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Program on Reproductive
Health and the Environment

UCSF

University of California
San Francisco

Non-targeted method for measuring multiple chemical exposures among pregnant women

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NIEHS, February 1, 2015



“... we must shift
...*burden of proof* from
the individual health care
provider and the
consumer to the
manufacturers *before* ...
chemicals are
....released into the
environment.” Dr.
Jeanne Conry, President
ACOG 2013



Linda C. Giudice, MD, PhD, President American Society for Reproductive Medicine and Jeanne C. Conry, MD, PhD, President, American Congress of Obstetricians and Gynecologists – October 2013, Washington, DC



Since PRHE's inception, we have seen great progress, and 2014 is no different. We know there is more to do in our overall goal towards an environment free of harmful chemicals—but we are proud of our work so far.

*Tracey Woodruff, PhD, MPH,
Professor and Director, UCSF PRHE*

*PEEC Faculty Development Investigator Roy Gerona
and PRHE Director Tracey Woodruff*



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Associate Professor



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Professor

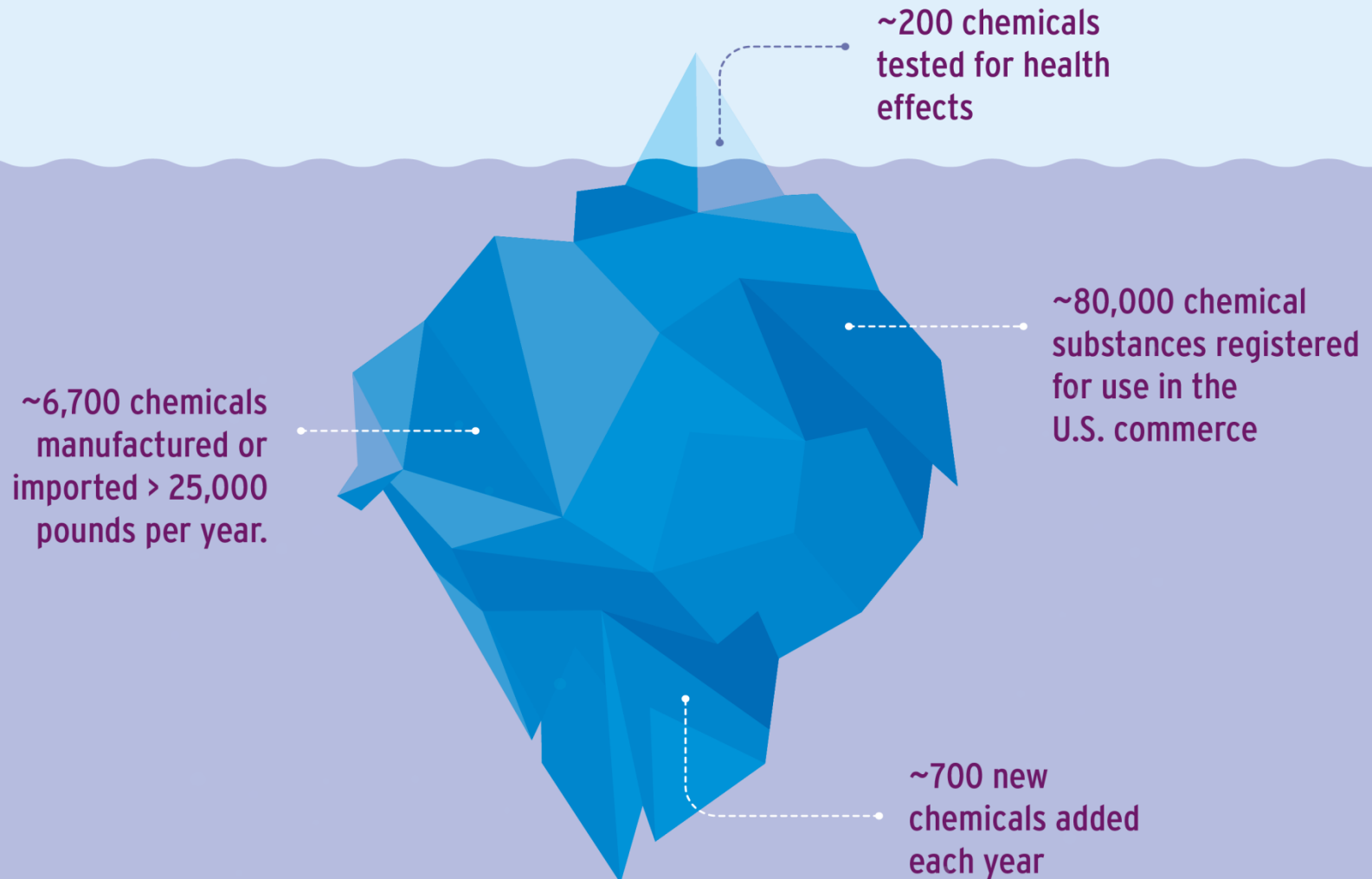
Industrial Chemicals in Virtually Every U.S. Pregnant Woman



