Urinary Biomonitoring for PFAS: Pilot Results and Challenges

Antonia M. Calafat

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

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J Environ Health 2014

Biomonitoring for Perfluorochemicals in a Minnesota Community With Known Drinking Water Contamination

Adrienne Landsteiner, MPH
Chronic Disease and Environmental Epidemiology
Minnesota Department of Health

Carin Huset, PhD
Environmental Division
Minnesota Public Health Laboratory

Allan Williams, MPH, PhD
Jean Johnson, MPH, PhD
Chronic Disease and Environmental Epidemiology
Minnesota Department of Health

JOEM 2006

Community Exposure to Perfluorooctanoate: Relationships Between Serum Concentrations and Exposure Sources

Edward Anthony Emmett, MD, MS
Frances Susan Shofer, PhD
Hong Zhang, MD, MPH
David Freeman, MS
Chintan Desai, BSc
Leslie Michael Shaw, PhD

Environ Sci Technol Letters 2016

Legacy and Emerging Perfluoroalkyl Substances Are Important Drinking Water Contaminants in the Cape Fear River Watershed of North Carolina

Mei Sun,[*,†,‡] Elisa Arevalo,[‡] Mark Strynar,[§] Andrew Lindstrom,[§] Michael Richardson,[∥] Ben Kearns,[∥] Adam Pickett,[⊥] Chris Smith,[#] and Detlef R. U. Knappe[‡]

Short communication

Int J Hyg Environ Health 2012

Perfluorinated compounds in the vicinity of a fire training area – Human biomonitoring among 10 persons drinking water from contaminated private wells in Cologne, Germany

Odulf Weiß[a,*], Gerhard A. Wiesmüller[a], Anne Bunte[a], Thomas Göen[b], Carsten K. Schmidt[c], Michael Wilhelm[d], Jürgen Hölzer[d]

J Environ Monit 2003

Occurrence and persistence of perfluorooctanesulfonate and other perfluorinated surfactants in groundwater at a fire-training area at Wurtsmith Air Force Base, Michigan, USA†

Cheryl A. Moody,[a‡] Gretchen N. Hebert,[b] Steven H. Strauss*[b] and Jennifer A. Field*[c]

Environ Sci Technol 2017

A Never-Ending Story of Per- and Polyfluoroalkyl Substances (PFASs)?

Zhanyun Wang,[†] Jamie C. DeWitt,[‡] Christopher P. Higgins,[§] and Ian T. Cousins*[∥]

Int J Hyg Environ Health 2018

Per- and polyfluoroalkyl substance (PFAS) exposure assessment in a community exposed to contaminated drinking water, New Hampshire, 2015

Elizabeth R. Daly[a,*], Benjamin P. Chan[a,*], Elizabeth A. Talbot[a,b], Julianne Nassif[a,1], Christine Bean[a], Steffany J. Cavallo[a,2], Erin Metcalf[a], Karen Simone[c,g], Alan D. Woolf[d,e,f]

PFAS are a diverse family

- Hundreds of chemicals with the perfluoroalkyl moiety (C_nF_{2n+1}–)

- Perfluoroalkylcarboxylic acids

  $CF_3(CF_2)_nCOOH$ e.g., PFOA

- Perfluoroalkane sulfonic acids

  $CF_3(CF_2)_nSO_3H$ e.g., PFOS

- Perfluoroalkane sulfonamidoacetic acids & salts

  $CF_3(CF_2)_nSO_2N(R)CH_2COOH$

  e.g., MeFOSAA

- Perfluoroalkyl ether carboxylic acids

  $CF_3(CF_2)_2OCFCOOH$ HFPO-DA (GenX)

  $CF_3O(CF_2)_3OCHFCF_2COOH$ DONA

- Perfluoroalkyl ether sulfonic acids

  $Cl(CF_2)_6O(CF_2)_2SO_3H$ 9Cl-PF3ONS

- Many others …

Some PFAS generalities

Legacy: Long alkyl chain

- PFCAs: C>7
- PFSAs: C>4
- Long $t_{1/2}$ in humans
- Use decreasing
- Detected in the environment
- Widespread human exposure
  - NHANES

