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EMORY

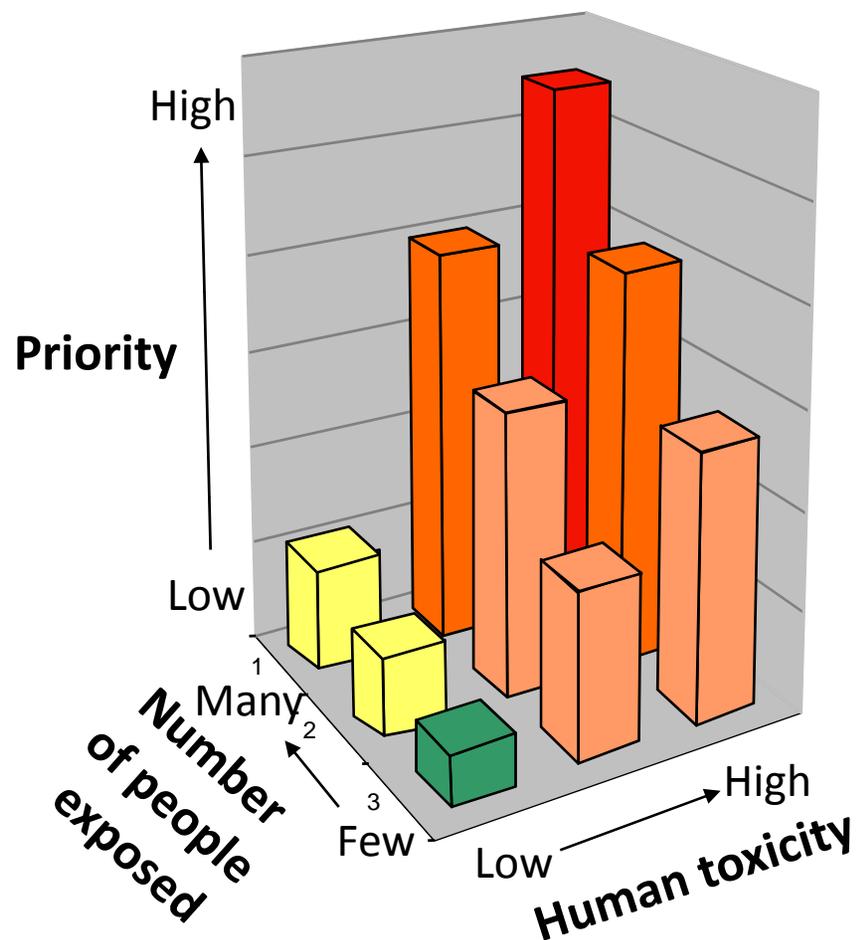
ROLLINS  
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HEALTH

# Biomonitoring of Environmental Chemicals for Exposure Assessment: is this our answer to exposure assessment?

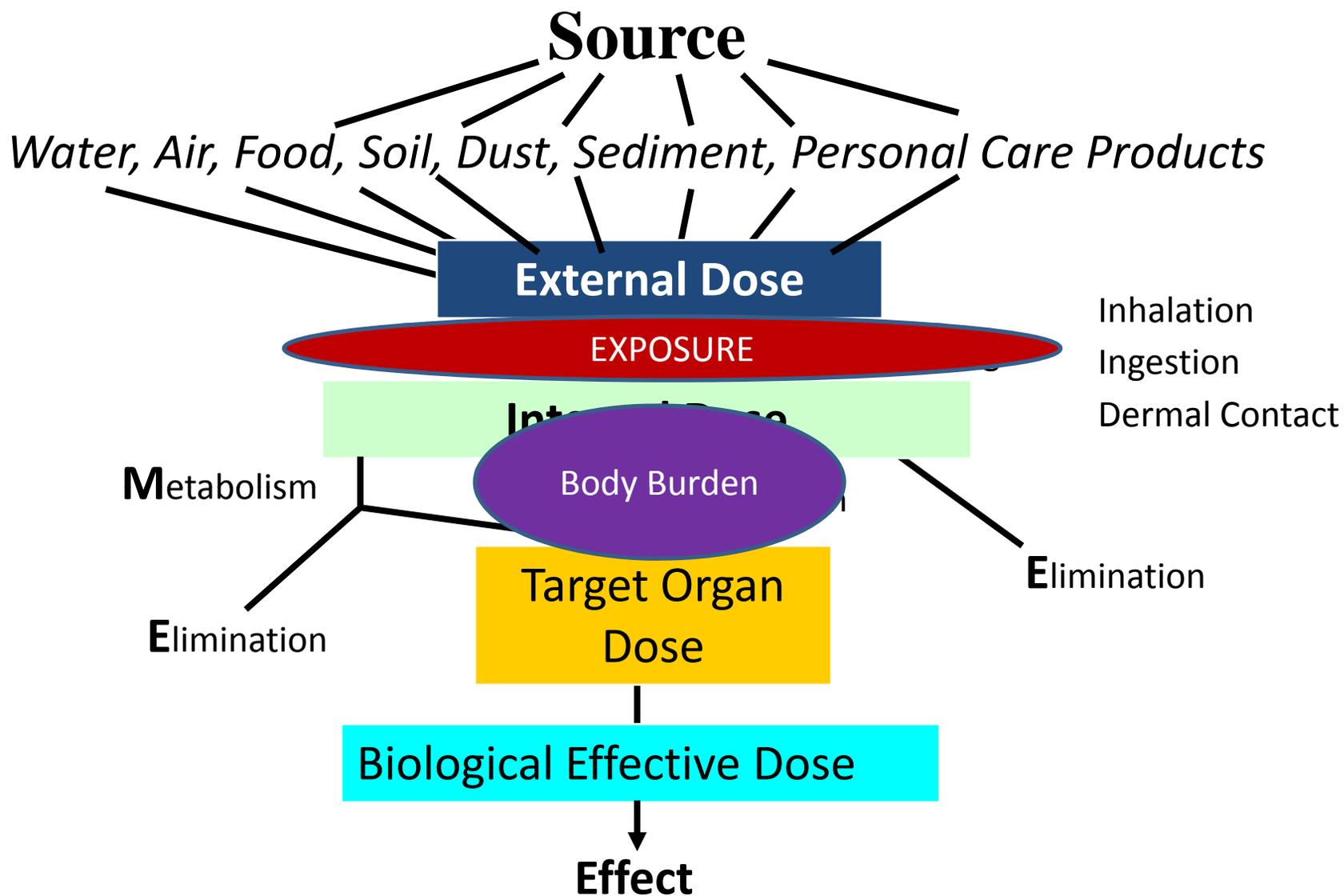
Dana Boyd Barr, Ph.D.  
Professor, Exposure Science and  
Environmental Health

# Exposure Science

- Is critical in risk assessment and risk mitigation
- No exposure, no risk, period!
- Our ability to accurately execute and evaluate resulting data is key

