Assessing Chemical Exposures: A Biomonitoring Update

Antonia M. Calafat

Organic Analytical Toxicology Branch
Division of Laboratory Sciences
National Center for Environmental Health

ILSI Annual Meeting
January 24-26, 2016
St. Petersburg, FL

Disclosure

This work was supported by the Centers for Disease Control and Prevention, U.S. Department of Health and Human Services

Human exposure to chemicals

The human exposure scenario

- Controlled conditions, as in animal studies, do not apply
- Numerous and even unknown exposure routes and sources
- Unknown dose, duration and timing
- People exposed to chemical "cocktails" (multiple/mixtures)
- How can we assess exposures?

Approaches to assess exposures

- Questionnaire/Historical Information
- Environmental monitoring
- Personal monitoring
  - Hand wipes
  - Personal samplers
- Biomonitoring

- Combine these approaches with calibrated and validated models

Biomonitoring

- Assessment of internal dose by measuring the parent chemical (or its metabolite or reaction product) in human samples
  - Integrates all sources/routes of exposure
  - Trace concentrations (vs environmental levels)
- We measure concentrations, not exposures
  - Analytical Chemistry foundation

Evaluation of human exposure using Biomonitoring at CDC – Examples

- Large –scale surveys
  - National Health and Nutrition Examination Survey (NHANES)
  - Others
- Epidemiological studies of specific populations
  - Susceptible/vulnerable
  - Highly exposed (e.g., occupational settings)
- Emergency investigations
- Disease clusters

NHANES

- **Annual survey (NCHS, CDC)**
  - US Congress funding
  - Clinical & nutritional data
- **Stratified, multistage probability sample of civilian, noninstitutionalized US population**
  - Yearly: ~5,000 persons, ~15 counties
  - Results for 2 -year cycles (e.g., 1999-2000)
- **Physical examination, collection of medical history, demographic, socioeconomic & behavioral data**
- **Also collects biological specimens**
  - Clinical chemistry tests
  - Nutritional biomarkers & environmental chemicals

http://www.cdc.gov/nchs/nhanes.htm

Biomonitoring in NHANES

- Limited amount of blood available; urine limited by age

Age (years)	Blood (mL)	Urine
1-2	9	No
3-5	22	No
6-11	38	Yes
12+	89-92	Yes

→ Yes in 2015+

→ Metals & NPs
Nutrition markers

↓

POPs (12+), Pb, Cd & Hg (1+), cotinine (3+)
Nutrition markers

- Randomly selected subsets of participants
  - Average sample size ~ 2500 people/chemical for each 2 -year cycle

National Reports on Biochemical Indicators of Diet and Nutrition

- Improve laboratory diagnosis and detection of nutrition-related diseases
- 27 biochemical indicators (2008): NHANES 1999-2002
- 58 biochemical indicators (2012): NHANES 1999-2006

Trace Elements

- Iodine (urine)
- Iron-Status Indicators
  - Ferritin (serum)
  - Iron (serum)
  - TIBC (serum)
  - Transferrin saturation (serum)
  - Protoporphyrin (erythrocyte)

Fat-Soluble Vitamins & Nutrients

- Vitamin A
- Vitamin E
- γ-Tocopherol
- α-Carotene
- *trans*-β-Carotene
- β–Cryptoxanthine
- Lutein/zeaxanthin
- *trans*-Lycopene
- 25OH-Vitamin
- Fatty Acids

Acrylamide HB Adducts

- Acrylamide
- Glycidamide

Water-Soluble Vitamins

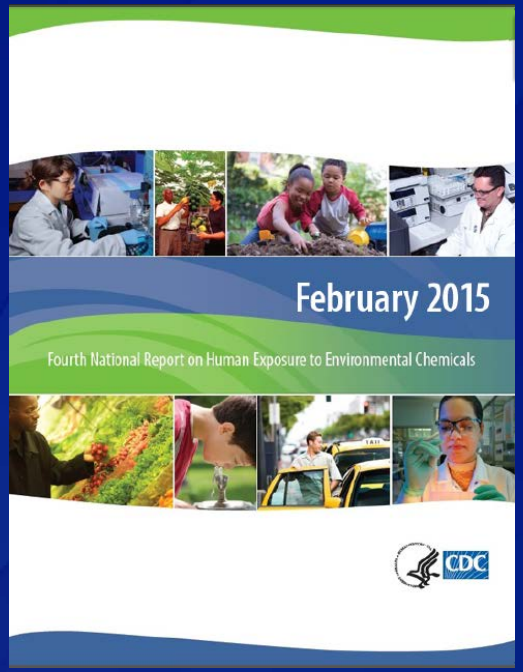
- Folate
- Vitamin B6
- Viatmin B12
- Homocysteine
- Methylmalonic acid
- Vitamin C

