ADDRESSING THE CHALLENGE OF EXPOSURE SCIENCE IN THE 21ST CENTURY: A STRATEGY FOR DEVELOPING MORE ROBUST EXPOSURE ASSESSMENT TOOLS

TODD GOUIN, IAN SORRELL, BEATE NICOL, OLIVER PRICE,
CLAIRE DAVIES, CATHERINE BARRATT

INTEGRATING HUMAN AND ENVIRONMENTAL RISK ASSESSMENT

» Common challenge related to linking exposure to the intrinsic toxicity a chemical may possess

- Need for efficient, reliable tools that enable accurate decisions regarding risk to be made

» NRC and risk assessment in the 21st century

- Rapid screening of large numbers of chemicals used in commerce
- Complementary use of in-vitro and in silico tools utilising high-throughput systems (i.e. ToxCast)

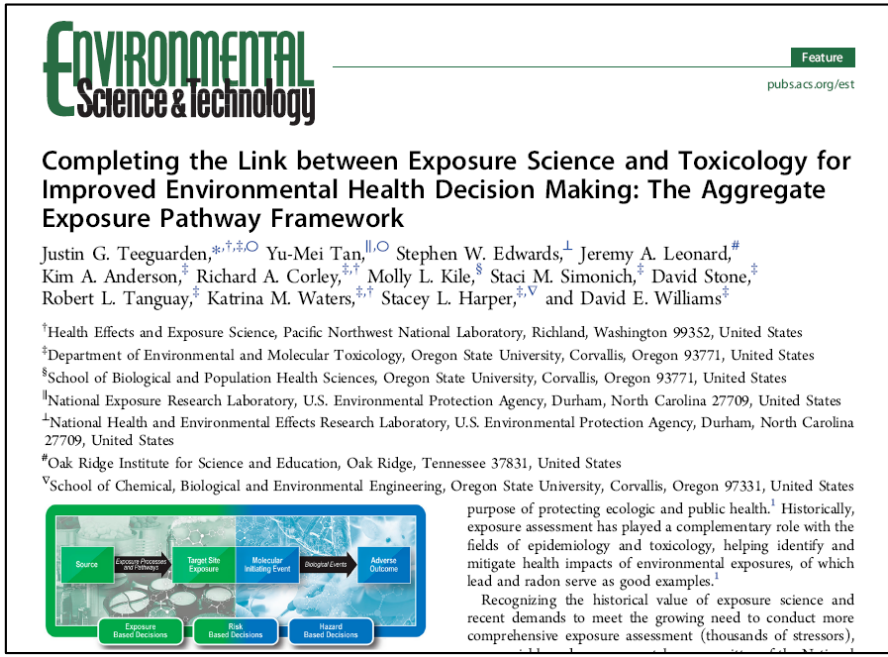
» Quantitative in vitro to in vivo extrapolation (QIVIVE)

Strategic vision needed to better characterize exposure

AGGREGATE EXPOSURE PATHWAY

- Organizational framework for enhancing our mechanistic understanding of the processes that influence exposure to chemicals by individuals and environmental systems.
- Complementary/analogous to adverse outcome pathways (AOPs)
- Key difference AOPs are not chemical specific, AEPs are chemical specific

Teeguarden et al. (2016). Completing the Link between Exposure Science and Toxicology for Improved Environmental Health Decision Making: The Aggregate Exposure Pathway Framework. Environ Sci Technol.



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Completing the Link between Exposure Science and Toxicology for Improved Environmental Health Decision Making: The Aggregate Exposure Pathway Framework

Justin G. Teeguarden,[*,†,‡,○] Yu-Mei Tan,[∥,○] Stephen W. Edwards,[⊥] Jeremy A. Leonard,[#] Kim A. Anderson,[‡] Richard A. Corley,[‡,†] Molly L. Kile,[§] Staci M. Simonich,[‡] David Stone,[‡] Robert L. Tanguay,[‡] Katrina M. Waters,[‡,†] Stacey L. Harper,[‡,▽] and David E. Williams[‡]

