Perspectives on Human Biomonitoring:
Enhancing Interpretation

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American Chemistry Council
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Enhancing Interpretation and Communication

How Scientists Look at Human Biomonitoring

My talk will cover:

- Explanation of the basic principles of chemistry, toxicology and risk
- Methods to express biomonitoring results in a risk context
- Fostering better understanding of what biomonitoring means

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Human Biomonitoring

- Definition: laboratory measurement of substances in blood, urine, or other human tissues
- Scientists have always known our bodies absorb chemicals by interacting with the environment
- Detection technologies continue to improve
- Can now detect trace concentrations of many natural and synthetic substances in our bodies (ppb, ppt levels)

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Population Based Biomonitoring Studies (CDC)

- Determine which chemicals get into members of the general population and at what concentrations
- Determine if exposure levels are higher in some groups than in others
- Track temporal trends in levels of exposure
- Assess the effectiveness of public health efforts to reduce exposure
- Establish reference ranges
- Determine the prevalence of people with levels above known toxicity levels
- Set priorities for research on human health effects

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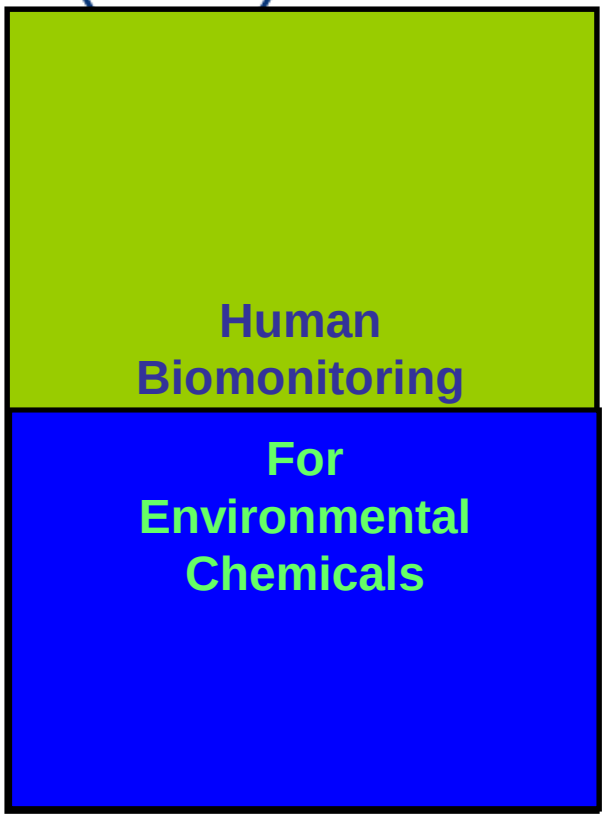
NAS Biomonitoring Report
(published July 2006)



"In spite of its potential, tremendous challenges surround the use of biomonitoring, and our ability to generate biomonitoring data has exceeded our ability to interpret what the data mean to public health"

Committee on Human Biomonitoring for Environmental Toxicants, National Research Council
http://books.nap.edu//catalog/11700.html#toc

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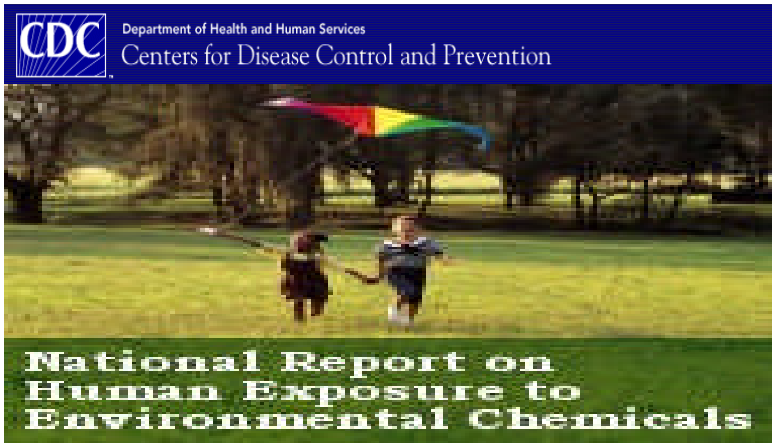
CDC and Interpretation of Human Biomonitoring



Mere detection in a biomonitoring study <u>does not</u> mean there's a health risk

"The measurement of an environmental chemical in a person's blood or urine does not by itself mean that the chemical causes disease." CDC goes on to say that the toxicity of a chemical is related to its dose or concentration and, "Small amounts may be of no health consequence, whereas larger amounts may cause adverse health effects."