Isoflavones & Lignans

- Genistein
- Daidzein
- O-DMA
- Equol
- Enterodiol
- Enterolactone

http://www.cdc.gov/nutritionreport/

CDC's National Reports on human exposure to environmental chemicals



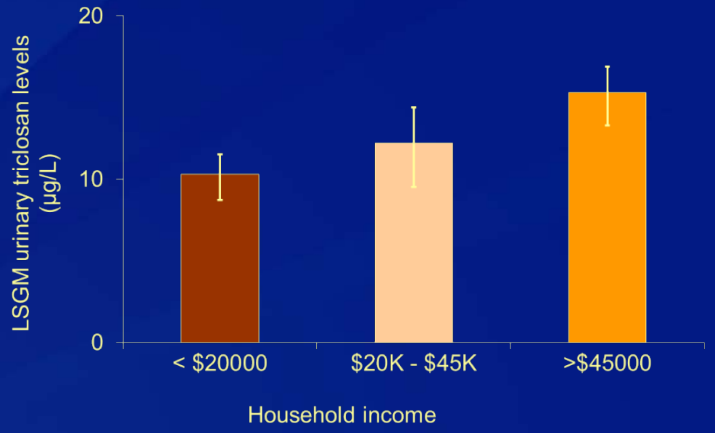
- Ongoing biomonitoring assessment of US population exposure to select metals, POPs, non-persistent chemicals
  - www.cdc.gov/exposurereport
- Set reference ranges
- Track temporal trends
- Monitor interventions
- Assist with priorities
- Exposure/risk assessment

The Exposure Reports have and don't have…

- **Limited data interpretation**
- **No health outcomes analysis**
  - The presence of a chemical in the body does not mean it causes disease
- **No identification of levels that may cause disease**
  - Additional exposure-health effect studies
- **Per NHANES design:**
  - No geographical (local, state or region) information
  - No seasonal data
  - No target populations with potential low/high exposures
    - Collaborative studies
    - National, state or local efforts
      - NYC HANES, Biomonitoring California, other
  - Limited biomonitoring data for the young

Who is exposed? How much? What chemicals?: Exposure to triclosan

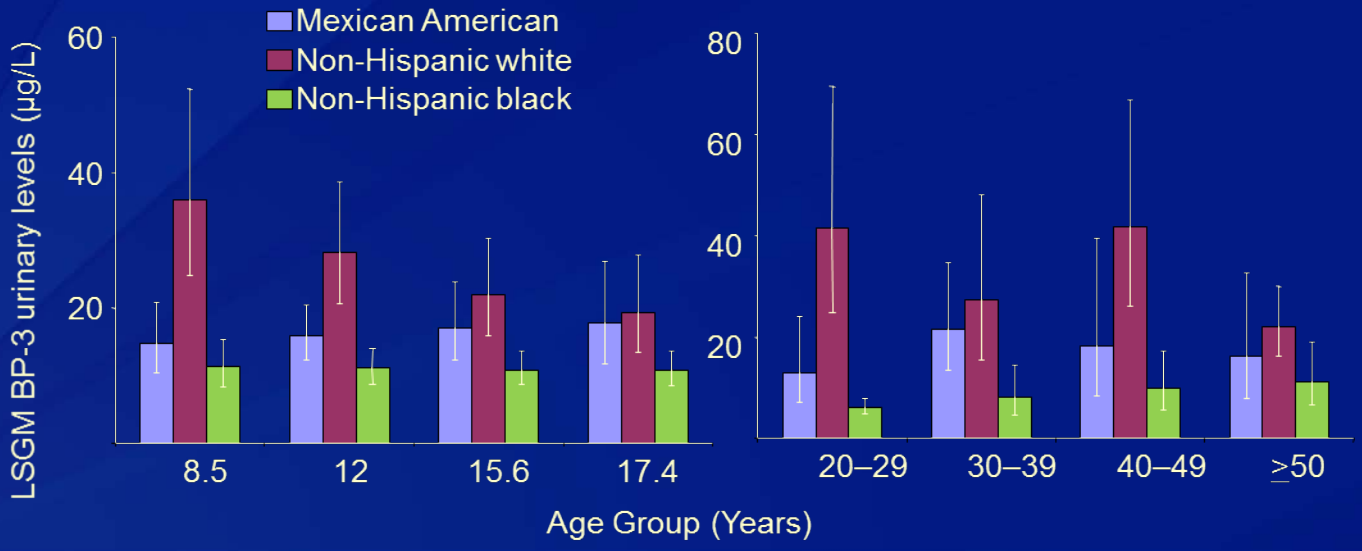
- No concentration differences by race/ethnicity or by sex
- Triclosan concentrations increase with household income