[†]Health Effects and Exposure Science, Pacific Northwest National Laboratory, Richland, Washington 99352, United States
[‡]Department of Environmental and Molecular Toxicology, Oregon State University, Corvallis, Oregon 93771, United States
[§]School of Biological and Population Health Sciences, Oregon State University, Corvallis, Oregon 93771, United States
[∥]National Exposure Research Laboratory, U.S. Environmental Protection Agency, Durham, North Carolina 27709, United States
[⊥]National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency, Durham, North Carolina 27709, United States
[#]Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee 37831, United States
[▽]School of Chemical, Biological and Environmental Engineering, Oregon State University, Corvallis, Oregon 97331, United States

purpose of protecting ecologic and public health.[1] Historically, exposure assessment has played a complementary role with the fields of epidemiology and toxicology, helping identify and mitigate health impacts of environmental exposures, of which lead and radon serve as good examples.[1]

Recognizing the historical value of exposure science and recent demands to meet the growing need to conduct more comprehensive exposure assessment (thousands of stressors),

EXPOSURE ASSESSMENT

- International Programme on Chemical Safety

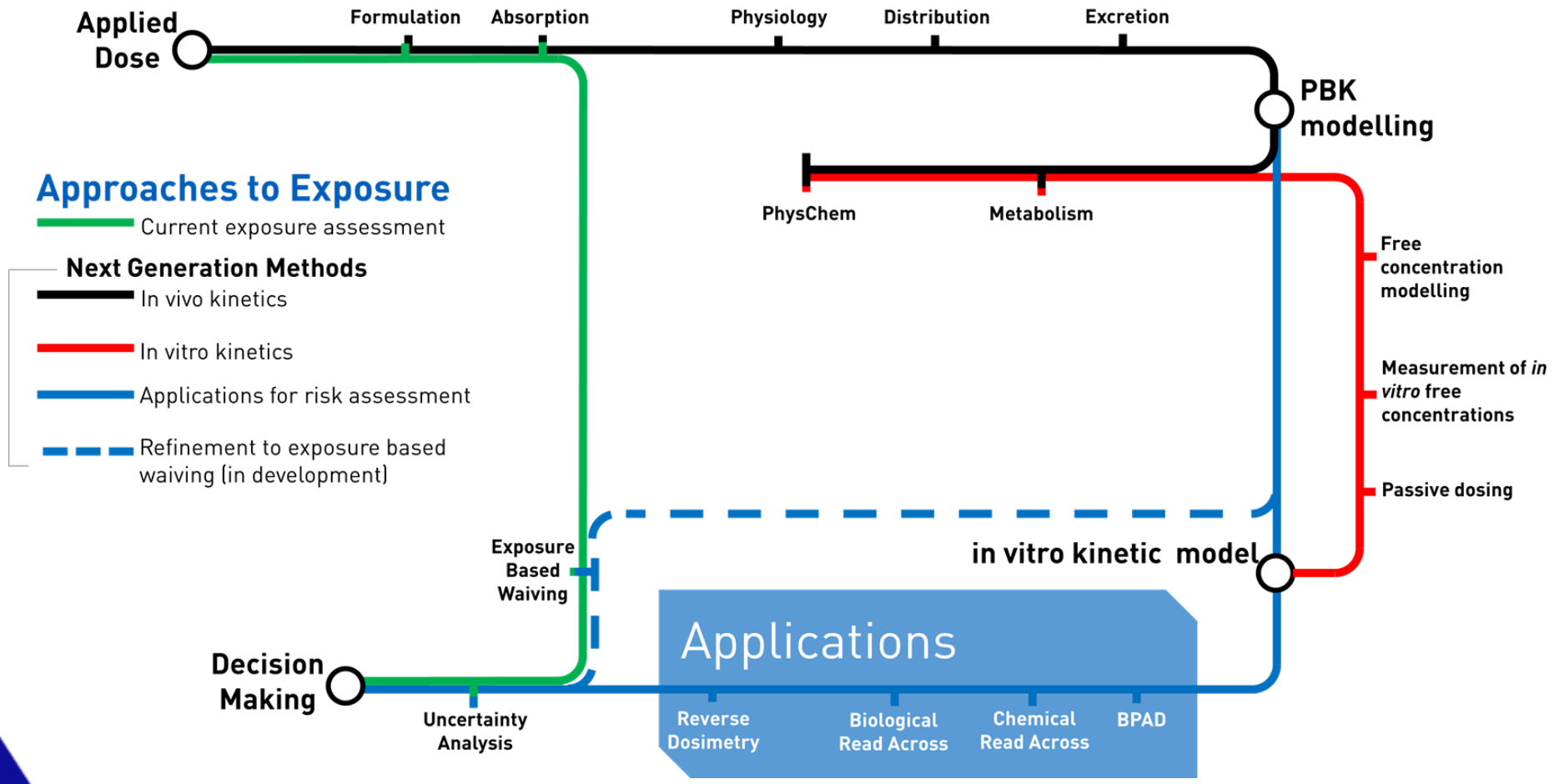
"The process of estimating or measuring the magnitude, frequency, and duration of exposure to an agent, along with the number and characteristics of the population exposed. Ideally, it describes the sources, pathways, routes, and the uncertainties in the assessment"