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Scientific Considerations

- Presence doesn't necessarily equate to risk -- paraphrasing CDC & others -- Just because people have an environmental chemical in their blood or urine does not mean that the chemical causes disease
- Can't interpret risk from biomonitoring data alone
- Can't determine source(s) of exposure from biomonitoring data alone
- Biomonitoring can't be used alone to establish toxicity or disease causality
- Research studies are required to determine what levels of chemicals in our bodies may cause toxicity and which levels are of negligible health concern

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Interpreting Biomonitoring Data

- FIRST & FOREMOST: Need to have confidence in the data
- – Study Design
  - – Population, procedures, scope, power,
  - – Sampling plan matched to characteristics of substance & metabolism
  - – Toxicokinetics (humans, animal models)
  - – Knowledge of analyte to parent compound & confidence the source of analyte is parent compound
- – Methods & Procedures
  - – Validated analytical methods, QA, QC, proficiency demonstrations, chain of custody, storage, handling, internal standards, sample blanks, lab blanks etc.

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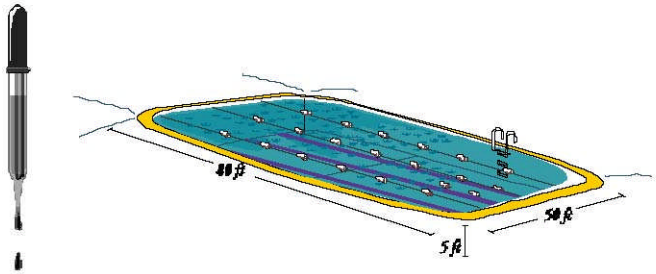
Biomonitoring: very low levels are detected in the population

- Exquisitely sensitive analytical chemistry techniques
- Biomonitoring data may be expressed as ppb
- What is a part per billion (ppb)?
  - Scientists understand ppb = 1ug/L
  - Public? analogies can help (round off)
    - 1 ppb = 1/32nd of a second in one year (1 min in 1990 yrs)
    - 1 drop in an Olympic-size swimming pool