Legacy: Short alkyl chain

- PFCAs: C≤7
- PFSAs: C≤4
- Short $t_{1/2}$ in humans
- Use on the rise
- Detected in the environment
- Human exposure less known
  - NHANES

Alternative & Emerging

- Fluorinated ether acids
- Other chemistries
- Short $t_{1/2}$ in humans
- Use on the rise
- Detected in the environment
- Human exposure less known

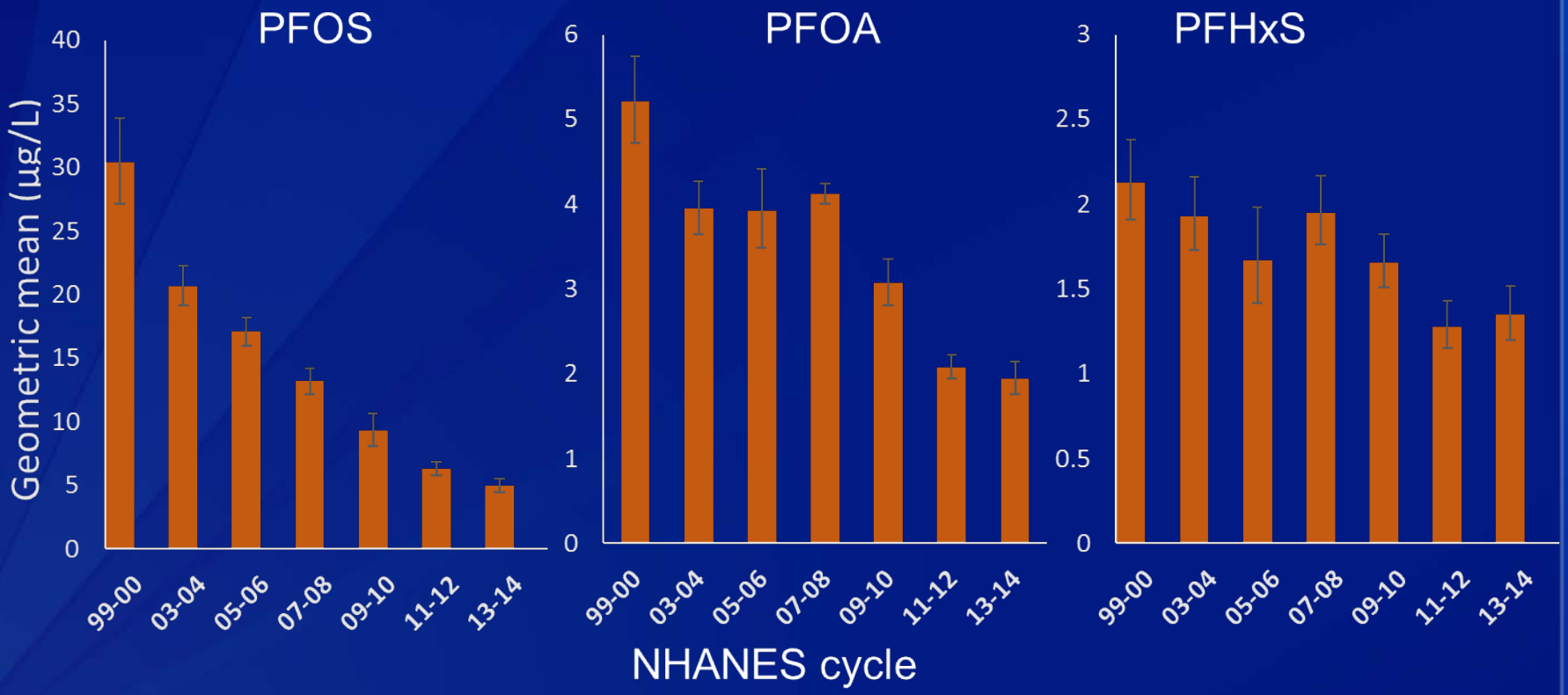
PFAS in NHANES

PFAS in serum		99–00	03–04 -----11–12	13–14
Short-alkyl chain	PFBS		X	X
	PFHpA	X	X	X
Long-alkyl chain	PFHxS	X	X	X
	PFOS	X	X	X[a]
	PFOA	X	X	X[a]
	PFNA	X	X	X
	PFDA	X	X	X
	PFUnDA	X	X	X
	PFDoDA	X	X	X
	FOSA	X	X	
	EtFOSAA	X	X	
	MeFOSAA	X	X	X
Alternative & emerging	e.g., GenX			

Not enough serum available in 2001-2. [a]Measured as isomers

Temporal trends: Long alkyl chain PFAS

- Before (1999-2000) & after (2003+) changes in manufacturing practices