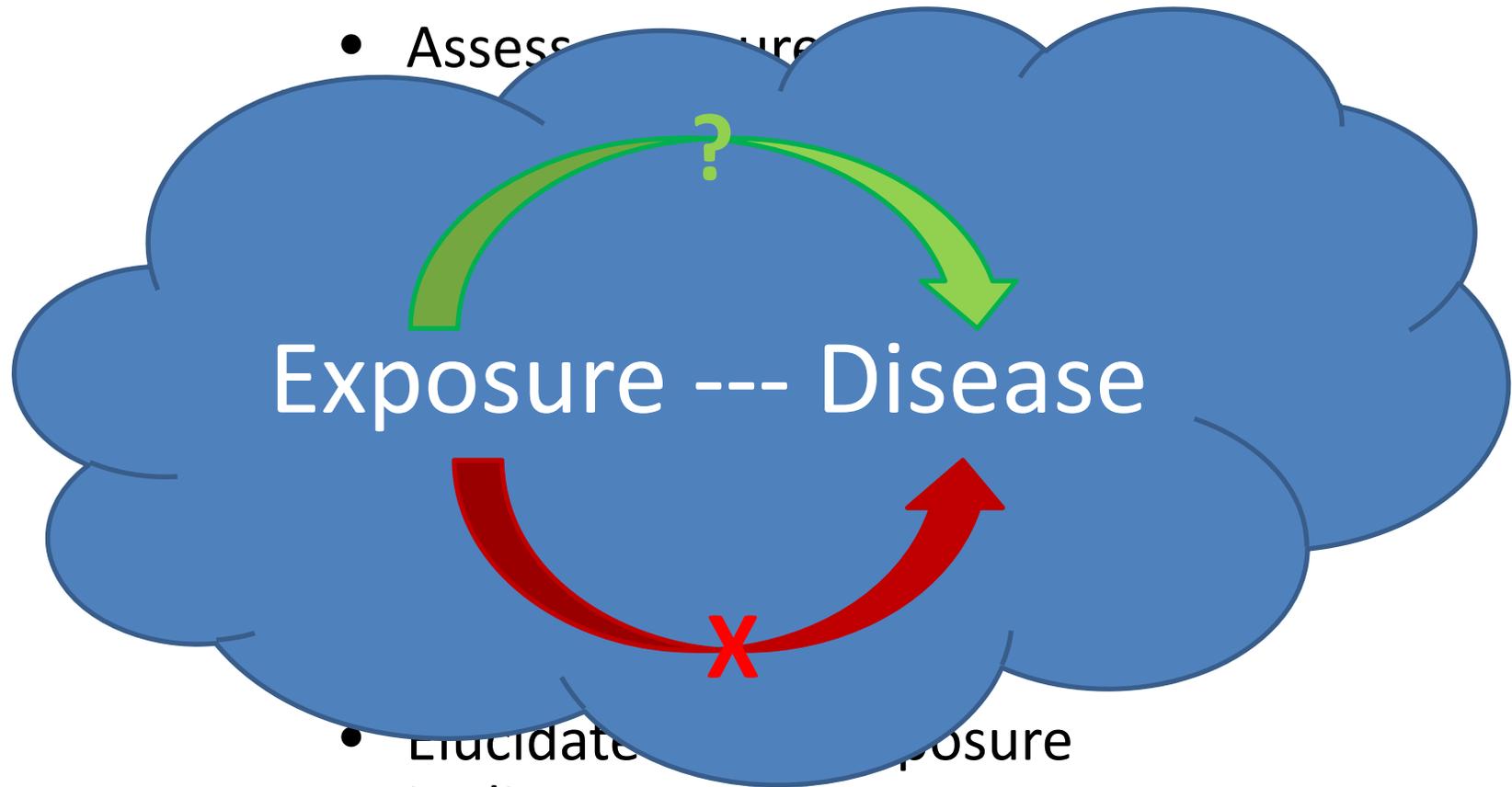


**Biomonitoring: Traditional definition ... the measurement of a chemical, metabolite or reaction product in a biological matrix ... may estimate the body burden or internal dose**



# Why are we biomonitoring?

- Assess exposure



- Elucidate exposure in disease

# From occupational to environmental applications

- Biomonitoring present in occupational applications since late 1800s.
- Garnered support b/c of utility in industrial hygiene
- Development of BEIs and BELs which have been worker protective
- Not directly transferable to non occupational exposure



# From occupational to environmental applications

## Occupational

- Exposure timing is usually known
- Exposure pathways and routes are typically known
- Frequency, duration and magnitude of exposures usually known
- Biomonitoring usually controlled (e.g., pre and post shift)
- Hydration correction is within a single individual but compared with relatively homogenous population

## Environmental

- Exposure timing is usually unknown
- Pathways and routes are typically multiple
- Frequency, duration and magnitude of exposures is typically unknown
- Biomonitoring is often spot measurement
- Hydration states compared among more heterogeneous populations

Essentially translated *controlled occupational monitoring* to a **more complex exposure scenario** without prior consideration of differences.

# Proposed New Definition of Biomonitoring

- The process by which one considered the following criteria in
  - **Selecting** a biomatrix for measurement
  - **Selecting** analyte(s) to measure
  - **Developing** and **validating** analytic methods
  - **Developing** data sets
  - **Interpreting** resultant datasets in a meaningful and useful manner
  - **Honing** steps above
- Criteria for consideration:
  - PK and other physical properties of the chemical(s)
  - Matrices for chemical
  - What species to measure?
  - Toxicological relevance of measured species
  - Intra- and inter-person variation
  - Exposure scenarios
  - Exposure route
  - Relevant coexposures

# Biomonitoring Data are **Not** Created Equally



Chosen biomarker

Coexposures

Inherent Characteristics of  
Exposure Scenario

Biologic Variability

Study design

Analytical methodology

Comorbidity

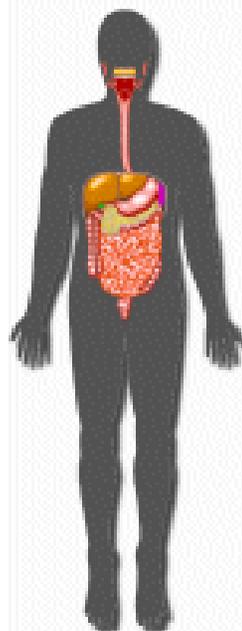
Preanalytic Considerations

# Focus Areas

- Species measured/matrix for measurement
- Exposure routes/pathways
- Relevant coexposures
- PK considerations (especially bioaccumulative fraction)
- Can biomarker and exposure ever be reconciled?
- Practical examples of biomonitoring successes and less successful applications