One drop of water is 1 ppb of a swimming pool full of water

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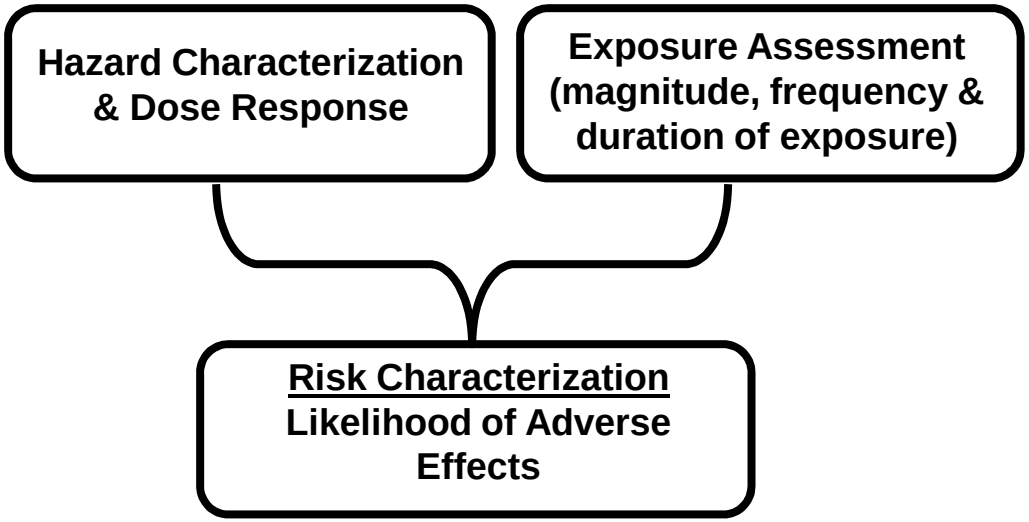
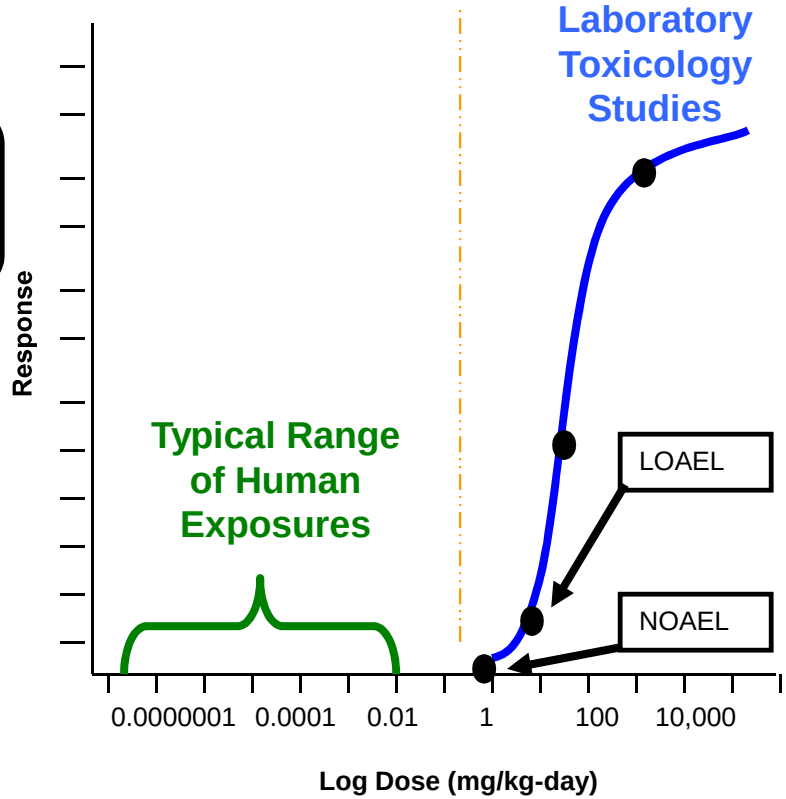
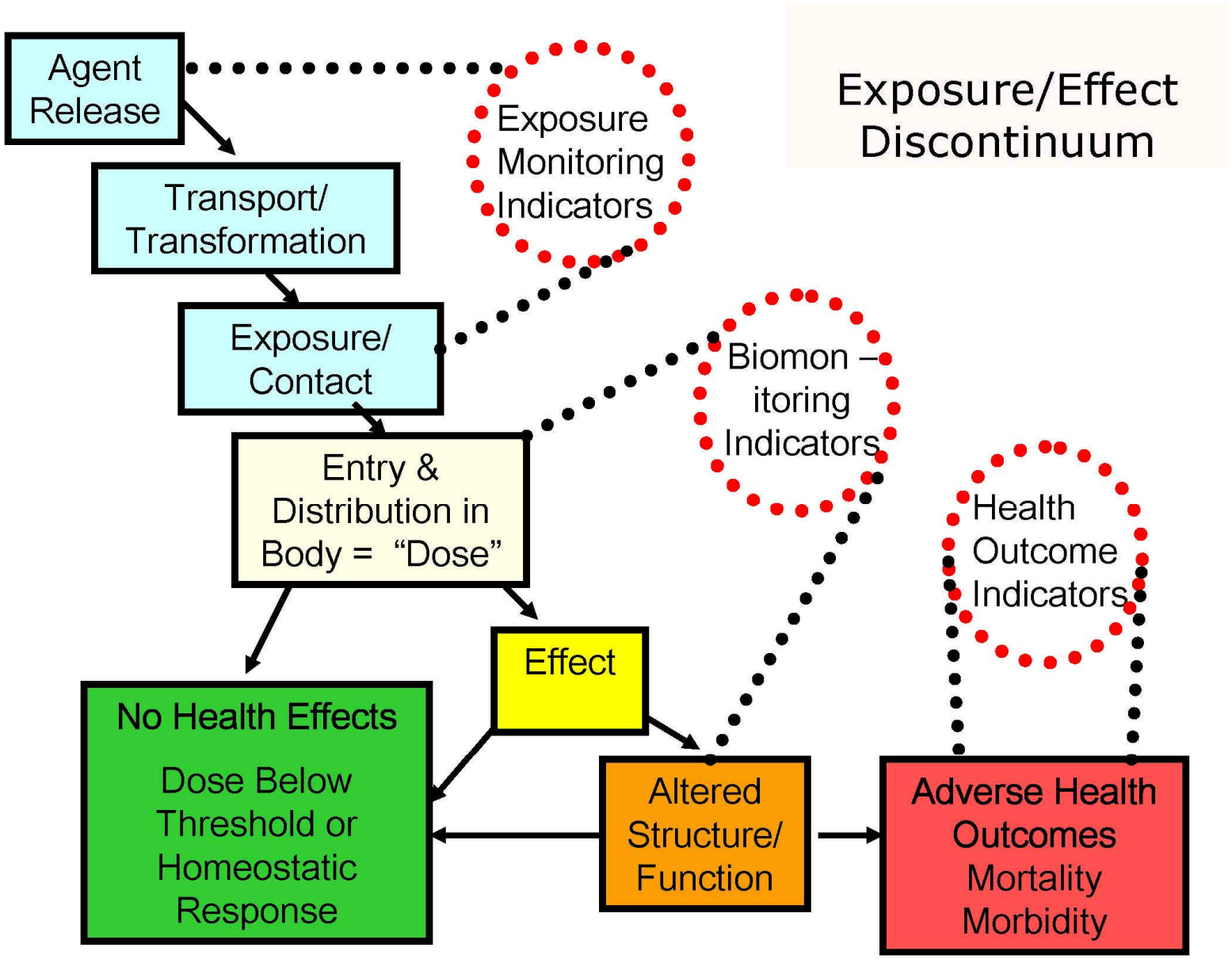
Principles: Chemistry, Toxicology and Risk