43



Majority of Chemicals Not Tested Before Entering the Market



Peer-Reviewed Articles

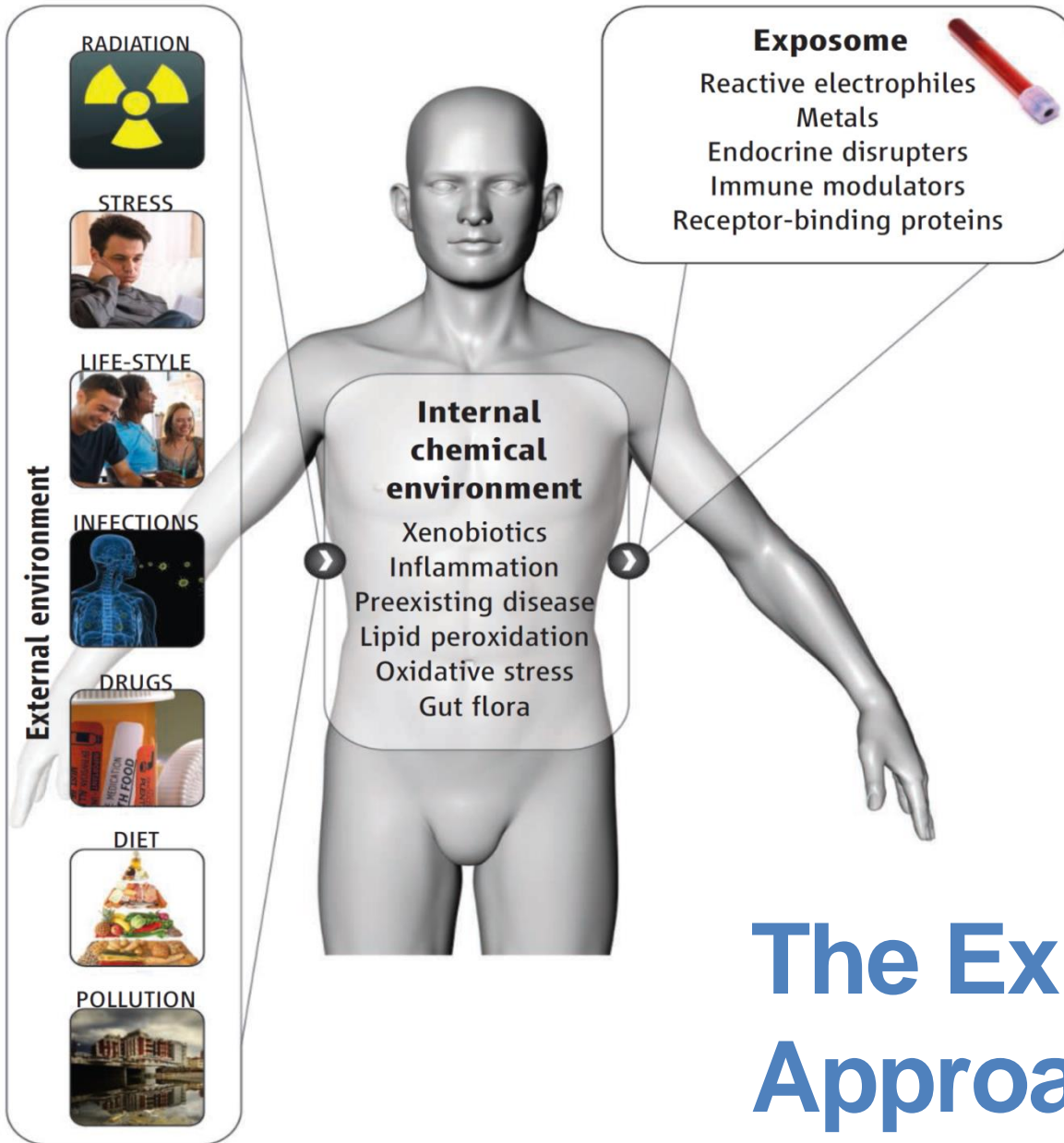


Decades



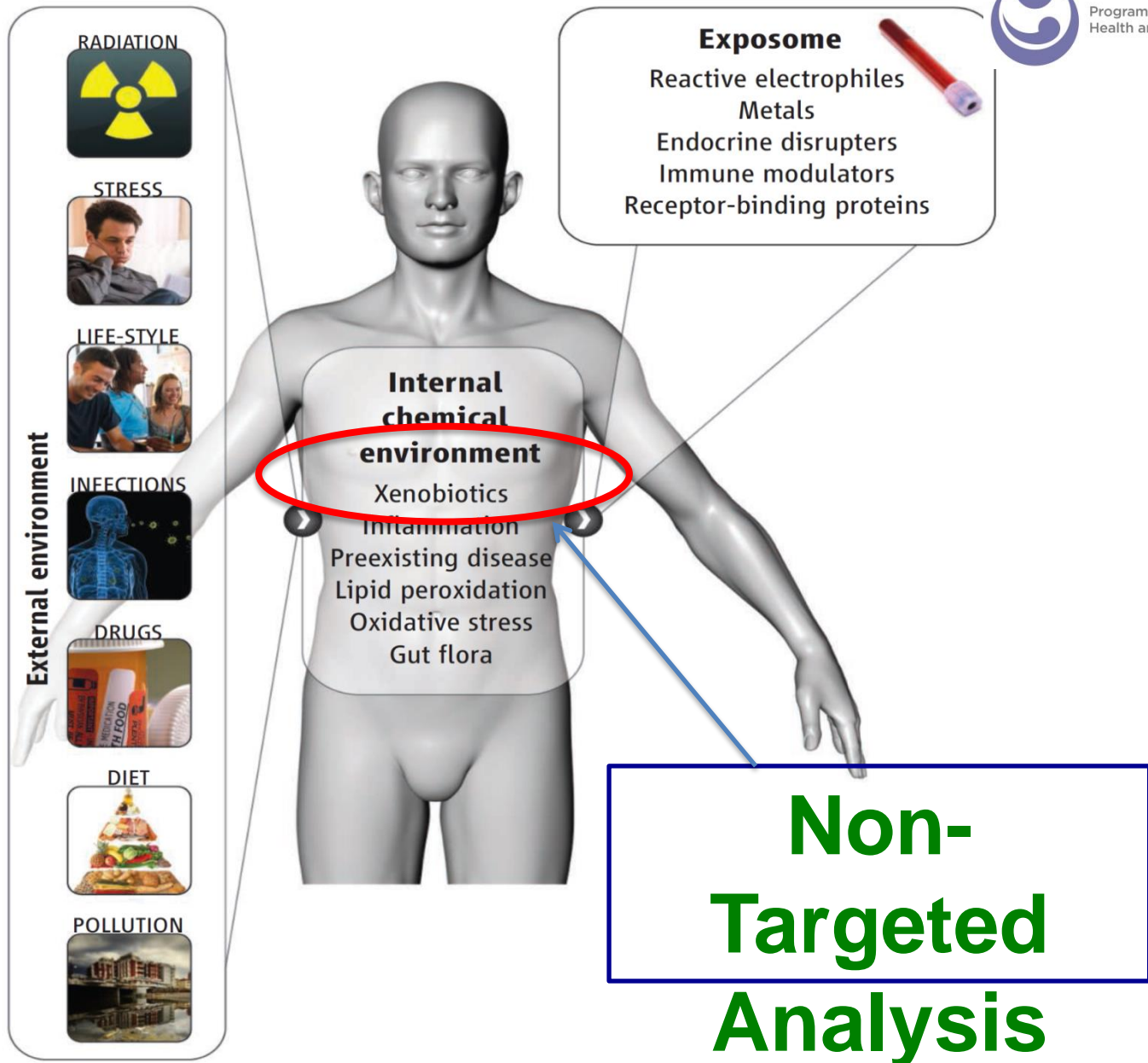
Linking Science to Action

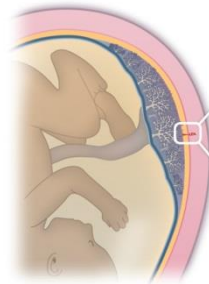




The Exposome Approach

The Exposome Approach



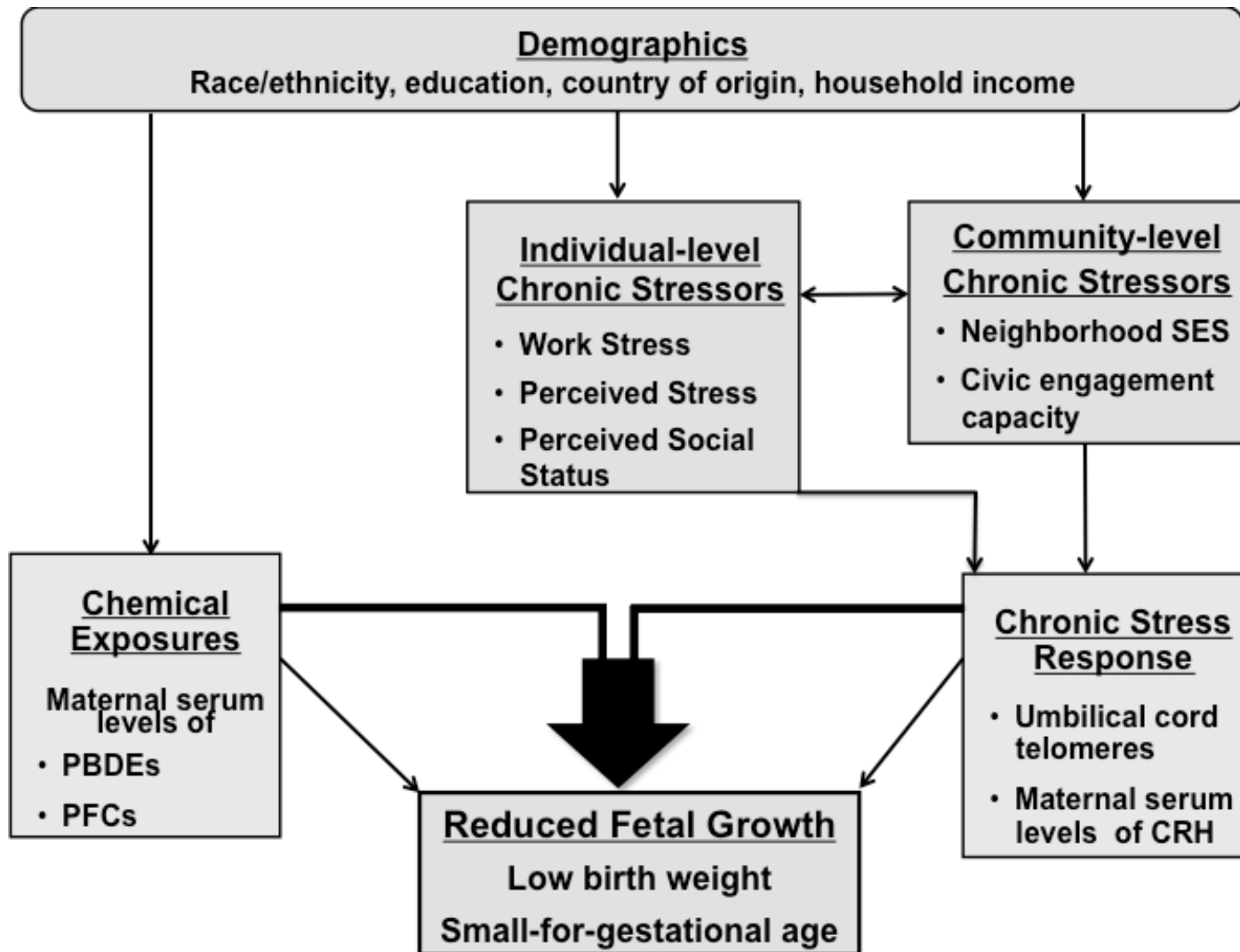


Pregnancy → Environmental Chemicals Center



Improves children's health by identifying and preventing harmful environmental chemical exposures that occur during pregnancy.

Figure 1. The Double Jeopardy of Prenatal Exposures to Chemical and Social Stressors That Affect Fetal Growth

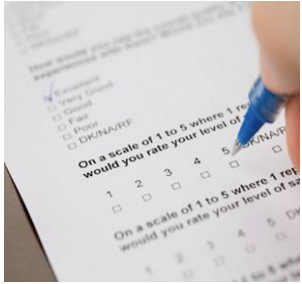




Chemicals in our Body Study

- **Stress Assessment Interview**
 - Information on demographics , stress, chemical exposure (ex: work, neighborhood, self-perceived stress, food security)
- **Biological specimens**
 - Maternal blood (2nd trimester)
 - Maternal and cord blood at delivery (3rd trimester)

Specimen	Collaborator
PBDEs (serum)	June-Soo Park
PFCs (serum)	Roy Gerona
CRH (plasma)	Mike McMaster Susan Fisher
Telomeres (whole blood)	Elizabeth Blackburn



Stress survey,
Medical charts data



Chemicals exposure levels (PBDEs, PFCs)



Infant birth outcomes



Pregnancy Exposures to
Environmental Chemicals
Children's Center



- **Pioneer a non-targeted screening method for Environmental Organic Acids (EOAs) LC-QTOF/MS to screen for multiple chemical exposures in pregnant women**
- **Use targeted methods to confirm the presence and identify levels of select EOAs detected through our non-targeted screen.**
- **Assess differences in exposure to six EOAs by race/ethnicity and socioeconomic status (SES)**

Study Design

Analytical Platform:

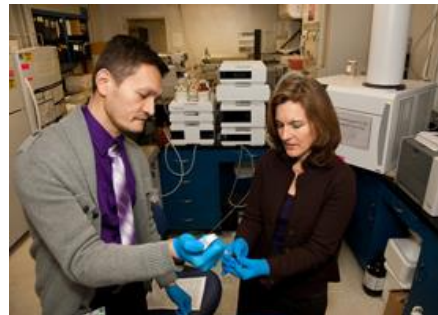
Quadruple Time-of-Flight Mass Spectrometer (LC-QTOF/MS) Agilent LC 1260- QTOF 6550

Study Population and biospecimen:

Serum samples from pregnant women. N = 200

Chemicals of Interest:

Environmental Organic Acids (EOAs), such as phenols, phthalates, acidic pesticides

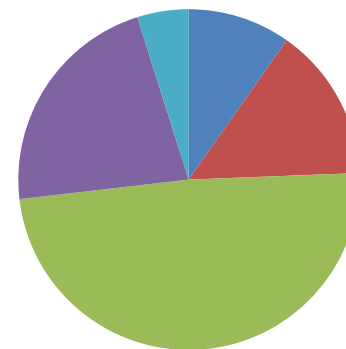
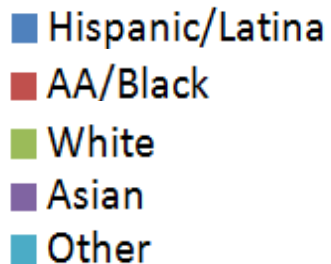
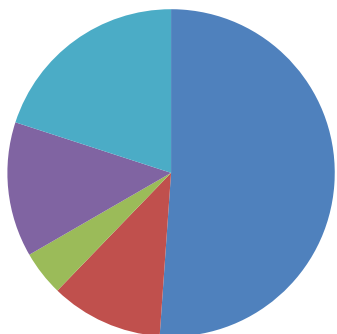


CiOB 2 – Demographics (N = 88)

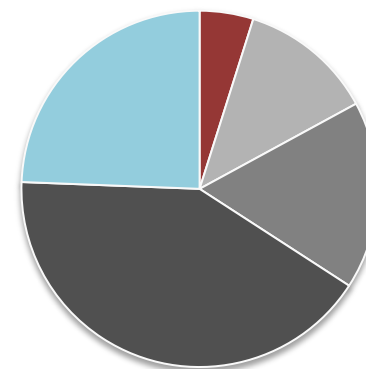
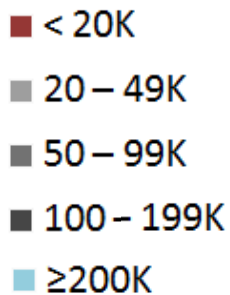
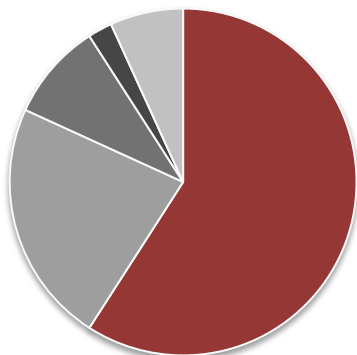
SF General Hospital = 47

Moffitt Long Hospital=41

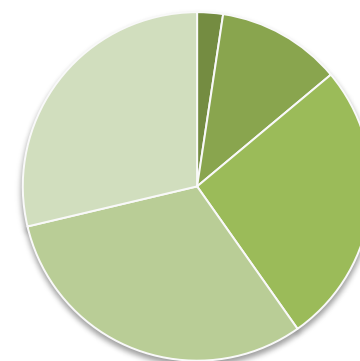
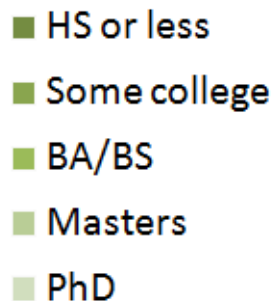
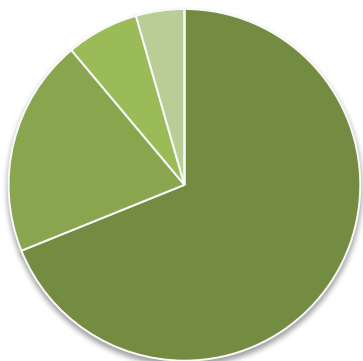
**Race/
Ethnicity**



**Combined
Household
Income**



**Educational
Attainment**

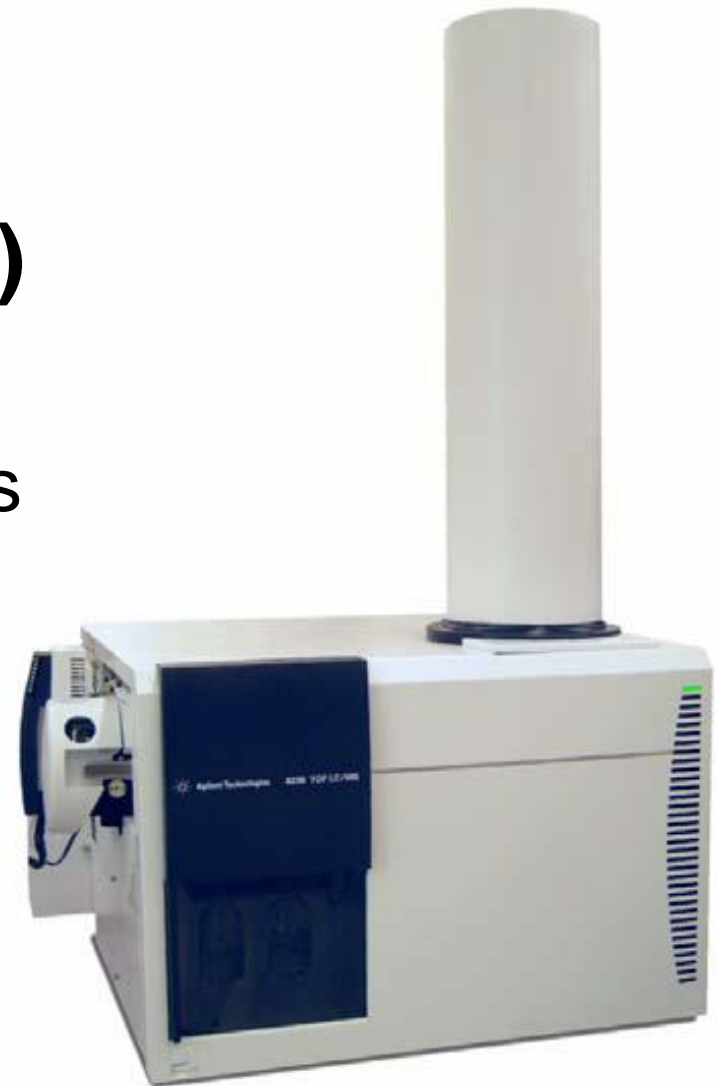


Non-Targeted Analytical Platform

Time-of-Flight Mass Spectrometer (TOF MS)

Separate molecules by ionization, and sorts by mass (molecular weight, MW).

Usually used in tandem with chromatography (LC or GC)



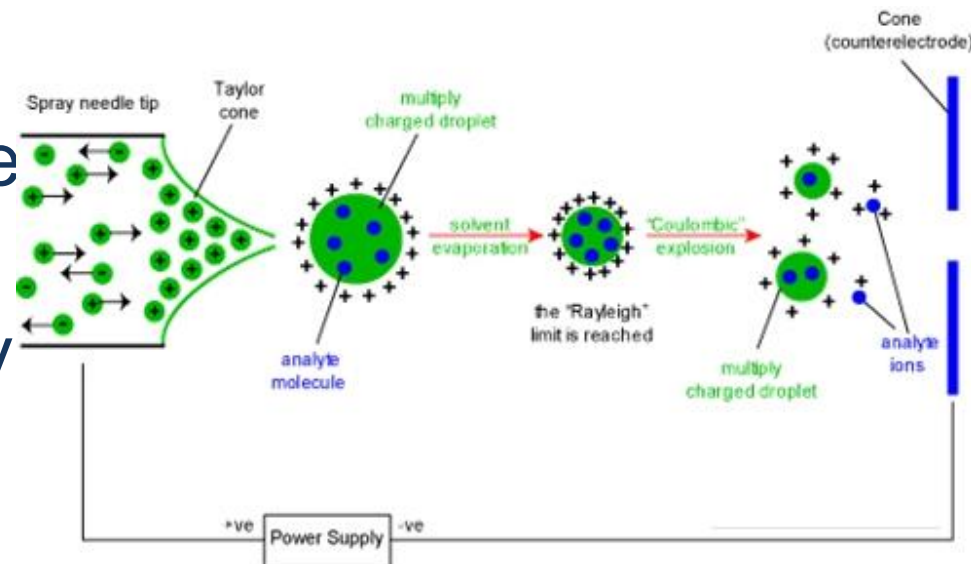
Mass Range: 75-600 amu (TOF); 75-600 amu (MS/MS)
LOD Range: 0.1 ng/mL – 10 ng/mL

TOF MS – Run Modes

Electrospray ionization (ESI)

→ ESI Positive

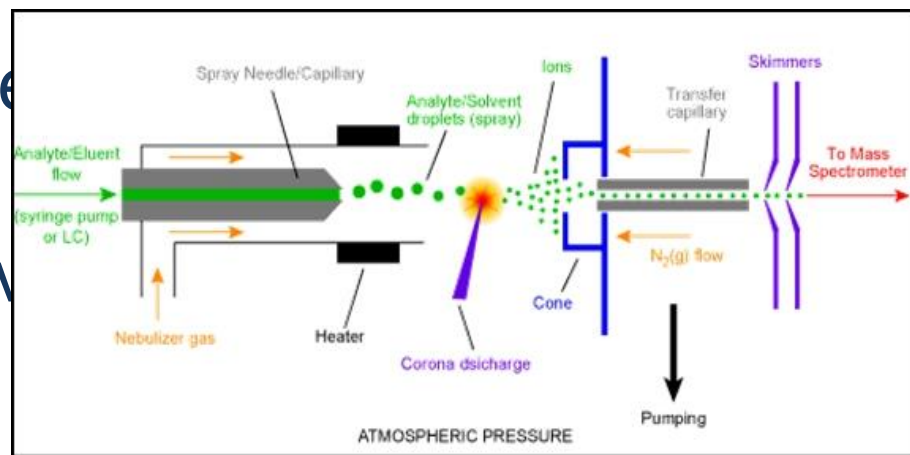
→ ESI Negative



Atmospheric pressure chemical ionization (APCI)

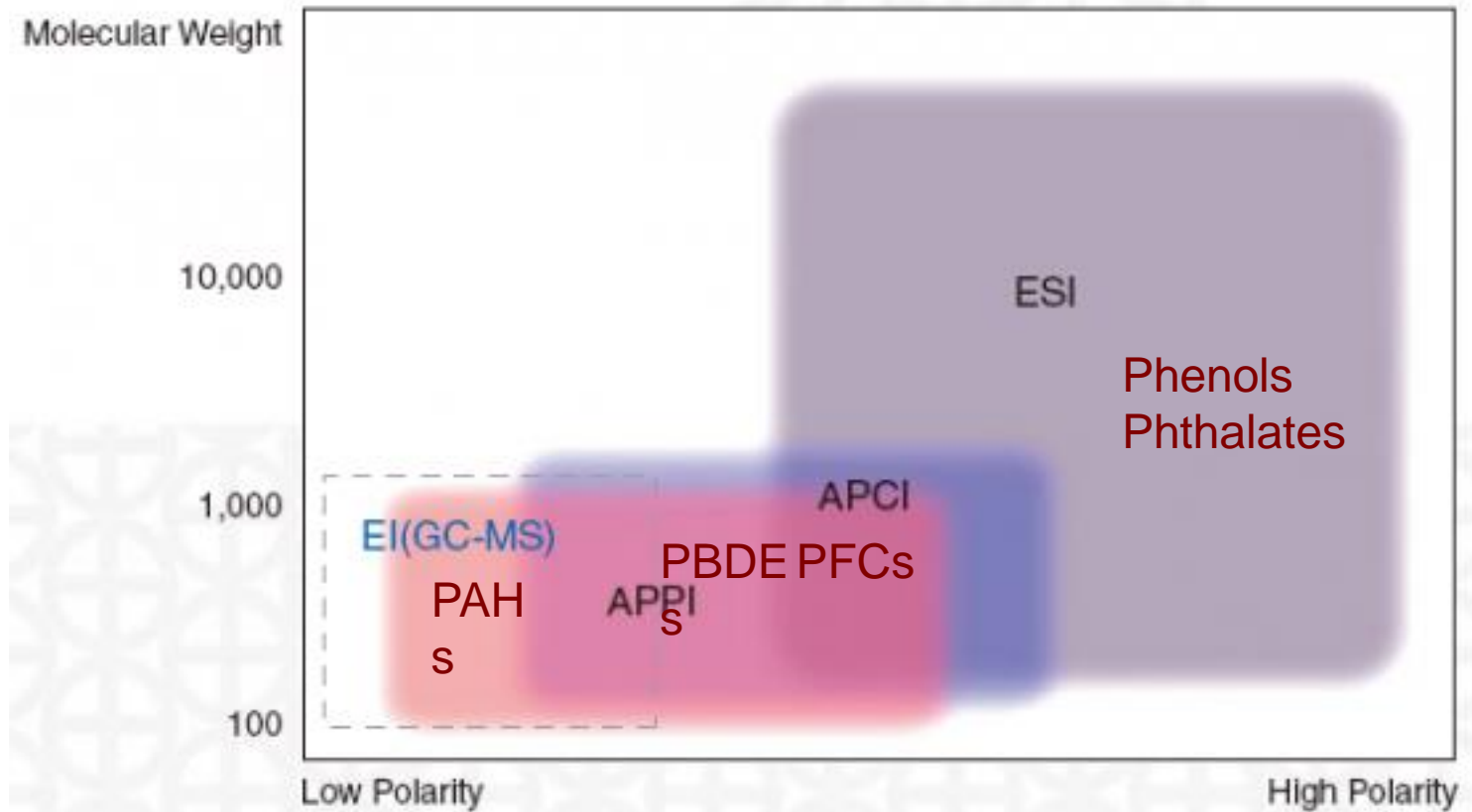
→ APCI Positive

→ APCI Negative

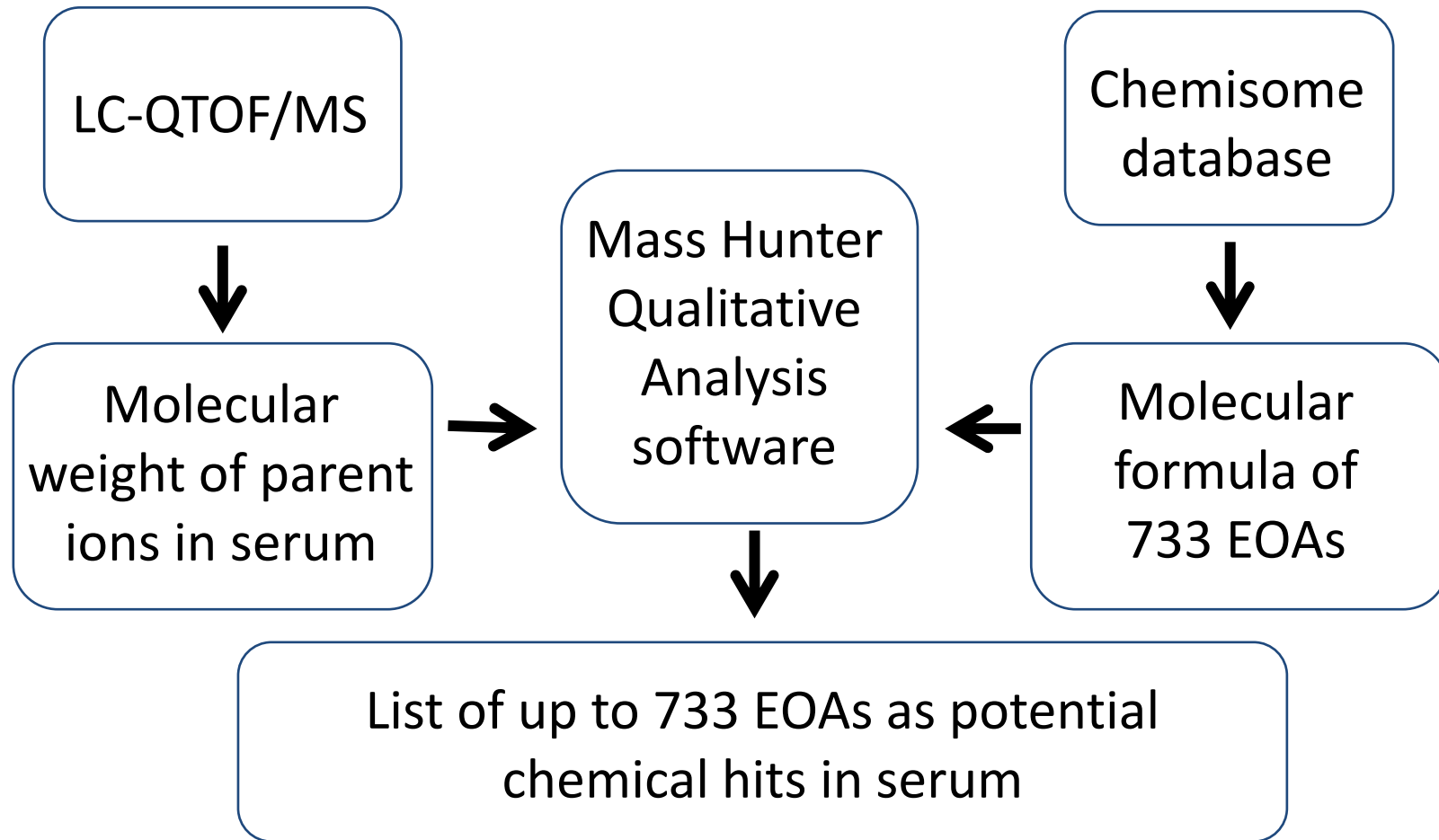


Goal is to capture full spectrum of chemicals, both positive, negative, and non-polar

Ion Source and Chemical Coverage



Matching QTOF-LC/MS output to Chemisome database



Chemisome Database

Priority:

1. High production volume & pesticides
3. Government priority

Sources:



N = 5,221

(TOF measurable n = 3,135)

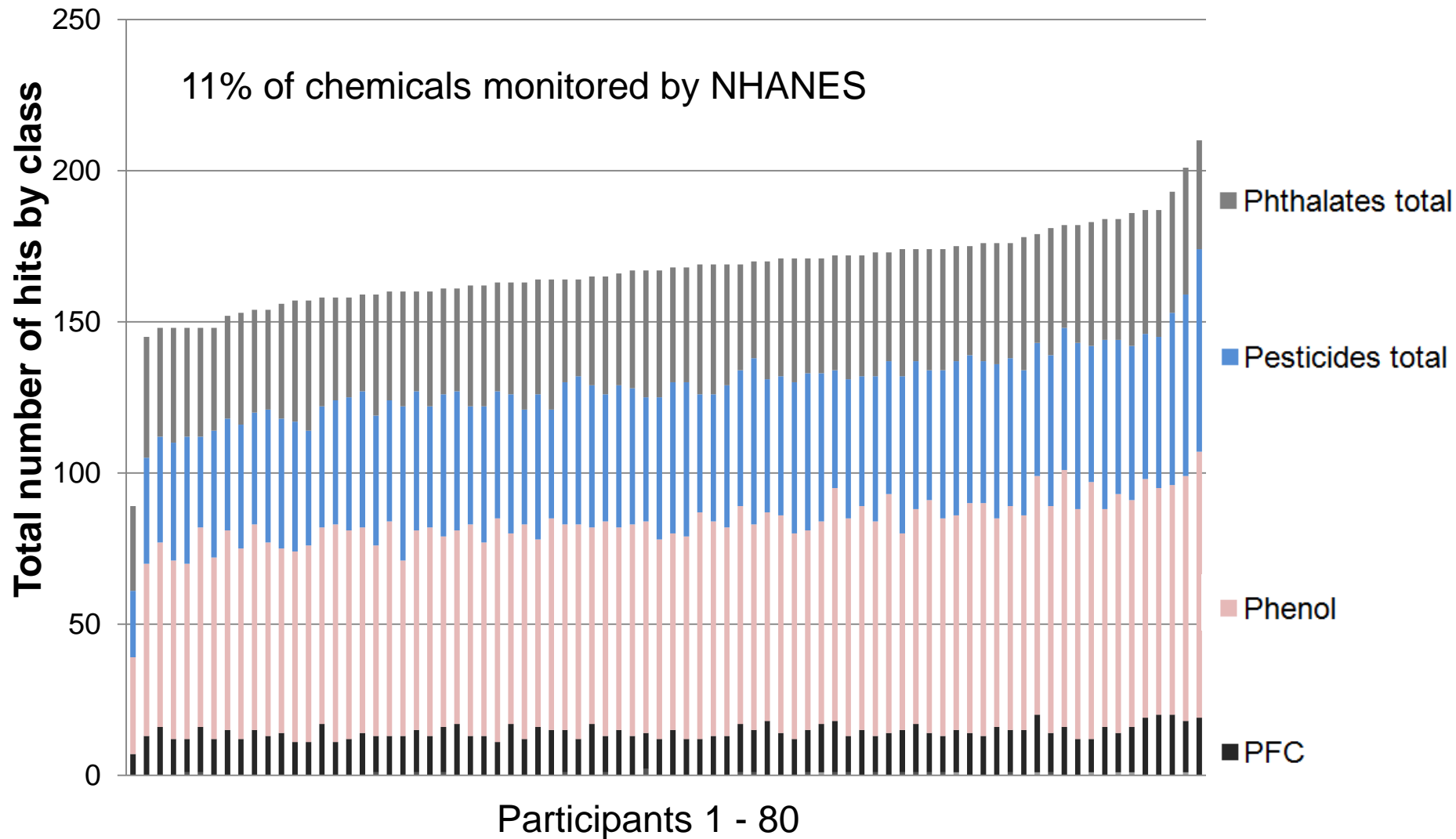
Name	CAS	Chemicalclass	Formula
zirconium dioxide	1314-23-4		ZrO2
zinc selenite	13597-46-1		ZnSeO3
zinc sulphide	1314-98-3		ZnS
tungsten trioxide	1314-35-8		WO3
tungsten carbide	12070-12-1		WC
Vanadium pentoxide (orthorhombic crystalline form)	1314-62-1		V2O5
divanadium trionide	1314-34-7		V2O3
titanium oxide sulphate	13825-79-6		TiOSO4
dichloride titanium oxide	13780-39-7		TiOCl2
Titanium dioxide	13463-67-7		TiO2
Titanium	7440-32-6	Metal	Ti22
Thorium dioxide	1314-20-1		ThO2
strontium sulphide	1314-96-1		SrS
strontium carbonate	1633-05-2		SrCO3
Sulfite liquors and Cooking liquors, spent	66071-92-9	Mixtures	SO3
tin sulphide	1314-95-0		SnS
Silicon dioxide	7631-86-9333		SiO2
Selenium sulfide	7446-34-6		SeS
selenium dioxide	7446-08-4		SeO2
Cocamide diethanolamine	68603-42-9		RCO(N)(CH2OH)2
phosphina	7803-51-2		PH3
lead titanium trioxide	12060-09-3		PbTiO3
lead telluride	1314-91-6		PbTe
lead selenide	12069-00-0		PbSe
lead sulphide	1314-87-0		PbS
lead monoxide	1317-36-8		PbO
lead diazide	13424-46-9		PbN6
lead sulfochromate yellow	1344-37-2		PbCrO4
orange lead	1314-41-6		Pb3O4
Lead	7439-92-1	Metal	Pb
diphosphorus pentasulphide	1314-80-3		P4S10
diphosphorus pentaoxide	1314-56-3		P2O5
zinc oxide	1314-13-2		ZnO
pentalead tetraoxide sulphate	12065-99-6		QPb5S
zinc bis(dihydrogen phosphate)	13598-37-3		OSBZn
tetralead trioxide sulphate	12202-17-4		OPb4S



Environmental Organic Acids

Class	# in Chemisome	Common Use			
Environmental Phenols	177				
Phthalates and Phthalate Metabolites	61				
PFCs	52		 <small>Aren't you glad you have Scotchgard!</small>		
PBDE/ PCB Metabolites	24				
Pesticides and metabolites	417				

Results – EOA hits by individual





Priorities

- Use in everyday consumer products and high volume use
- Identified in at least 80% of study participants
- Novel chemical exposures not measured in large biomonitoring studies or in pregnant women.



Targeted analysis candidate chemicals

Mono-n-pentyl phthalate

(Di-n-pentyl phthalate
metabolite -
plasticizers, PVCs)



No production volume
information on DnPP

Benzophenone-1

(UV absorber)

National Production
Volume (IUR 2006)

< 500,000 lbs



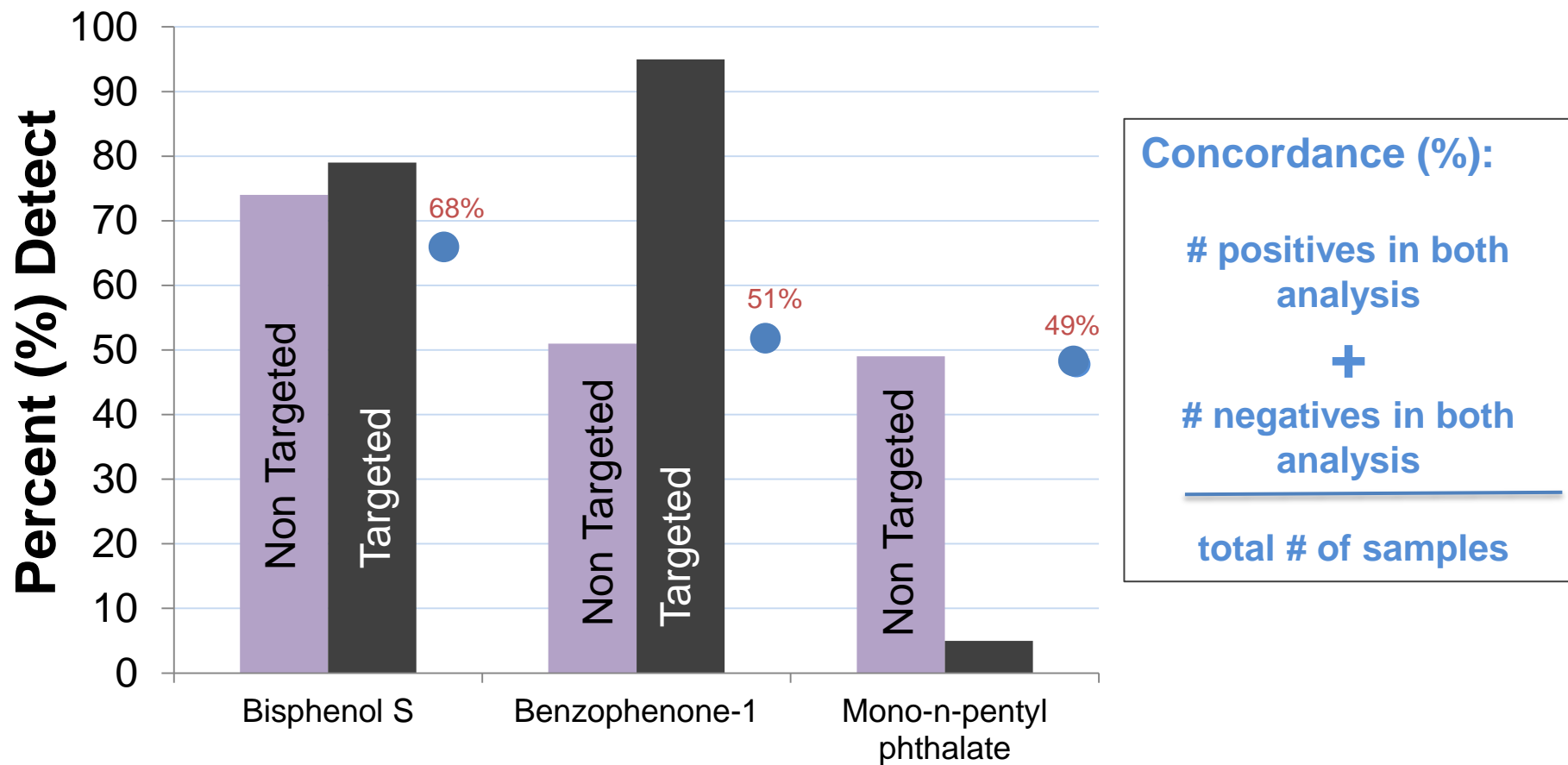
Bisphenol-S

(Bisphenol-A substitute)

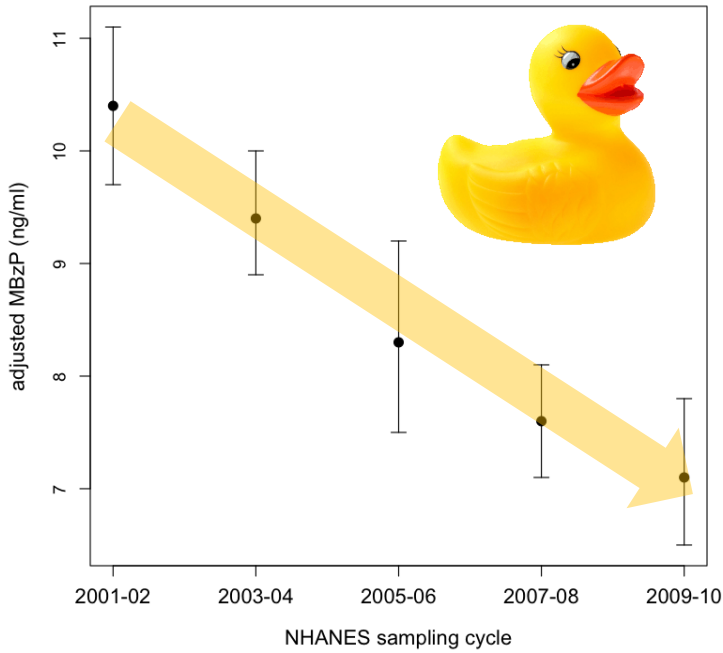
BPA substitute,
confirmed by reference
standards



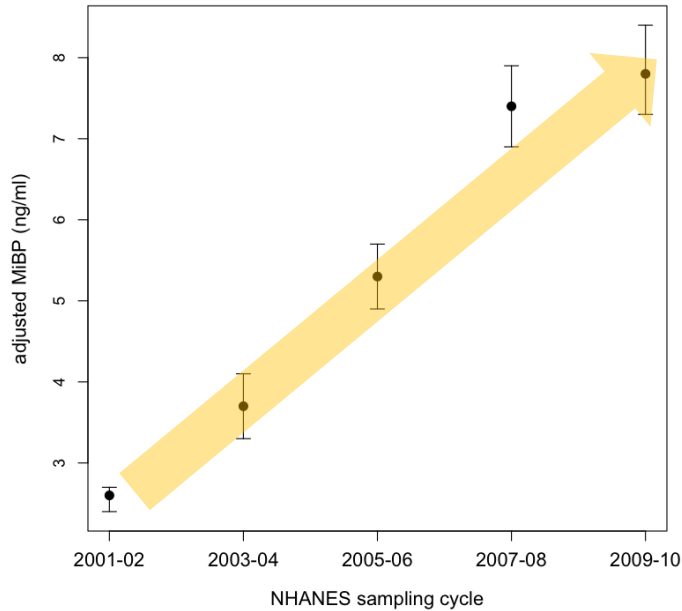
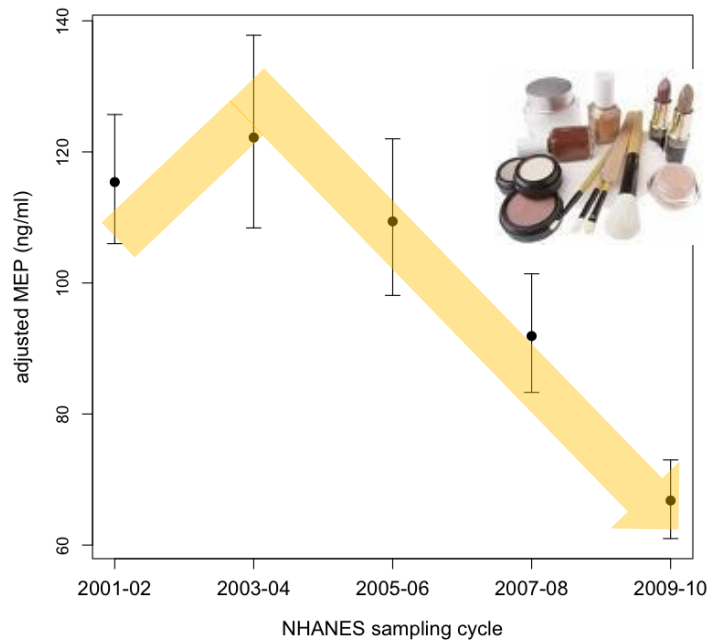
Results – Targeted analysis



Banned Phthalates



Phthalates Targeted in Market Campaigns



Phthalates not Banned (Replacements)

Study Personnel

Project 2

- ❖ PI: Tracey Woodruff, PhD, MPH
- ❖ Collaborator: Roy Gerona, PhD, Saunak Sen, PhD, Rachel Morello-Frosch PhD, MPH (UC Berkeley)
- ❖ Study Assistants: Jackie Schwartz, MPH, Cheryl Godwin de Medina, BS, Priscila Valdez Lopez, BS, Cynthia Melgoza Canchola, MPH, Matt Friesen, BS, Thomas Lin, BS



Summary

1. ~50 participants recruited
2. Goal to add cord serums
3. Need identification of sources
4. Move toward prevention





PRHE

Information for Families

Resources to help your family reduce their environmental exposures



Clinical Practice

Resources for health care professionals to promote environmental health



Research

Targeted research to inform clinical decision making and public policy



Policy

Resources to advance science-based policy solutions.



Mission: To create a healthier environment for human reproduction and development by advancing scientific inquiry, clinical care, health policies that prevent to chemicals in our



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