  - PFOS reduced by 83% since 1999-2000
- Widespread exposure



Temporal trends: Short alkyl chain PFAS

- Limited exposure to short alkyl chain PFAS

OR

- Is serum the best biomonitoring matrix?

NHANES	PFBS (C4)	PFHpA (C7)
	95th percentile (95% conf. interval) in µg/L	
1999–2000	n/a	0.70 (0.50-1.00)
2003–2004	<0.40	0.40 (<0.30-0.50)
2005–2006	0.10 (<0.10-0.20)	0.70 (<0.40-1.70)
2007–2008	<0.10	0.50 (0.40-0.80)
2009–2010	<0.10	0.20 (0.20-0.30)
2011–2012	<0.10	0.22 (0.18-0.26)
2013–2014	<0.10	0.20 (0.10-0.20)

LOD = 0.1 µg/L (2009+)

Choice of biological matrix is critical

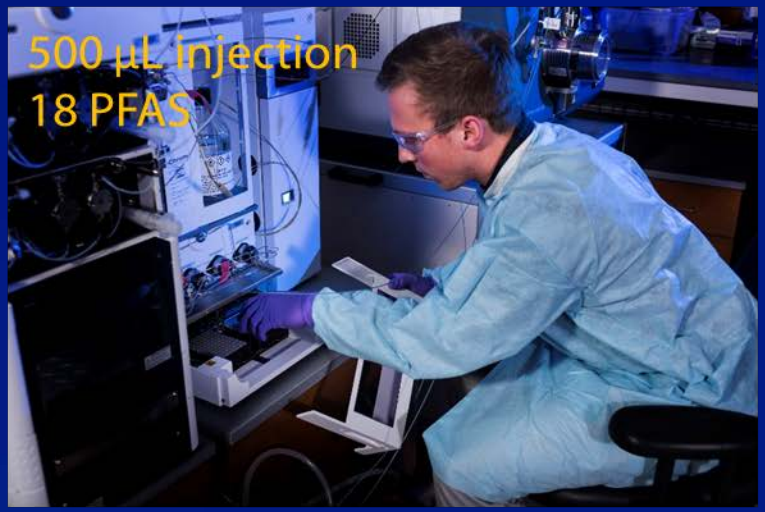
- Chemical's $t_{1/2}$ in humans*
  - Non-persistent chemicals: Urine
  - Persistent chemicals: Blood
- Many analytes can be measured simultaneously, but additional information is needed to demonstrate the utility of these analytes as exposure biomarkers