- Chemistry: IS everything and everywhere; as we interact with our environment we encounter chemicals in all that we do
- Toxicity information alone is insufficient for risk assessment
- Exposure information alone is insufficient for risk assessment

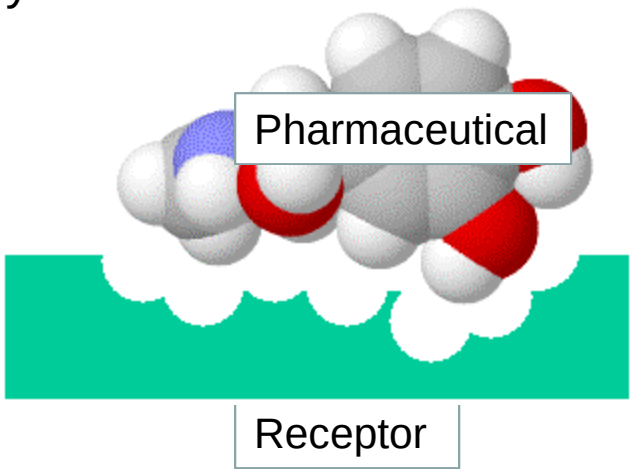


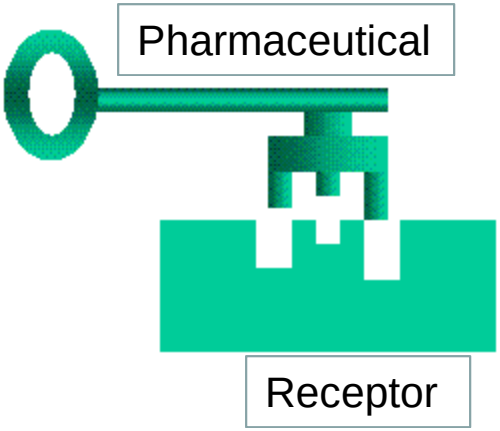



Exposure/Effect Discontinuum
Agent Release
Transport/ Transformation
Exposure/ Contact
Entry & Distribution in Body = "Dose"
Exposure Monitoring Indicators
Biomon – itoring Indicators
Health Outcome Indicators
Effect
No Health Effects
Dose Below Threshold or Homeostatic Response
Altered Structure/ Function
Adverse Health Outcomes
Mortality
Morbidity

Potency: Another Scientific Concept That's Important

Potency is the dose of a substance required to produce a specific effect of given intensity





- Pharmaceuticals are designed to have the precise molecular composition and structure to interact with the receptor sites in cells – they are very potent
- Small doses of a pharmaceutical cause effects

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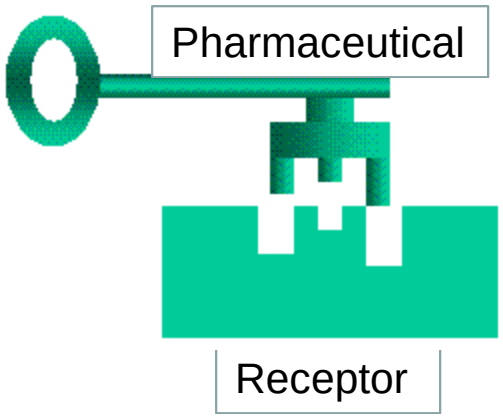
Potency (continued)

- Commodity chemicals are not designed to be biologically active
- They do not have the precise molecular composition and structure to fit into the receptor ("the key doesn't match the lock" – therefore generally are very much less potent than pharmaceuticals
- At high concentrations – 1,000 or 10,000 or 100,000 times higher than a pharmaceutical a chemical may act "like a sledge hammer to open the lock"



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Dose

- The larger the dose, the larger the response
- Threshold: dose below which no effects are produced
- Examples: ethanol, juice

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Communicating What Biomonitoring Means and What it Doesn't Mean

- Scientists need to explain what biomonitoring actually means - Draw on the principles of chemistry, biology, toxicology and risk
- How can complex information be better communicated?
  - Oversimplification can be misleading if the fundamental principles of chemistry, biology and toxicology are ignored
    - Just because chemicals produce adverse health effects at high doses in animal studies does not mean that these substances will cause adverse effects in humans exposed to much lower levels; levels that are 100s, 1000s, 10000s times less
  - Risk: the integration of exposure and hazard is the appropriate metric
    - Examples: ethanol, aspirin etc.

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Interpreting Biomonitoring Data

Reference Range	• Statistical description of levels in general population • Classify measures as “Typical” or “Atypical” • No information on potential health impacts
Clinical-Based Benchmarks	• “Gold standard”; human exposure-response data • Resource intensive • Available for very few chemicals (Lead; Ethanol)
Risk Assessment-Based Benchmarks	• Leverages existing chemical toxicology and risk assessments • Requires animal or human pharmacokinetic data

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Biomonitoring Equivalents

- Experts in risk assessment, pharmacokinetics, communication, medical ethics
- Provided guidance on the BE concept, methods, and communication.
- Results from pilot project available in *Regul. Toxicol. Pharmacol*., Vol. 51, No. 3, Supplement 1 (2008)
  - Guidelines for Derivation
  - Guidelines for Communication
  - Case Studies

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www.biomonnitoringequivalents.net

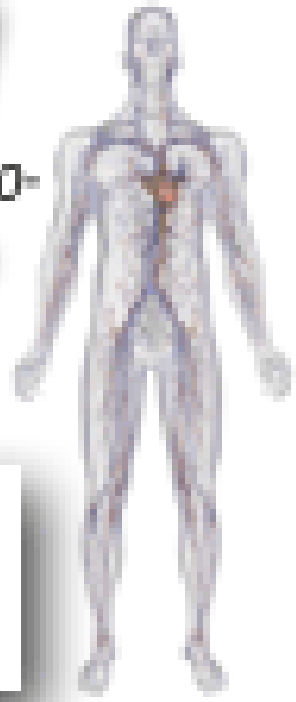
Laboratory animal data

Safety Factors

"Safe" Human Dose - RfD, MRL

Animal Pharmaco-Kinetics

Human Pharmaco-Kinetics



Rat Blood Level

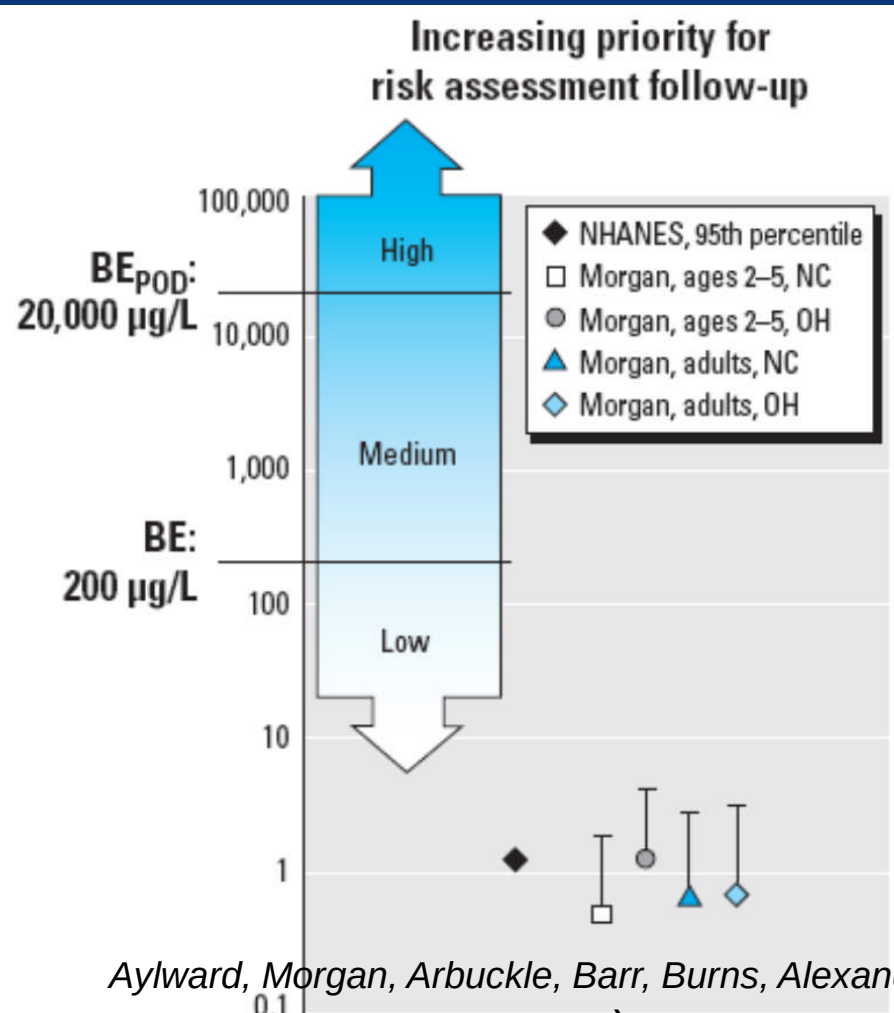
Modified Safety Factors

Human Blood Level

Example:
Use of BE to Help Interpret Data

- Herbicide with recent USEPA risk assessment
- RfD: 0.005 mg/kg-d
  - Derived from rat data
  - No-observed-effect level for bodyweight changes and biochemical endpoints: 5 mg/kg-d
  - 1000-fold UF applied
- Biomonitoring data for general population:

  <1 to 3 µg/L in urine
- What do these levels mean?



Aylward, Morgan, Arbuckle, Barr, Burns, Alexander, Hays (2010; EHP 118:117-181)

Chemicals with BE Values

Completed and Published

2,4-D
Cyfluthrin
Cadmium
Inorganic arsenic
Hexachlorobenzene
Bisphenol A
Triclosan
Diethyl phthalate
Dibutyl phthalate
Benzyl butyl phthalate
Di-2(ethylhexyl) phthalate
Dioxin TEQ (29 compounds)
Acrylamide
Chloroform
Bromoform
Dibromochloromethane
Bromodichloromethane
Methylene chloride
Carbon tetrachloride
Methyl-tert-Butyl Ether (MTBE)

n-Nonane
1,1,1-Trichloroethane
1,1,2-Trichloroethane
n-Decane
1,2,3-Trichloropropane
1,1,1,2-Tetrachloroethane
1,1,2,2-Tetrachloroethane
1,2-Dibromoethane
Hexachloroethane
1,1-Dichloroethene
cis-1,2-Dichloroethene
trans-1,2-Dichloroethene
Trichloroethene
Tetrachloroethene
Benzene
Toluene
Styrene
Ethylbenzene
Xylenes, mixed
Methyl isobutyl ketone

Dibromomethane
n-Hexane
1,1-Dichloroethane
1,2-Dichloroethane
n-Heptane
n-Octane
Acrylonitrile
Furan
Tetrahydrofuran
1,4-Dioxane
Hexabromocyclododecane

In Submission or Preparation

Di-isononylphthalate
DDT/DDE/DDD
PBDE 99
Deltamethrin

Conclusions: Meeting the Challenges Posed by Human Biomonitoring

- How Scientists Look at Human Biomonitoring
  - Scientists apply the principles of chemistry, toxicology and risk to interpret the data
  - Scientists focus on authoritative sources
  - Presence alone doesn't signify health risk
  - Research to improve methods for detecting chemicals and understanding what these levels mean is ongoing and industry is contributing to this research in a responsible manner

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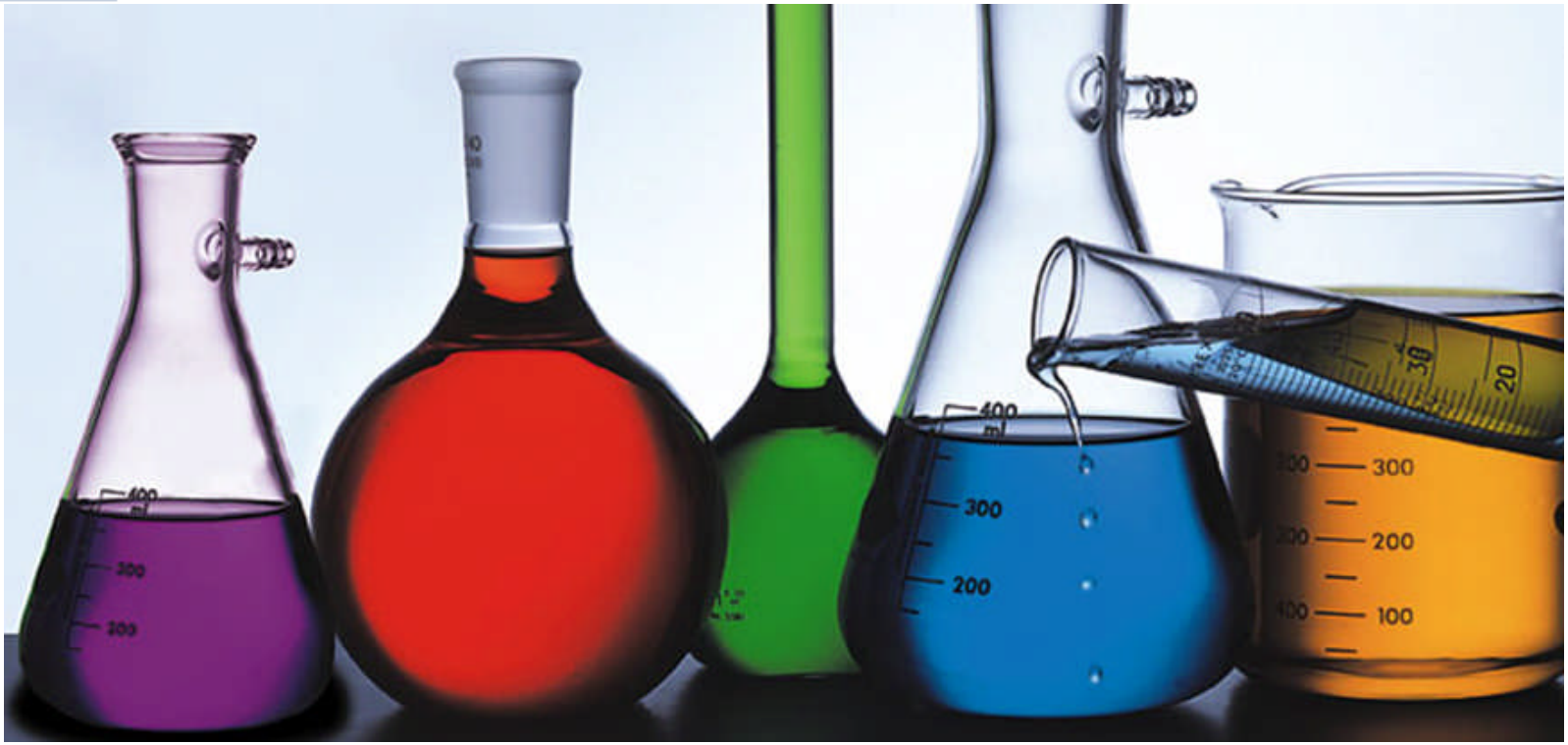
Thank You



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