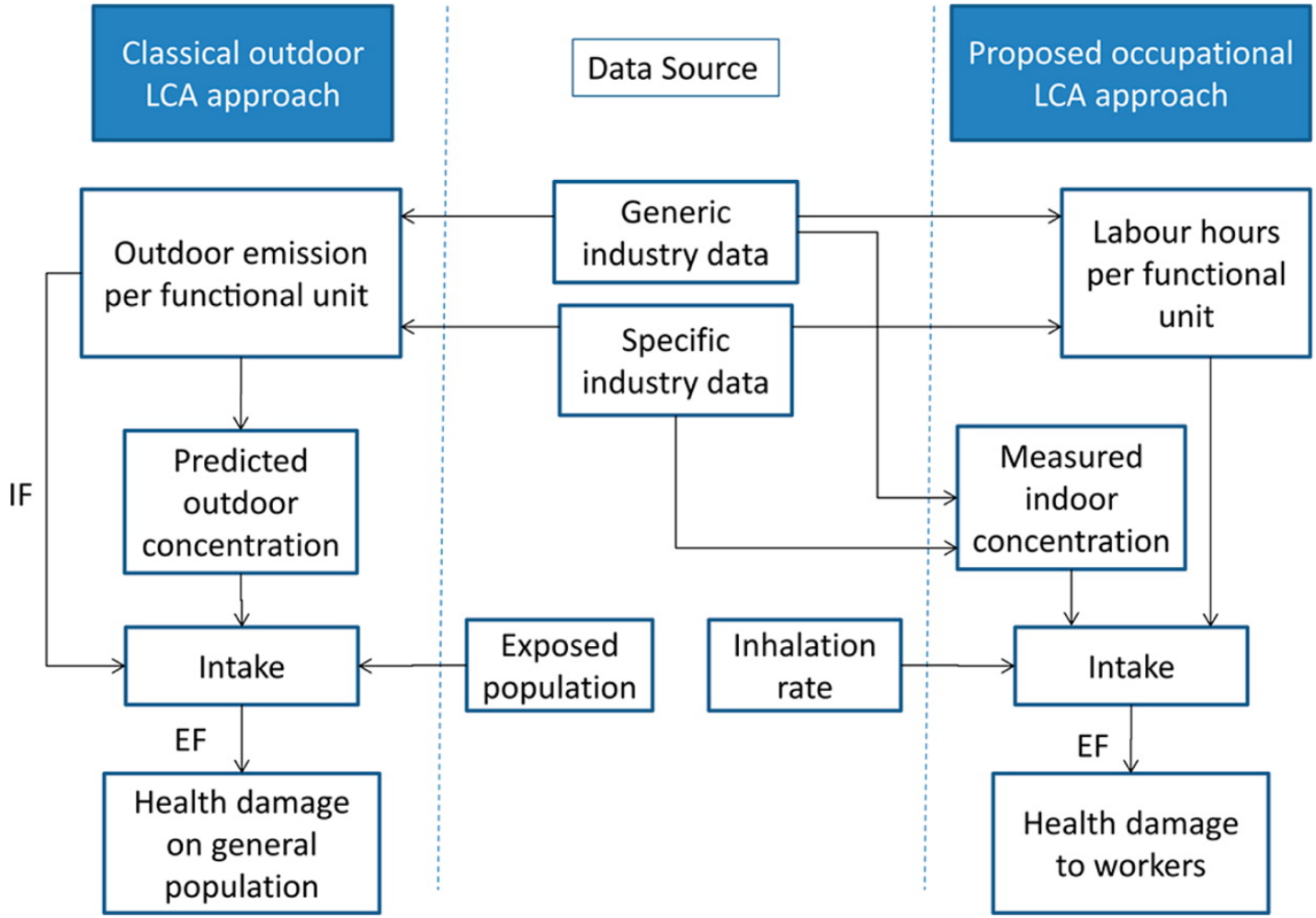
- ChemSTEER is an EPA model used to estimate workplace exposures and environmental releases for chemicals manufactured and used in industrial/commercial settings
- ChemSTEER is not intended to be a high throughput exposure model, but instead features menu-driven interfaces to allow users to “build” assessments
- Contains pre-defined, industry-specific generic scenarios scenarios which user may then customize
- ORD is working to create a high throughput version, which we can then evaluate with the available data



https://www.epa.gov/tsca-screening-tools/chemsteer-chemical-screening-tool-exposures-and-environmental-releases

Work led by Katherine Phillips

Model for Predicted Intake from Occupational Exposure



Kijko et al. (2015)

Proposed Occupational SEEM Analysis

- Model OSHA data to determine averages for different levels of NAICS (i.e., industries)
- Setzer et al. method will identify the level of granularity informed by the data
- Use the available average chemical measurements to evaluate models (ChemSTEER, Kijko, et al. 2015) and chemical properties (e.g., vapor pressure) for ability to predict
    - Develop calibrated predictive model and empirically estimate uncertainty
- Apply calibrated predictive model to those chemicals without monitoring data

Summary

- Models incorporate Knowledge, Assumptions and Data
- The trick is to know which model to use and when
- Rough exposure assessments may be potentially useful if the uncertainty can be quantified and is acceptable (i.e., “fit for purpose”)
- EPA relies on the Systematic Empirical Evaluation of Models (SEEM) framework to develop consensus models
- Using SEEM, various predictors of exposure are combined according to calibrated weights reflecting estimates of their predictive ability based on monitoring data

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