Calafat et al. EHP 2008, 116:303-7

Reference ranges: Sunscreen exposures

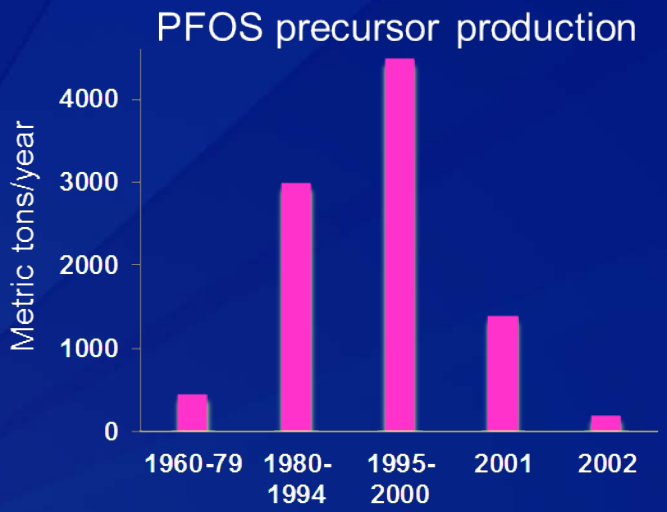
- Regardless of age, benzophenone-3 geometric mean concentrations are:
  - Higher in females than in males
  - Higher in non-Hispanic whites than in non-Hispanic blacks
- Same trends at the 95 th percentile concentrations



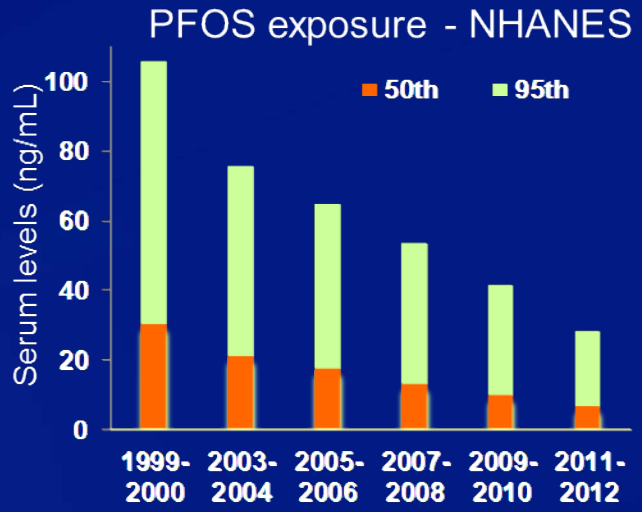
Calafat et al. EHP 2008, 116:893-7

Monitor time trends: Human exposure to PFOS

- PFCs Surfactants: Persistent, bioaccumulative & toxic
- PFOS precursors phased out (2000 -2)
  - PFOS human levels reduced by 78% since 1999 -2000
- PFOS precursors still produced in China