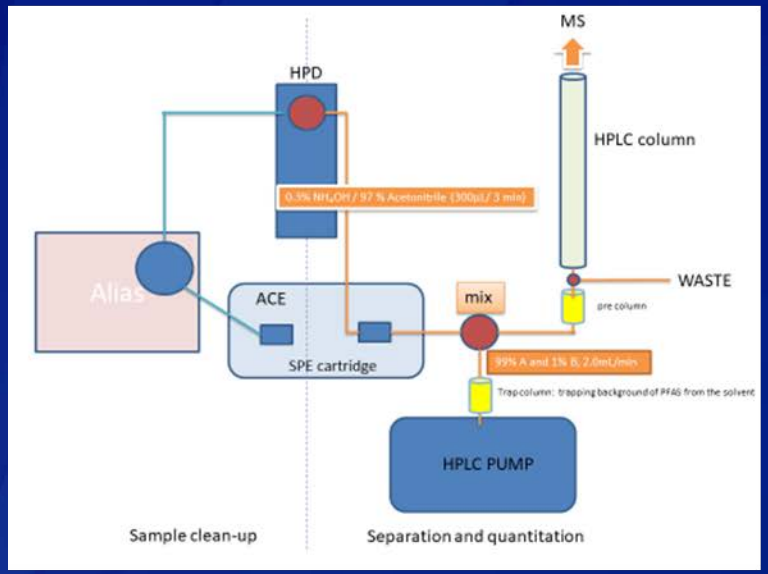
*With exceptions

PFAS quantification in urine

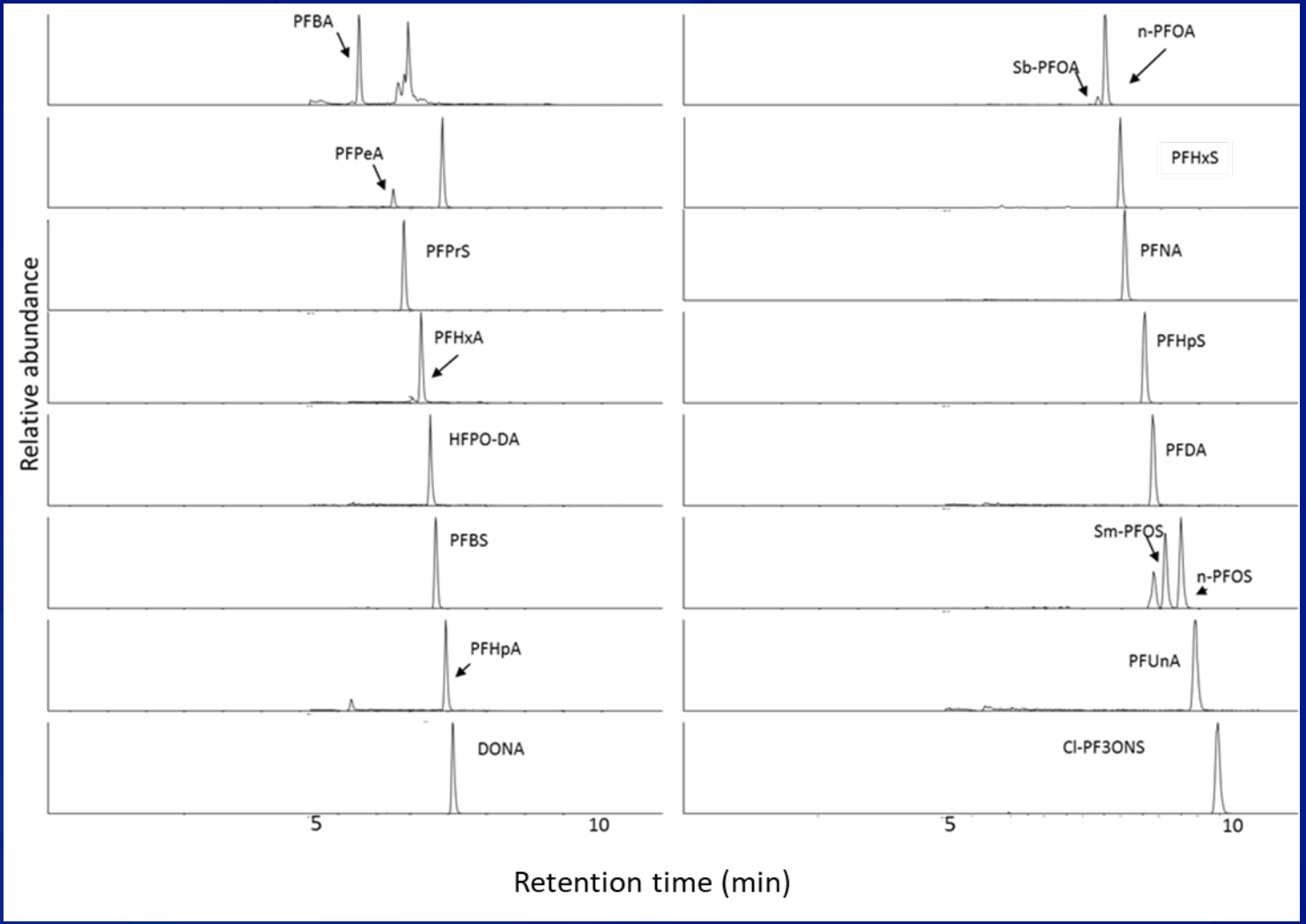
Incubate (37 °C, 2 hrs)