- Exposure to chemicals can be multi-faceted, influenced by differences in routes and duration of exposure.
- Particularly relevant in assessing chemicals used in PCPs.
  - For instance, product categories include both 'leave-on' and 'wash-off' use scenarios, where depending on the nature of the product, exposure can vary between timescales of seconds to hours (ref).

» Key exposure routes include inhalation, dermal, oral, or a combination of routes.

» Need to consider variance in consumer use habits

APPROACHES TO EXPOSURE



CURRENT EXPOSURE ASSESSMENT

- Formulation effects poorly addressed within human health risk assessment
- Maximum inclusion level in product based on human safety data for individual chemical
- Absorption is based on conservative assumptions:
- Human health risk assessment assumes 100% systemically available
- Environmental risk assessment assumes 100% emitted to environment

» Exposure based waiving adopted when inclusion levels well below toxicological threshold concentration (TTC)

NEXT GENERATION METHODS

- in vivo kinetics
- Absorption, Distribution, Metabolism, Excretion (ADME) data coupled with physiologically based biokinetic (PBBK) models
- Refinement of physicochemical properties

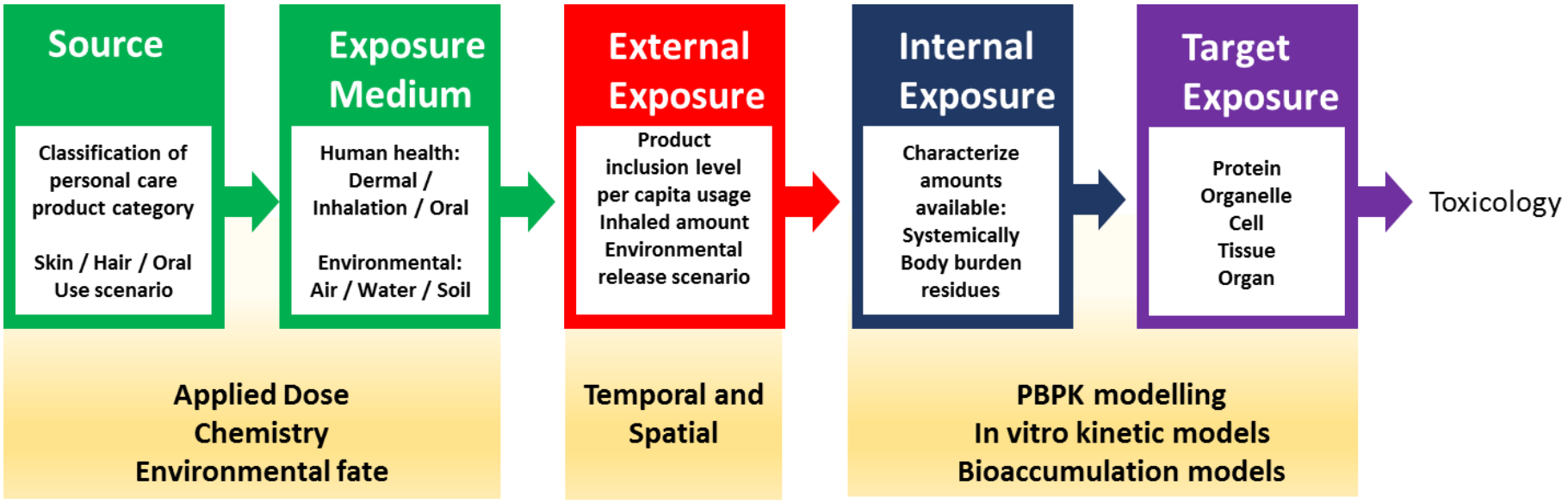
» in vitro kinetics

- Characterization of freely dissolved concentration in in vitro test system coupled with the need to better understand behaviour of parent and/or transformation product(s) in test system in relation to behaviour in vivo