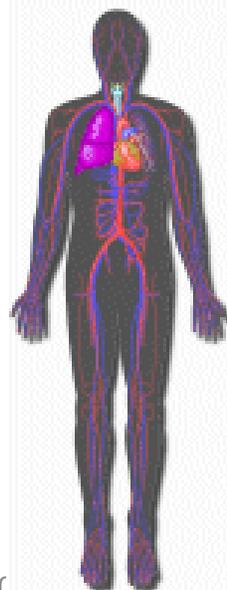
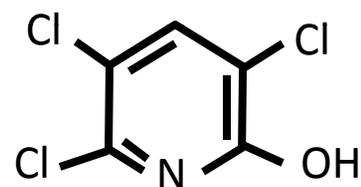
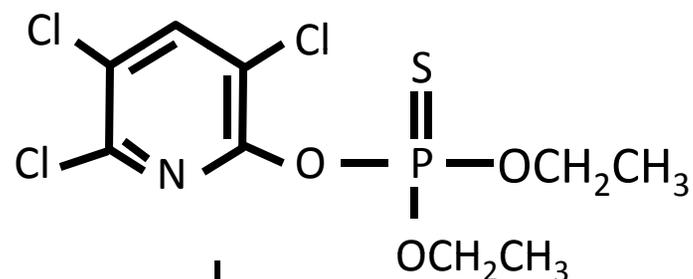


# Two similar exposures with varied toxicities



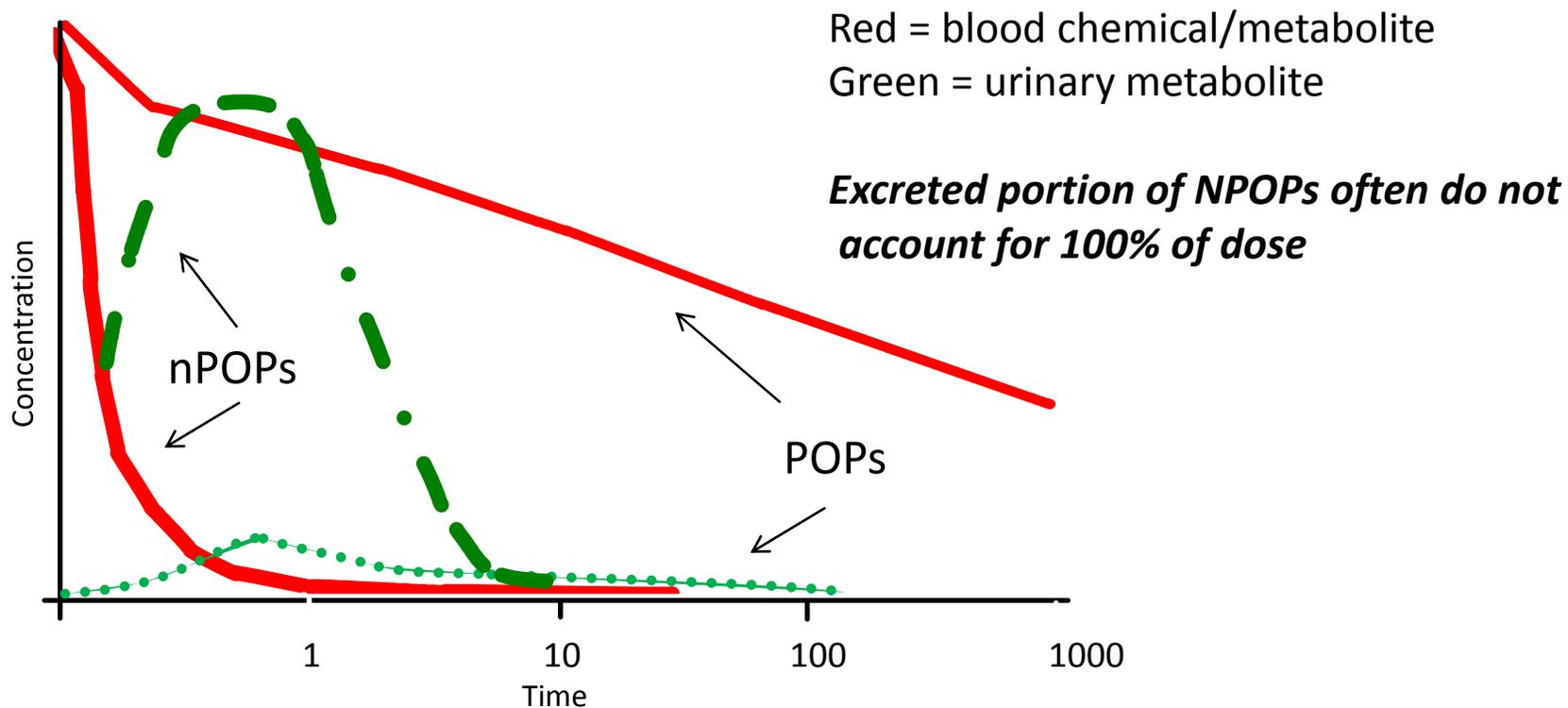
*Exposure* → *Measure*

100 mg chlorpyrifos → 100 ng/mL TCPy



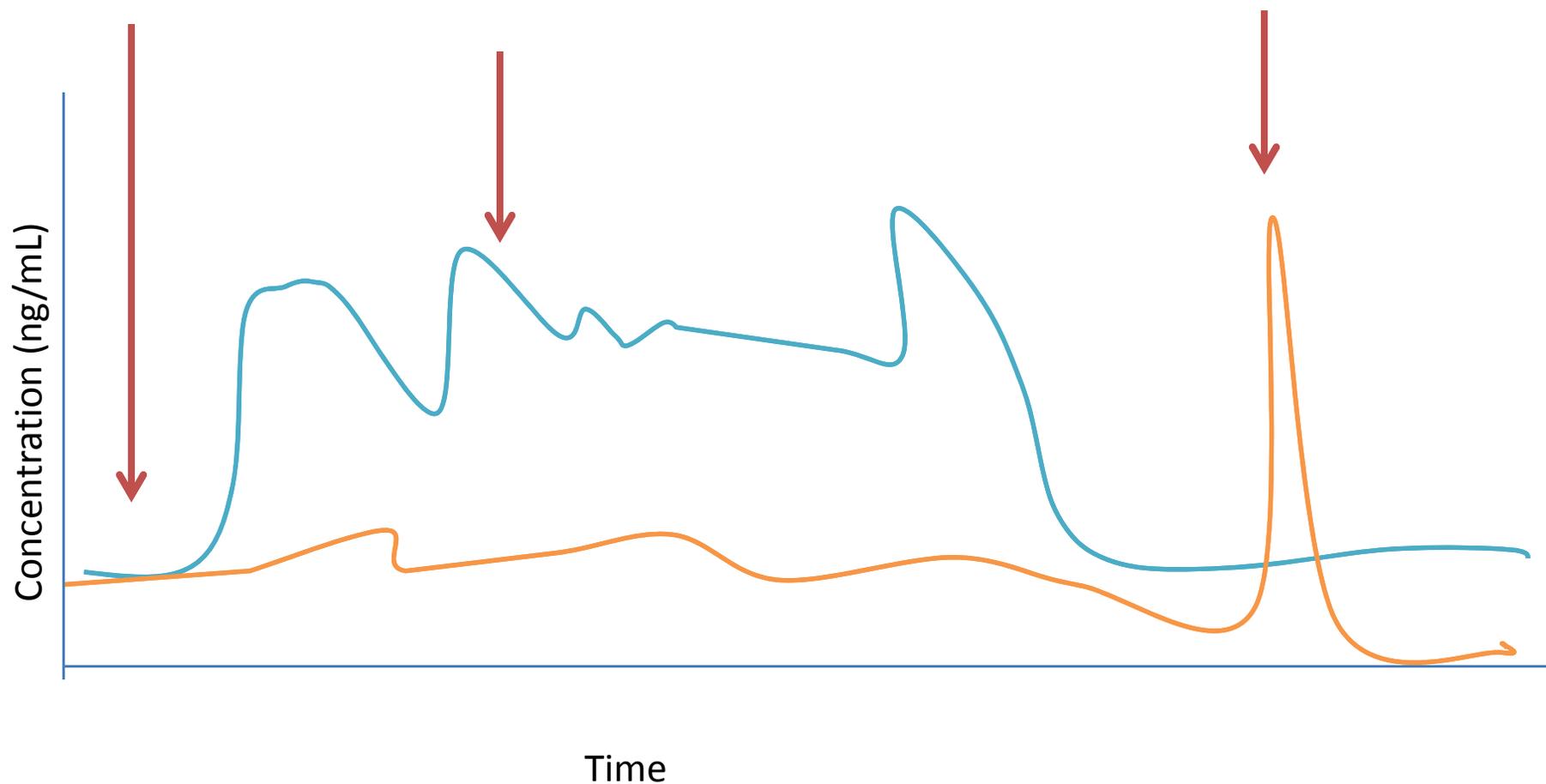
**Would the exposure route effect the toxicity?**

# Biological Persistence is a Key Factor for Consideration



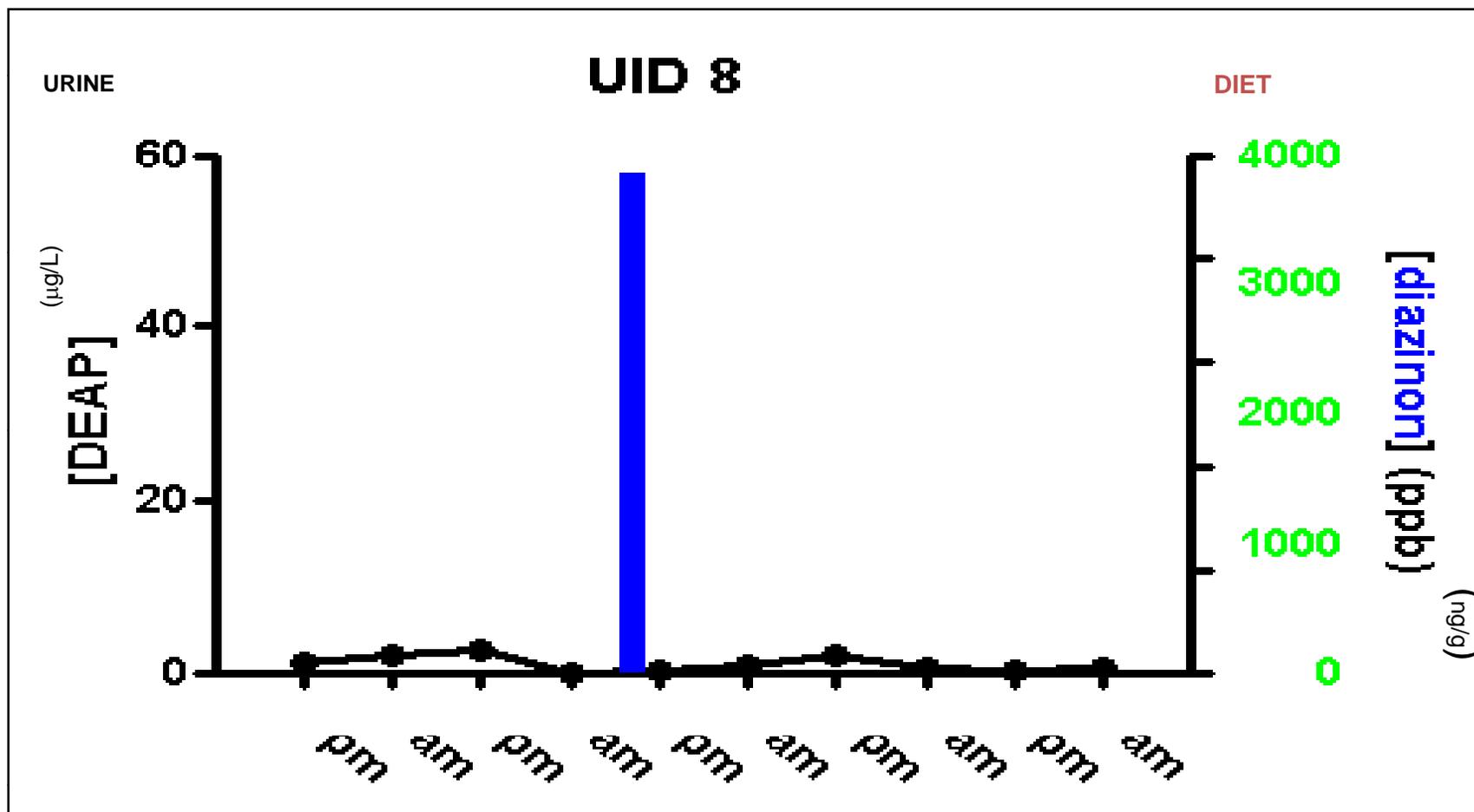
Needham and Sexton, JEAEE 10:611-629 (2000)

# Exposure Classification: High/Low

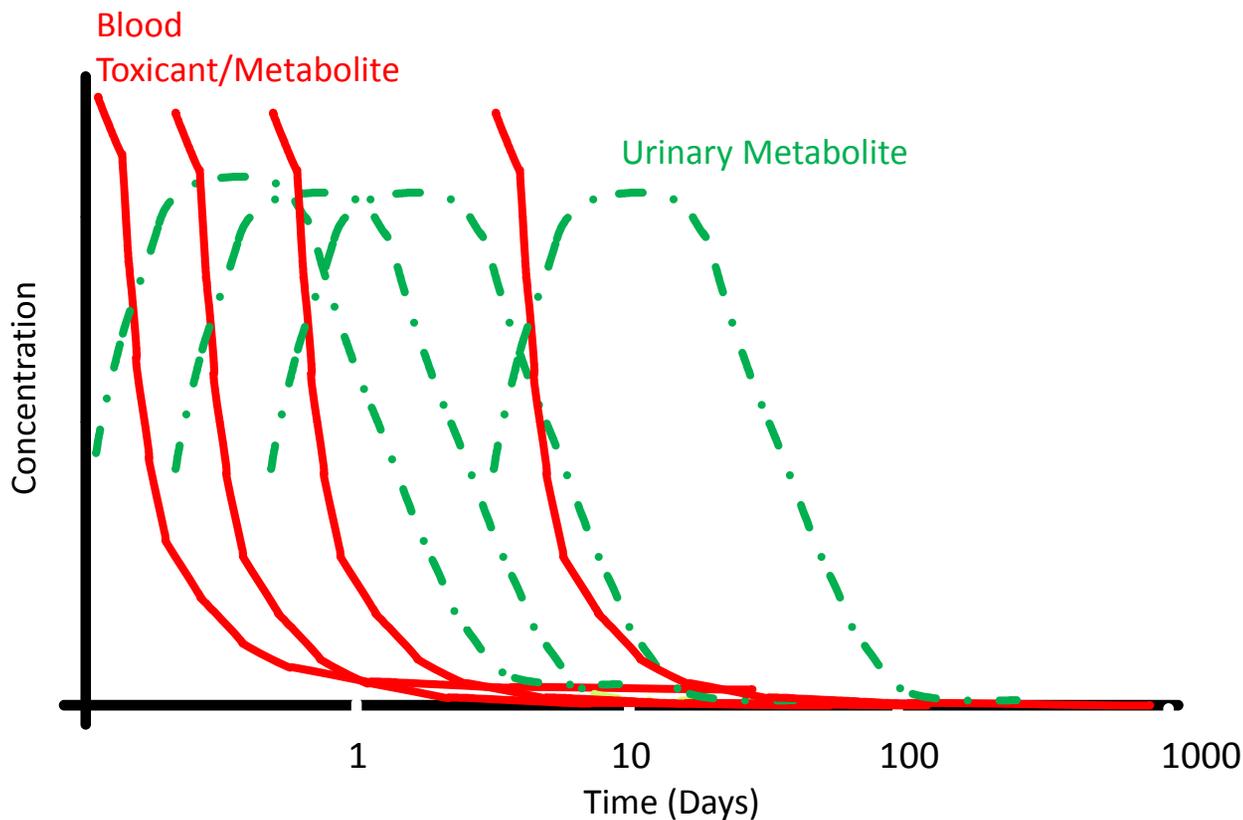


***High degree of likelihood of exposure misclassification without repeated measures***

# Can one exposure measure suffice?



# Chronic Exposure: A different story



Barr, Wang, and Needham. Environ. Health Perspect 113(8):1083-1091 (2005)

10-11-2005 Needham, Barr, and Calafat. Neurotoxicology 26:547-53(2005)

# Are we considering the “unaccounted for” fraction?.....

- Not all POPs persist biologically
- Not all nPOPs fail to bioaccumulate
- Varies not only among persons but also within persons

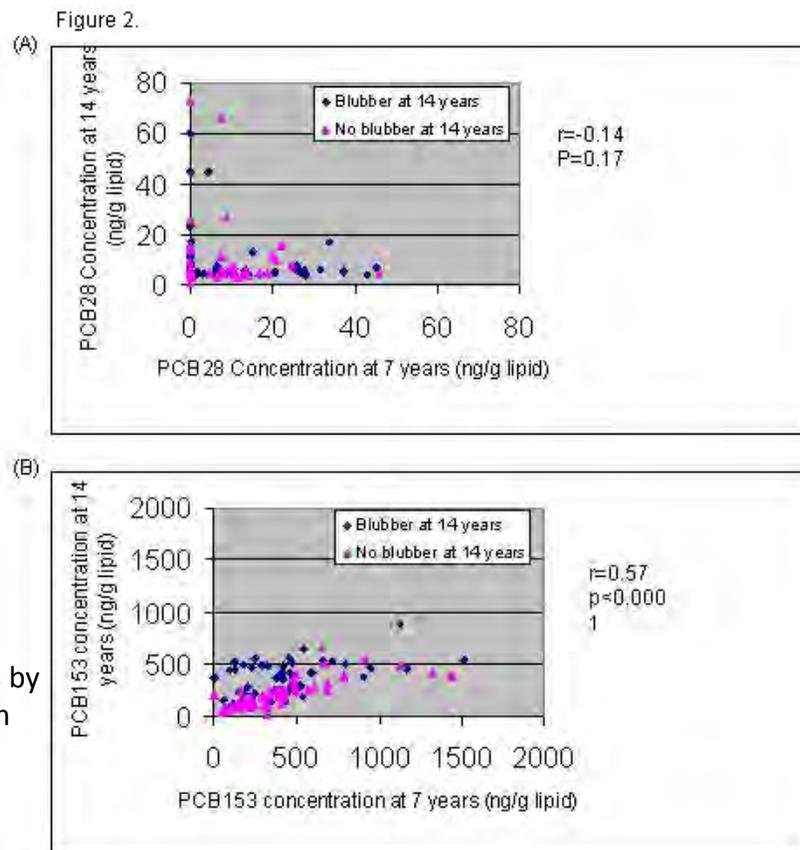
Needham LL. Assessing exposure to organophosphorus pesticides by biomonitoring in epidemiologic studies of birth outcomes. *Environ Health Perspect.* 2005;113(4):494-8

Barr DB, Weihe P, Davis MD, Needham LL, Grandjean P. Serum polychlorinated biphenyl and organochlorine insecticide concentrations in a Faroese birth cohort. *Chemosphere.* 2006;62(7):1167-82.

10-11-2011

EPA PPDC 21st Century Toxicity

16



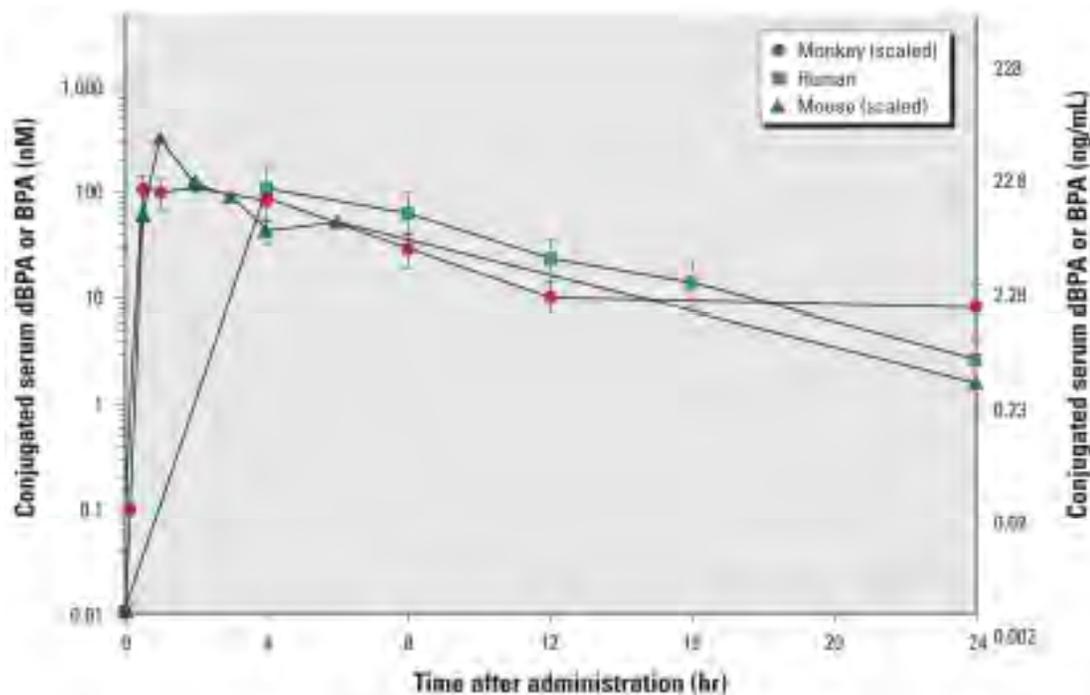
# Should we measure it because we can? BPA and drinking bottles

- Intervention study where bottled water bottles were replaced with BPA-free bottles
- BPA was measured along with other alkylated phenols
- Other alkylated phenols used as “negative” controls
- **Bottom line:** Change in bottle decreased exposure
- **Caveat:** One negative control 3BP demonstrated a change but they tried to explain away findings

[Carwile et al. Environ Health Perspect.](#) 2009 Sep;117(9):1368-72

# Measurement of Toxicologically Relevant Species?

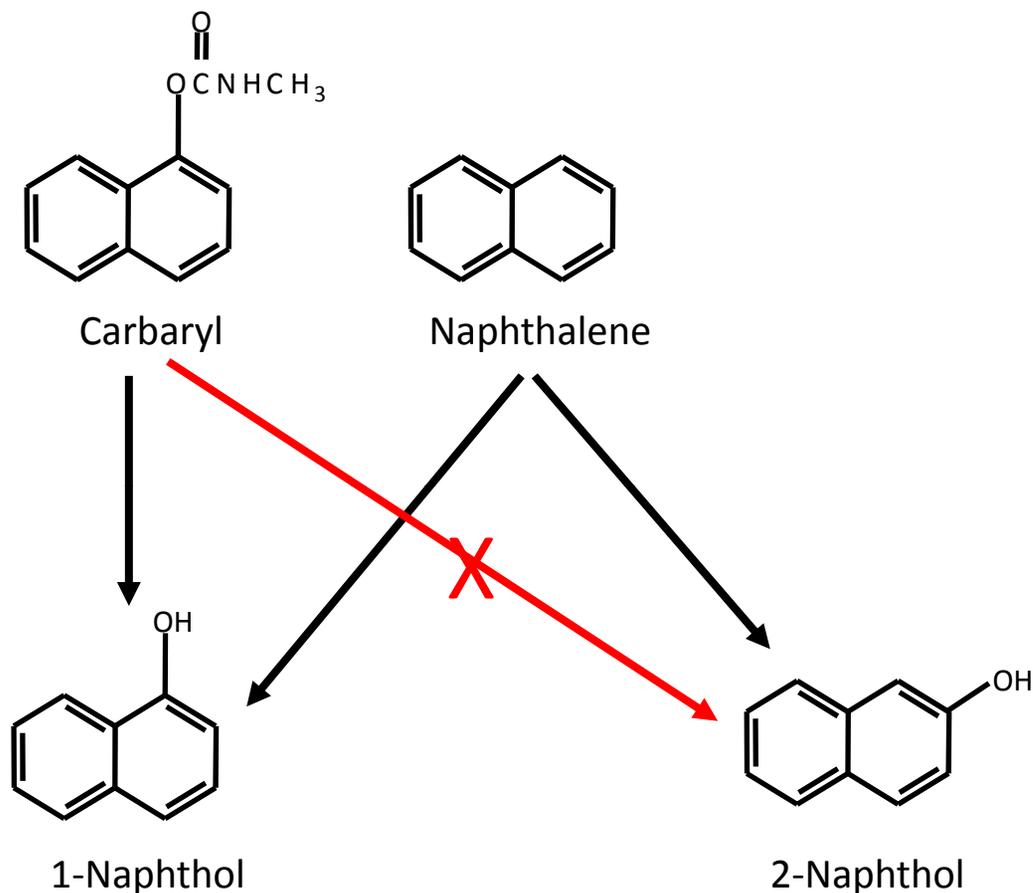
- BPA is a classic example



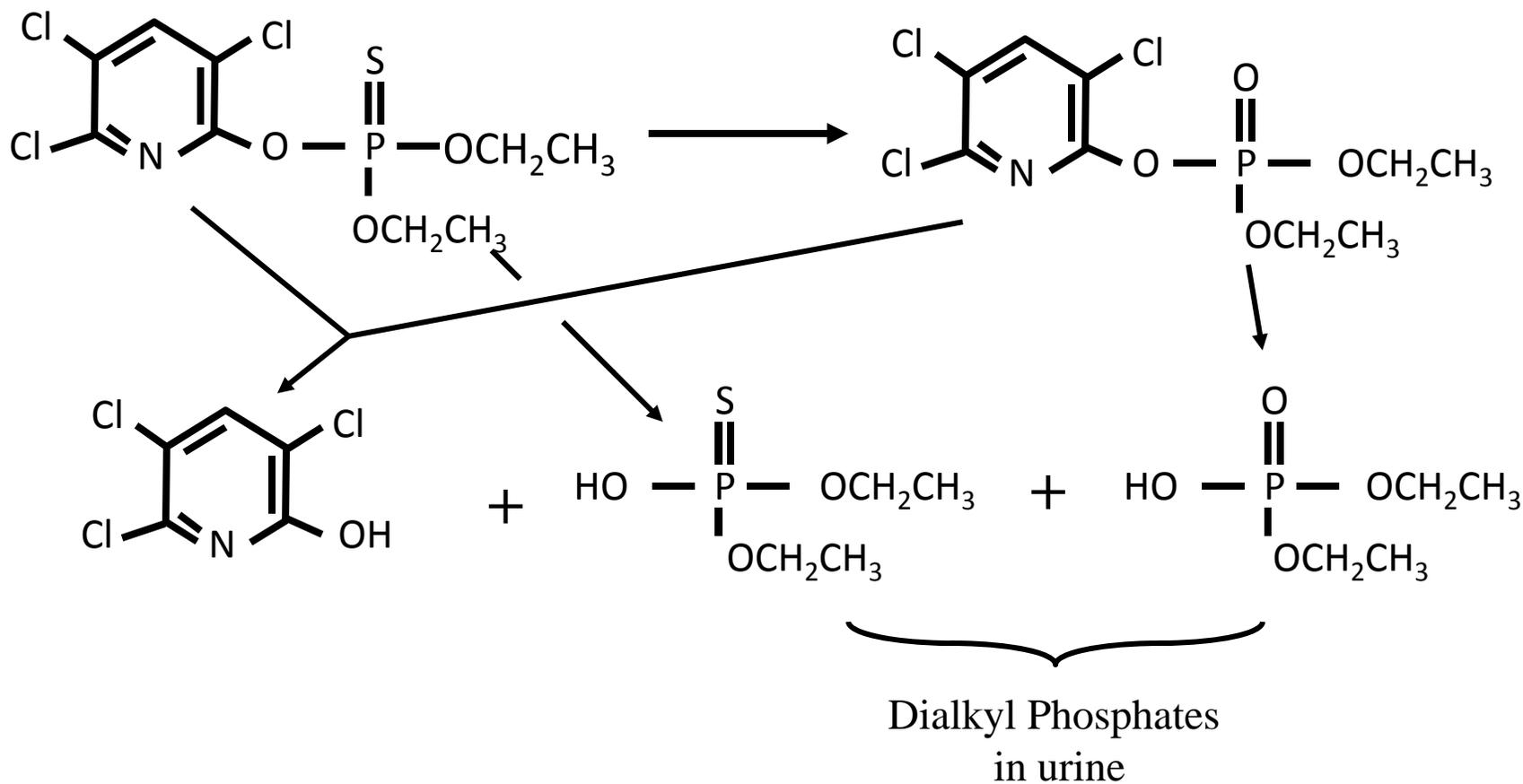
Taylor et al. Environ Health Perspect. 2011 Apr;119(4):422-30

# Specificity of Species Measured

- Is the biomarker selective for the chemical/agent it represents?
- Likely differs based upon the exposure scenario

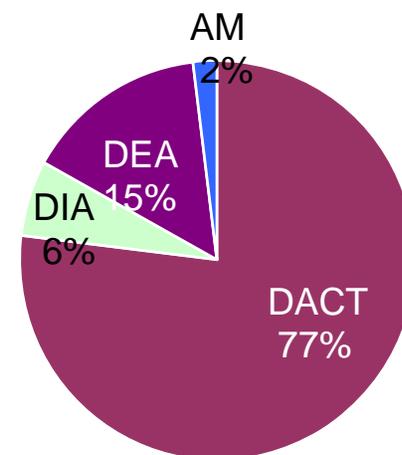
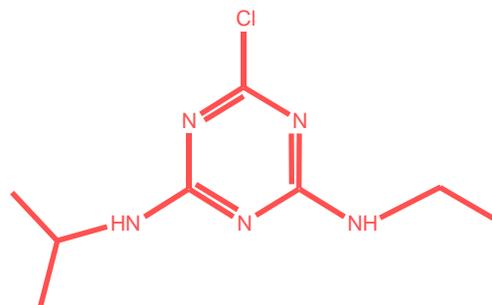


# Confounding by preformed metabolites....

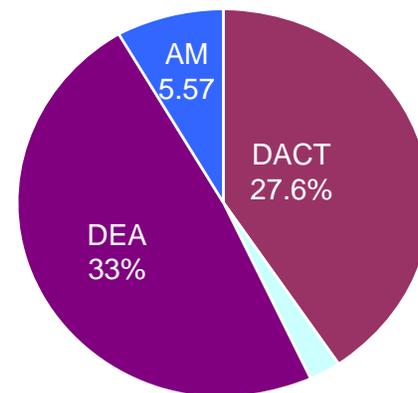


# Exposure Scenario can also dictate the chemical exposure or species to be measured

- Atrazine has >12 metabolites
- Which to measure?
- Exposure scenario is important
- Degradates become predominant in environmental exposure scenarios

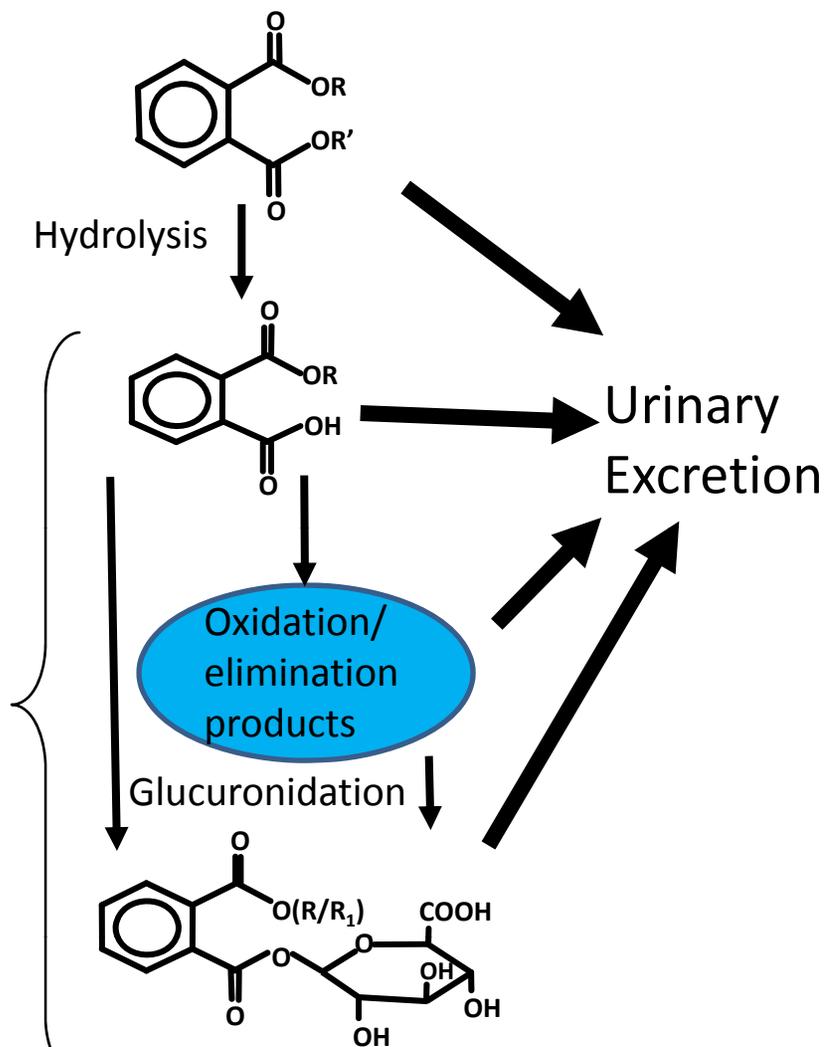
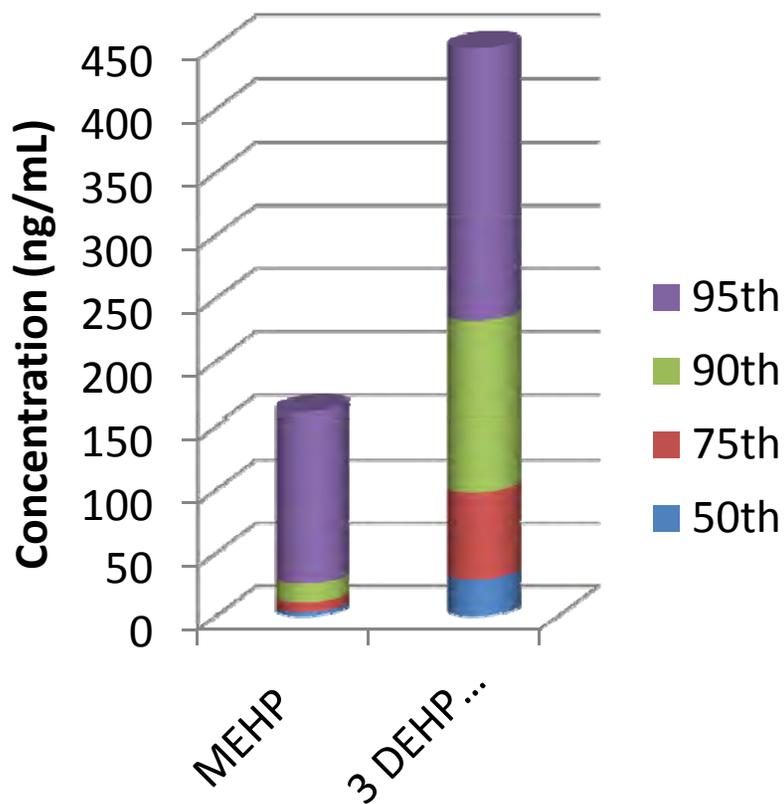


Env'l exposures



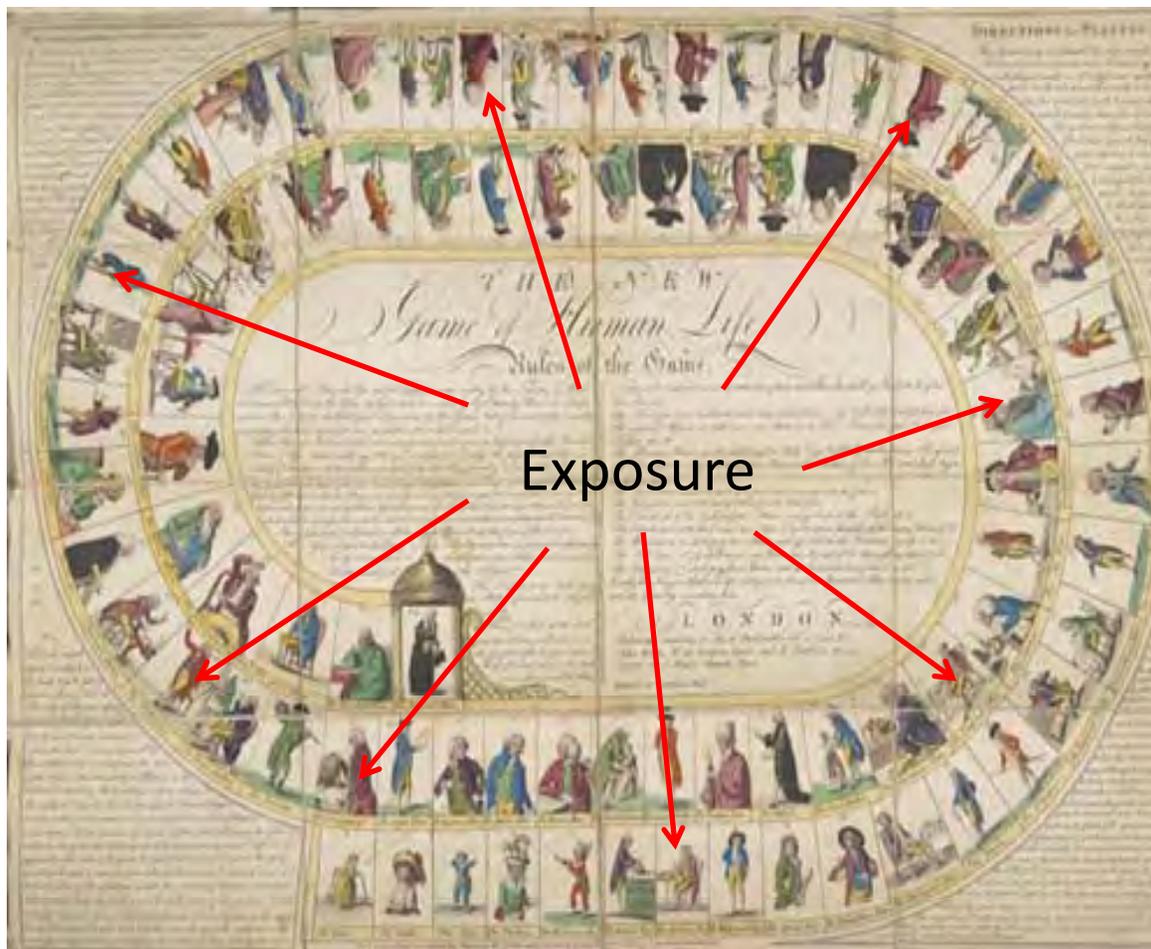
Low level acute exposures

# Phthalate Metabolism and Excretion



# Biomonitoring Hinges on the Study Design

- Exposure is dynamic
- Predicting exposure becomes difficult unless repeated empirical data are available



The New Game of Human Life: John Wallis, 1790  
EPA PPDC 21st Century Toxicity

# Contextual Parameters for Exposure

- Position in overall distribution
- Reference Ranges
- Provide context related to common exposures and biological measurements and ***how these alter our bodies' ability to handle exposures***
  - Caffeine
  - Acetaminophen
  - Aspirin

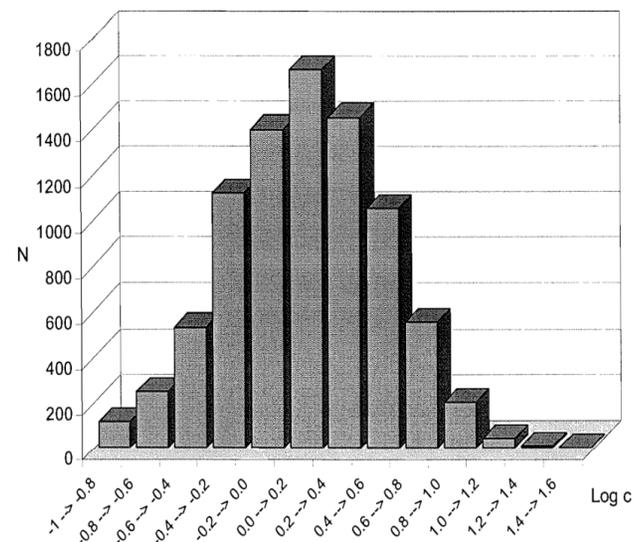


Figure 2: Distribution of log-transformed urinary caffeine concentrations of urine samples exceeding the LOQ of the analytical method.

Units mg/L

[http://proceedings.live-record.de/proceedings\\_12\\_pdf/12\\_27.pdf](http://proceedings.live-record.de/proceedings_12_pdf/12_27.pdf)

# The Unexplored Territory: Mixtures



Mixtures do not always occur by chemical class so should biomonitoring always occur by class?



# What is critically missing from current biomonitoring attempts?

- Chemicals measured are guided by convenience rather than science
- Analytic measurement quality is given precedence over the other overarching considerations
  - Toxicological relevance
  - coexposures
- One measurement is often considered sufficient without data supporting *low intra-person variability*
- Sometimes we make measurements just because we can
- Analytics have outpaced interpretive capabilities

# Successes and Pitfalls

- We've come a long way, baby!
  - Understand more now than ever
  - Idea of what we do not know
  - Biomonitoring successes
- Too narrowly focusing our efforts can be our demise



A *simple* tool used to solve a *complex* problem doesn't necessarily result in a *simple* solution.

~ Larry Wall

The process of biomonitoring is a useful tool but its reliable and effective use requires careful study design, careful chemical/analyte selection, repeated measures and the understanding of the impact of intra- and inter-person variability.



In loving memory of  
Dr. Larry L. Needham

Biomonitoring guru  
Broad thinking scientist  
Beloved mentor  
Dear friend