425 µL 0.1M formic acid





Kato et al. Chemosphere 2018



Typical HPLC-MS/MS chromatograms in a QC sample (~0.5-2.8 ng/mL, depending of the analyte)

PFAS in paired urine/serum

- 50 paired urine/serum specimens collected anonymously from U.S. adults in 2016
- PFBA, PFPeA, PFHxA, PFBS, PFPrS, HFPO-DA, DONA, Et FOSAA, FOSA, and 9Cl-PF3ONS not detected in any serum samples
- Only PFBA detected in urine

	Serum											Urine
	PFHpA	PFOA	Sb-PFOA	PFNA	PFDA	PFUnDA	PFHxS	PFHpS	n-PFOS	Sm-PFOS	MeFOSAA	PFBA
Frequency (%)	2	98	2	100	40	8	92	96	98	86	42	56
median	<LOD	0.7	<LOD	0.5	<LOD	<LOD	0.5	0.3	1.7	0.7	<LOD	0.2
90th percentile	<LOD	2.0	<LOD	1.0	0.2	<LOD	1.2	0.7	5.0	2.1	0.3	0.5
95th percentile	<LOD	2.4	<LOD	1.2	0.3	0.1	1.7	0.8	5.1	2.3	0.4	0.6
Maximum	0.1	4.0	0.1	1.3	0.6	0.2	2.0	1.0	10.3	4.4	0.5	0.8

LODs were 0.1 µg/L in urine and serum for all analytes. LODs & concentrations in µg/L

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Temporal trends of PFAS in urine?

- 478 archived urine specimens collected anonymously from convenience samples of US male and female adults

Analyte	LOD	2001 (N=198)		2009 (N=127)		2012 (N=83)		2015 (N=70)	
		Detection Frequency (%)	90th %tile	Detection Frequency (%)	90th %tile	Detection Frequency (%)	90th %tile	Detection Frequency (%)	90th %tile
PFBA	0.2	0	<LOD	0	<LOD	0	<LOD	40	1.1
PFBS	0.1	0	<LOD	0	<LOD	0	<LOD	0	<LOD
PFPeA	0.1	0	<LOD	0	<LOD	0	<LOD	11	0.1
PFHxA	0.1	0	<LOD	0	<LOD	0	<LOD	3	<LOD
PFHpA	0.1	19.2	0.2	0	<LOD	0	<LOD	3	<LOD

LODs & concentrations in µg/L

How do these U.S. data compare to other data?

- 120 children 5-13 years old in (South Korea, 2012)

Table 1
Summary of perfluorinated compound concentrations (ng/mL) in serum from children and urine from children and adults.