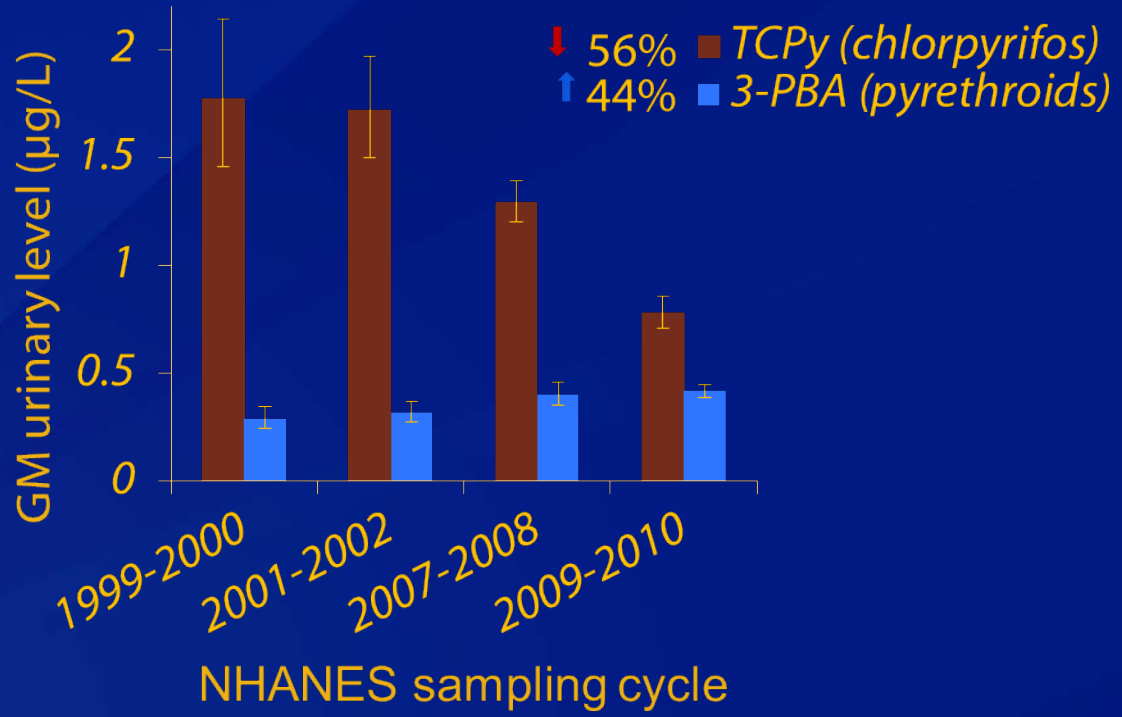
Prevedouros et al. ES&T 2006



www.cdc.gov/exposurereport

FQPA reduced exposure to organophosphate insecticides

- Phase -out residential use of chlorpyrifos (2000-1)



Error bars represent 95% confidence intervals

www.cdc.gov/exposurereport

Prevalence above thresholds: U.S. children with blood lead levels ⩾5 µg/dL

- Focus to primary prevention
- Reference level set in Oct 2012
- Based on the 97.5th percentile of blood lead distribution in NHANES 1-5 year old children
- CDC will update the reference value every four years using the two most recent NHANES datasets
- Chelation therapy considered when a child has a blood lead test result ⩾45 µg/dL

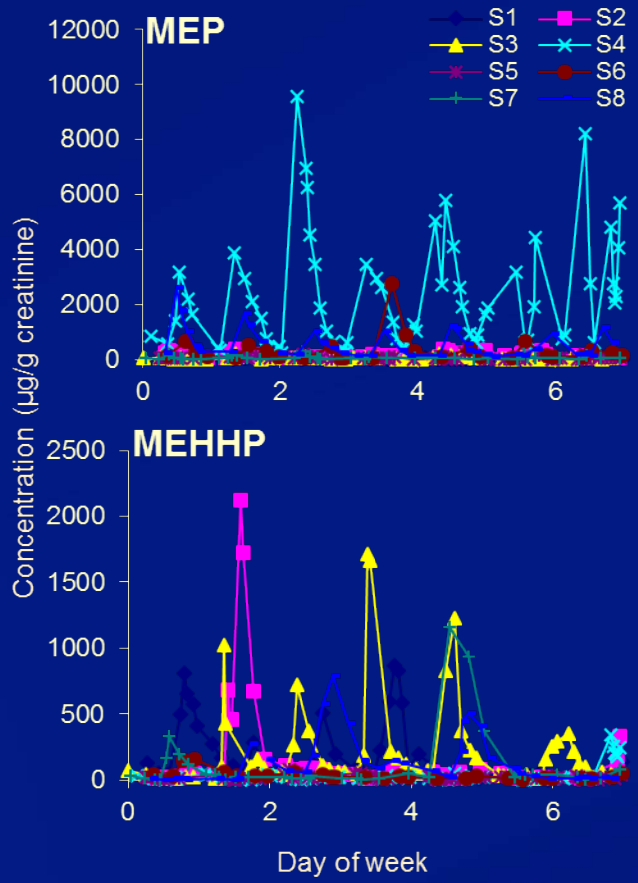
http://www.cdc.gov/nceh/lead/ACCLPP/blood_lead_levels.htm

NHANES Biomonitoring data show …

- **Widespread exposure to chemicals/chemical classes**
  - Multiple sources & exposure pathways
- **Differences in prevalence and magnitude of exposure among demographic groups**
  - Children vs adults and adolescents
    - Exposure driven (e.g., lifestyle)
    - ADME related
  - Race/ethnicity & sex differences
    - Exposure and/or genetic factors
  - SES differences
    - Lifestyle, diet, etc
- **Exposure trends**

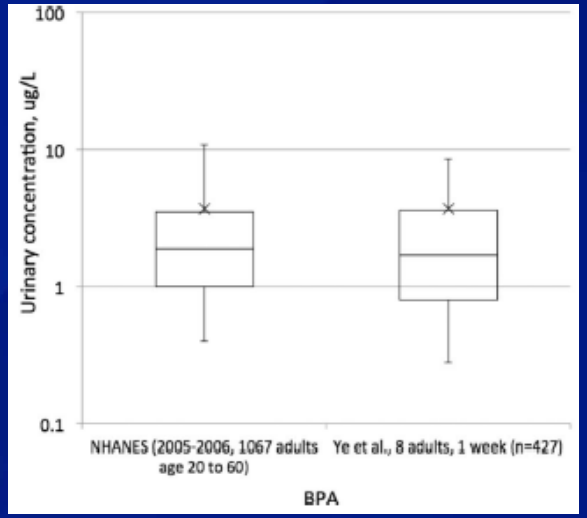
Non-persistent chemicals & variability in urinary concentrations

- **Variability is unavoidable**
  - MEP (PCP use): Mostly between-person variability
  - MEHHP: (diet) Mostly within-person variability
- **Variability factors**
  - Chemical properties
  - Nature of exposure & population
  - Timing of urine collection



Preau et al. EHP 2010, 118(12):1748-54

Can one sample be used to assess exposure?

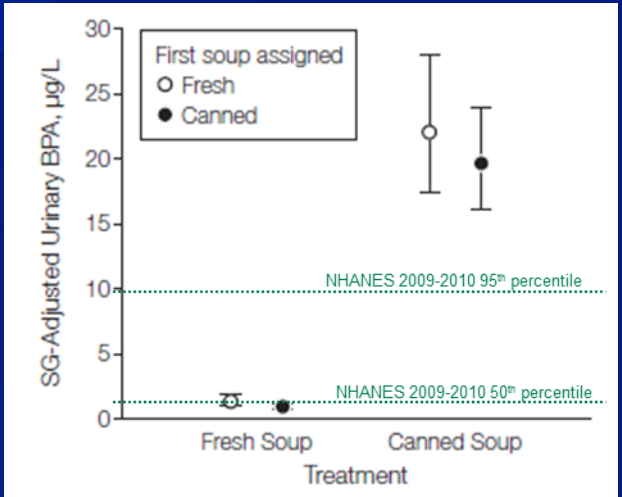


- Comparable distribution of spot sample concentrations from eight persons over one week and from NHANES 2005–2006 adults
- Range of population average urinary concentrations over time are less variable than suggested by the distribution of spot sample concentrations for compounds with rapid elimination relative to exposure frequency

Aylward et al. J Toxicol Environ Health B Crit Rev. 2014;17(1):45-61

Population variability

- BPA urinary concentrations are highly variable
  - Short-lived chemical & episodic exposures
- Urinary levels of BPA increased by 1221 per cent in people who ate canned soup compared with those who ate fresh soup



N = 75 persons

Carwile et al. JAMA 2011 306:2218-20

Take home messages – Biomonitoring

- **One tool for exposure assessment**
  - Integrates sources/routes of exposure
  - Trace vs environmental levels
  - Requires complex analytical methods
- **Interpretation of Biomonitoring data**
  - More than a laboratory measurement
  - Multiple samplings may be needed (NPs)
    - Variability
  - Collection & handling considerations (how/when/where?)
    - Stability (analyte & matrix)
    - Potential contamination
- **Used properly, biomonitoring undoubtedly improves exposure assessment**

Take home messages – NHANES

- NHANES can provide ongoing data on the exposure of the U.S. population to select environmental chemicals
- Biomonitoring, clinical and nutritional NHANES parameters can be linked to evaluate health outcomes
- NHANES per design cannot answer all public health issues
  - Need for additional studies to assess exposures in select populations
  - Separate studies of varying exposure levels and health effects are required to determine which blood and urine levels are safe and which may result in disease
- Biomonitoring NHANES data can be/have been used to support public health guidelines

Acknowledgements

DLS

NCHS

Our collaborators

THANK YOU!

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
Visit: www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info