» Application

- QIVIVE modelling

AEP FOR CHEMICALS USED IN PERSONAL CARE PRODUCTS (INTEGRATING HRA AND ERA)



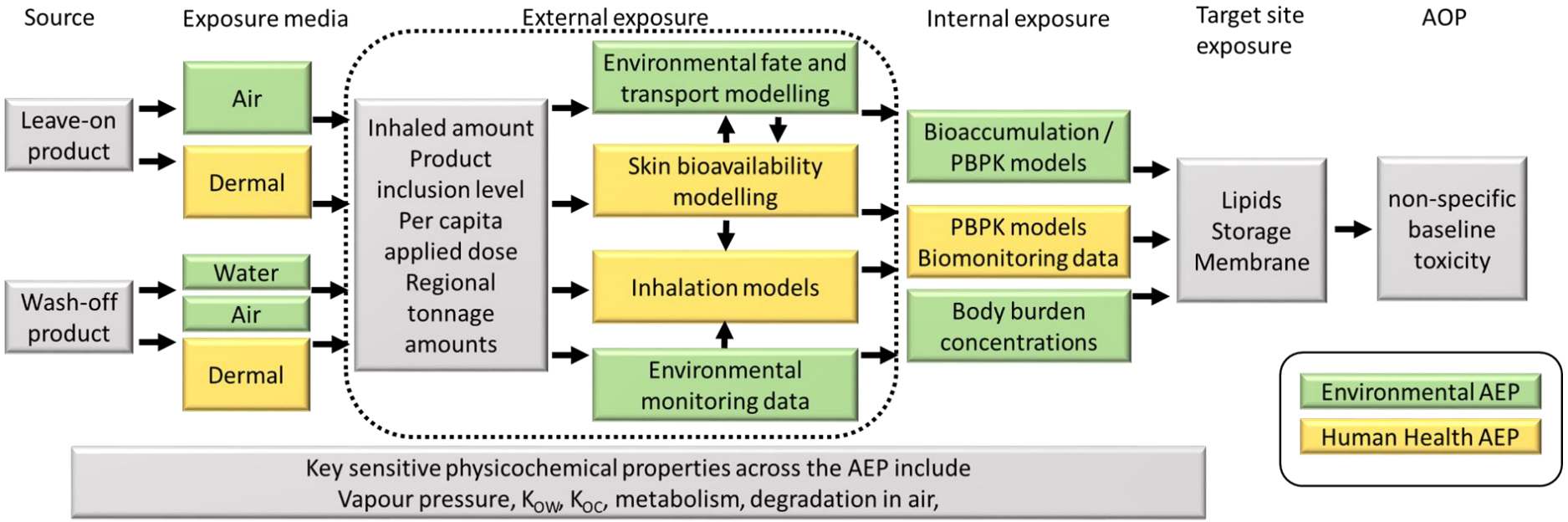
Adapted from Teeguarden et al. (2016)

ILLUSTRATIVE EXAMPLES

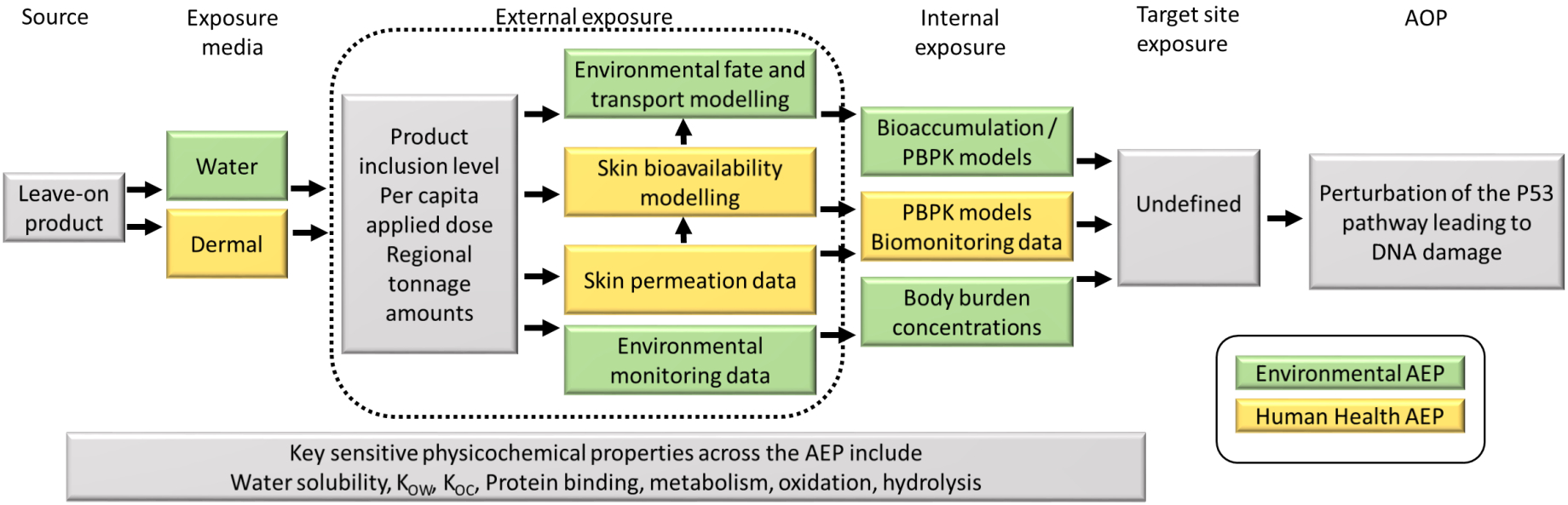
- D5 (Gouin et al. Chemosphere, 2013)
- Volatile organic, highly hydrophobic
- Used in both leave-on and down-the-drain products

- Quercetin (Adeleye et al. Toxicology, 2015)
- Highly soluble
- Used in leave-on products

D5


Source
Exposure media
External exposure
Internal exposure
Target site exposure
AOP
Leave-on product
Wash-off product
Air
Dermal
Water
Air
Dermal
Inhaled amount
Product inclusion level
Per capita applied dose
Regional tonnage amounts
Environmental fate and transport modelling
Skin bioavailability modelling
Inhalation models
Environmental monitoring data
Bioaccumulation / PBPK models
PBPK models
Biomonitoring data
Body burden concentrations
Lipids
Storage
Membrane
non-specific baseline toxicity
Environmental AEP
Human Health AEP
Key sensitive physicochemical properties across the AEP include
Vapour pressure, K_{OW}, K_{OC}, metabolism, degradation in air,

QUERCETIN


Source
Exposure media
External exposure
Internal exposure
Target site exposure
AOP
Leave-on product
Water
Dermal
Product inclusion level Per capita applied dose Regional tonnage amounts
Environmental fate and transport modelling
Skin bioavailability modelling
Skin permeation data
Environmental monitoring data
Bioaccumulation / PBPK models
PBPK models Biomonitoring data
Body burden concentrations
Undefined
Perturbation of the P53 pathway leading to DNA damage
Environmental AEP
Human Health AEP
Key sensitive physicochemical properties across the AEP include
Water solubility, K_{OW}, K_{OC}, Protein binding, metabolism, oxidation, hydrolysis

CONCLUSIONS

- Continuing challenges in assessing exposure of chemicals used in personal care products
- Need to develop robust exposure assessment strategy to better characterize and quantify associated uncertainties in relation to both HRA and ERA
- Adoption of AEP framework provides an effective organizational framework that helps to identify and communicate key chemical specific exposure events
  - Critical in prioritizing addressing key data gaps needed for improved characterization of uncertainty
  - Enables greater confidence in decision making process