	PFBA[a]	PFPeA[a]	PFHxA[a]	PFHpA[a]	PFOA[a]	PFNA[a]	PFDA[a]	PFUnDA[a]	PFDoDA[a]	PFTrDA[a]	PFTeDA[a]	PFBS[a]	PFHxS[a]	PFHpS[a]	PFOS[a]	PFDS[a]
Serum (Children)																
DF[b] (%)	47	37	8	36	100	78	90	100	0	34	0	11	100	75	100	0
Mean	0.346	0.497	0.353	0.312	5.15	1.72	0.604	0.748	–	0.306	–	0.105	1.13	0.203	6.58	–
Range	ND–0.611	ND–0.942	ND–0.576	ND–0.856	1.09–8.49	ND–3.30	ND–1.19	0.228–2.09	–	ND–0.627	–	ND–0.165	0.260–2.46	ND–0.338	1.84–14.3	–
Urine (Children)																
DF[b] (%)	0	70	11	36	0	0	0	0	0	0	0	1	0	0	0	0
Mean	–	2.34	0.731	1.35	–	–	–	–	–	–	–	0.492	–	–	–	–
Range	–	ND–11.6	ND–2.34	ND–4.44	–	–	–	–	–	–	–	ND–0.492	–	–	–	–
Urine (Adult)																
DF[b] (%)	1	25	5	7	0	0	1	0	1	0	0	0	0	0	0	0
Mean	1.72	2.39	1.38	0.495	–	–	0.495	–	0.442	–	–	–	–	–	–	–
Range	ND–1.72	ND–17.6	ND–5.63	ND–1.08	–	–	ND–0.495	–	ND–0.442	–	–	–	–	–	–	–

[a] PFBA = perfluorobutanoic acid; PFPeA = perfluoropentanoic acid; PFHxA = perfluorohexanoic acid; PFHpA = perfluoroheptanoic acid; PFOA = perfluorooctanoic acid; PFNA = perfluorononanoic acid; PFDA = perfluorodecanoic acid; PFUnDA = perfluoroundecanoic acid; PFDoDA = perfluorododecanoic acid; PFTrDA = perfluorotridecanoic acid; PFTeDA = perfluorotetradecanoic acid; PFBS = perfluorobutane sulfonate; PFHxS = perfluorohexane sulfonate; PFHpS = perfluoroheptane sulfonate; PFOS = perfluorooctane sulfonate; PFDS = perfluorodecane sulfonate.
[b] Detection frequency; LOD varied from 0.0574 to 0.281 ng/mL in serum and 0.0875–0.225 ng/mL in urine samples (specific LOD value of each PFCs are given in the SI, Table S3).

- $[PFPeA, PFHxA, PFHpA]_{urine} > [PFPeA, PFHxA, PFHpA]_{serum}$
- Long-chain PFASnot detected in urine

Kim et al. Environ Pollut 2014

Of note

- PFAS levels in drinking water are in ppt range
- NHANES serum data since 1999
  - Medians of long alkyl chain PFAS in the low ppb range
  - 95th percentiles of short alkyl chain PFAS (PFBS, PFHpA) <0.2 ppb
- Pilot serum/urine results
  - Frequently detected long alkyl chain PFAS in serum, but not in urine
  - Hardly detected short alkyl chain PFAS (e.g., PFBS, PFPeP, PFHxA) or fluorinated alternatives (e.g., HFPO-DA, DONA) in serum or urine

Take home messages

- Method for trace-level quantification of 15 C_3-C_{11} PFAS, and three fluorinated alternatives in 50 µL urine
- Updated current "serum" method to quantify PFAS & three fluorinated alternatives in serum
- Paired urine/serum pilot data
  - Serum for long alkyl chain PFAS exposure assessment
  - Urine for short alkyl chain PFAS exposure assessment

Future work

- Continue NHANES
  - Serum
- Urine (2013-2014)
  - PFAS & alternatives
- PFAS concentrations in paired urine/serum samples in exposed populations
- Continue R&D on alternative PFAS

Acknowledgements

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NCHS

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
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov