Health Consultation

Exposure Investigation

Biological Sampling of Per- and Polyfluoroalkyl Substances (PFAS[1]) in the Vicinity of Lawrence, Morgan, and Limestone Counties, Alabama

NOVEMBER 28, 2016

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Agency for Toxic Substances and Disease Registry
Division of Community Health Investigations
Atlanta, Georgia 30333

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HEALTH CONSULTATION

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Prepared By:

U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry (ATSDR)
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[1] In the past ATSDR has referred to this class of chemicals as “perfluorinated compounds” or “PFCs.” In an effort to be more precise, ATSDR now uses the “per- and polyfuoroalkyl substances” or “PFAS.”

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Abbreviations and Acronyms

ADEM	Alabama Department of Environmental Management
ALT	Alanine aminotransferase
ATSDR	Agency for Toxic Substances and Disease Registry
CTE	Central Tendency Exposure
DCHI	Division of Community Health Investigations
EPA	Environmental Protection Agency
Et-PFOSA-AcOH	2-(N-ethyl-Perfluorooctane sulfonamido) acetic acid
g	gram
GGT	gamma-glutamyl transferase
HDL	high density lipoprotein
LDL	low density lipoprotein
Me-PFOSA-AcOH	2-(N-methyl-Perfluorooctane sulfonamido) acetic acid
Ml	milliter
MRL	minimalrisk level
NCEH	National Center for Environmental Health
Ng	Nanogram
NHANES	National Health and Nutrition Examination Survey
PBPK	physiologically-based pharmacokinetic modeling
PFAS	per- and polyfluoroalkyl substances
PFBuS	perfluorobutane sulfonic acid
PFC	perfluoroalkyl compounds
PFDeA	perfluorodecanoic acid
PFDoA	perfluorododecanoic acid

PFHpA	perfluoroheptanoic acid
PFHxS	perfluorohexane sulfonic acid
PFNA	perfluorononanoic acid
PFOA	perfluorooctanoic acid
PFOS	perfluorooctane sulfonic acid
PFOSA	perfluorooctane sulfonamide
PFUA	perfluoroundecanoic acid
Pg	Pictogram
ppb	parts per billion
RfD	reference dose
RME	reasonable maximum exposure
UCMR3	Unregulated Contaminant Monitoring Rule 3
UGA	University of Georgia

Executive Summary

In January and February 2016, the Agency for Toxic Substances and Disease Registry (ATSDR) collected blood and urine samples from 45 people from Morgan, Lawrence, and Limestone Counties, Alabama who previously participated in a 2010 Exposure Investigation (EI). This investigation:

- **Provided a public health service to the community:** The investigation provided information to community members about their body burden of per- and polyfluoroalkyl substances (PFAS), including an assessment of how their PFAS-serum concentrations compare to national reference populations. Participants also learned how their current serum concentrations compare to those measured in 2010.
- **Generated hypotheses regarding pathways of exposures in the community:** Each individual participant received an interpretation of what their biomonitoring results suggest about how they are being exposed, and whether sources of PFAS exposure other than drinking water may exist. ATSDR recommended actions to further reduce exposure as appropriate.
- **Advanced the scientific understanding of the pharmacokinetics of PFAS in humans:** Very few estimates of biological half-life for PFAS exist in the scientific literature. This investigation generated the data necessary to calculate biological half-life for perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS), and perfluorohexane sulfonic acid (PFHxS). ATSDR will analyze this data and report the resulting estimates of biological half-life separately.

Conclusions

1. Exposure to PFAS is decreasing over time in the people tested. Geometric mean serum concentrations of PFOA, PFOS, perfluorononanoic acid (PFNA), and 2-(N-methyl-Perfluorooctane sulfonamido) acetic acid (Me-PFOSA-AcOH) were significantly lower (49%, 53%, 58%, and 60%, respectively) in 2016 than in 2010. Observed changes in the geometric mean serum concentrations of PFHxS and perfluorodecanoic acid (PFDeA) were not statistically significant.
2. Historical PFAS exposures amongst participants in the investigation were likely higher than exposures to the general U.S. population and were lower than or similar to exposures that occurred in other communities located near PFAS manufacturing or use. Geometric mean levels for three PFAS (PFOS, PFHxS, and PFOA) were elevated in EI participants compared to the U.S. general population as defined by the 2011 – 2012 National Health and Nutrition Examination Survey (NHANES) 95th percentile. However, geometric mean serum concentrations of PFOA and PFOS were lower than or similar to levels found in other U.S. communities with known exposures to PFAS.
3. Geometric mean serum concentrations for five PFAS (PFNA, PFDeA, Me-PFOSA-AcOH, 2-(N-ethyl-Perfluorooctane sulfonamido) acetic acid [Et-PFOSA-AcOH], and perfluorooctane sulfonamide [PFOSA]) were similar to or lower than the U.S. general population as defined by the 2011 – 2012 NHANES 95th percentile.
4. Exposure to PFAS in drinking water is not a current public health hazard for any age group. Concentrations of PFOA and PFOS measured in the West Morgan East Lawrence Municipal Water Authority are currently below the United States Environmental Protection Agency's (EPA's) lifetime health advisory (LTHA).

5. Drinking water from the West Morgan East Lawrence Municipal Water Authority in the past is not expected to be harmful for adolescents or adults (anyone over the age of two).
6. Infants and young children whose primary drinking water source was the West Morgan East Lawrence Municipal Water Authority and who drank average or above average quantities of this water at the maximum concentrations detected may have an increased risk of harmful effects resulting from additive exposure to PFOA and PFOS. ATSDR makes this conclusion based on the following:
    - Based on the assumptions used in our exposure dose calculations, the hazard index exceeds 1.0 for children under the age of one under both the Reasonable Maximum Exposure (RME) and Central Tendency Exposure (CTE) scenarios. The hazard index exceeds 1.0 for children between one and two only when the RME scenario is applied. While a hazard index greater than 1.0 increases the level of concern for the potential hazard of the mixture, there are no studies that quantitatively evaluate the cumulative risk of exposure to PFOA and PFOS.
    - Evidence suggests that people in this community, including infants and young children, were likely exposed to PFOA through non-drinking water sources in the past.
    - Health effects have been associated with serum PFAS concentrations comparable to or lower than those observed in this population, and young children have been identified as potentially sensitive to health effects resulting from exposure to PFOA and PFOS.

Recommendations

1. ATSDR recommends that community members concerned about exposures to PFAS consult with their physicians.
2. In light of the evidence that people living in the vicinity of Morgan, Lawrence, and Limestone Counties have blood levels of some PFAS that are elevated compared to national reference populations, ATSDR recommends that water systems downstream of PFAS facilities on the Tennessee River, including the West Morgan East Lawrence Municipal Water Authority, continue conducting routine monitoring of PFAS concentrations in finished drinking water and take steps to ensure that concentrations of PFAS in finished drinking water remain below the current EPA Lifetime Health Advisory for PFOA and PFOS (0.07 µg/L).

Background

Health Effects of Per- and Polyfluoroalkyl Substances (PFAS)

PFAS are used in industrial and consumer applications and products, including fire-fighting foams and oil, stain, grease, and water repellent coatings on carpet, textiles, leather, and paper [1]. PFOS, PFOA, PFHxS and perfluorononanoic acid (PFNA) have been more widely studied than other PFAS. For the most part, laboratory animals exposed to high doses of PFAS, including those mentioned above, have shown changes in liver, thyroid, and pancreatic function, as well as some changes in hormone levels.

A variety of epidemiological studies have been conducted to assess the relationship between PFAS exposure and health effects in humans. These studies have been conducted in occupationally exposed populations, residential populations exposed to PFAS through contaminated drinking water, and the general United States population. Scientists are not yet certain about the possible health effects resulting from human exposure to PFAS at levels typically found in our water and food. Some, but not all studies in humans have shown that certain PFAS may affect the developing fetus and child, including possible changes in growth, learning, and behavior. In addition, they may decrease fertility and interfere with the body's natural hormones, increase cholesterol, affect the immune system, and increase cancer risk. These associations have been observed at a range of exposure levels, including those occurring in the general United States population. However, more research is needed to confirm or rule out possible links between health effects of potential concern and exposure to PFAS.

Epidemiological studies have demonstrated a positive association between serum PFOA and high cholesterol in occupational and non-occupational populations; though no consistent trend between serum PFOA and low density lipoprotein (LDL) and high density lipoprotein (HDL) is evident [2-5]. Findings from longitudinal and cross-sectional studies find positive associations between serum PFOA and PFOS and LDL cholesterol levels [2, 4]. PFOA and PFOS have been shown to modulate expression of genes related to cholesterol metabolism and transport in men and women [6].

Evaluation of liver enzymes suggests that there is a positive association between serum PFOA and liver enzymes and a negative association between serum PFOA and bilirubin levels [3-5, 7, 8]. This association is evident in both occupational and non-occupational populations. A positive relationship between liver enzyme gamma-glutamyl transferase (GGT) and PFOA serum concentration was observed in an occupational cohort [4]. A positive association between serum PFOA and serum PFOS concentrations and serum alanine aminotransferase (ALT) levels was observed in a large residential study [7].

There is evidence to suggest a positive association between serum PFOA and chronic kidney disease [9, 10] and early menopause [11] in the general population.

PFOA has been associated with kidney and testicular cancer in a survivor cohort living near a chemical plant [9]. A retrospective cohort study showed an association between length of employment at 3M Chemical Division and prostate cancer [12].

Epidemiological studies suggest a positive association between serum PFOA and serum PFOS concentrations and suppressed antibody responses to vaccines. *In vitro* studies with human cell lines suggest that PFOA inhibits cytokines that help regulate immune responses [13, 14].

There are several studies that evaluate systemic end points in children living near PFAS manufacturing facilities [15-22]. Cross-sectional studies provide some evidence for associations between exposure to PFAS and asthma-related outcomes in children, though this is not yet well studied [16, 20]. Animal studies have reported impacts on pup mortality following gestational exposure [23]; however, human studies have found no evidence of association between human maternal serum PFOA or PFOS and preterm birth [24]. A modest negative association between maternal PFOS serum concentration and low birth weight in full term infants has been observed [24].

In animals, adverse health effects have been seen in response to PFOA and PFOS exposure [25, 26]. These studies identify increased liver weight as one of the primary critical effects [25, 27-31]. Other effects include changes in spleen and thymus [28, 32] as well as developmental effects [26, 33]. However, it is important to note that extrapolation from animals to humans is uncertain because of pronounced differences in biological half-life and substantial variability across species [34-36]. These uncertainties have been accounted for in the development of ATSDR's draft Minimum Risk Levels (MRLs) and EPA's Reference Doses (RfDs) for PFOA and PFOS, which are based on animal studies [1, 37, 38].

Ongoing Efforts to Reduce Exposure

PFAS have historically been released to the environment by manufacturing facilities during use as a processing aid or as a result of the use and disposal of PFAS-containing consumer products. Some PFAS are also found in the environment as a result of degradation of precursor species including fluorotelomer alcohols, olefins, and perfluoroalkyl sulfonamido substances. PFAS are detected in >98% of people tested as part of the CDC's National Health and Nutrition Examination Survey (NHANES), which suggests that exposure is widespread [39]. In communities without contaminated drinking water supplies, the majority of exposure can be attributed to incidental ingestion and diet. For populations with contaminated drinking water supplies, drinking water exposure is an important contributor to PFAS body burden [40].

Production of PFAS peaked between 1970 and 2002 and has diminished greatly since then. In 2000, 3M (one of the major producers) announced a phase out of all eight carbon PFAS [41]. As a result of an increasing body of evidence demonstrating that long-chain PFAS are persistent, biologically accumulative, and potentially harmful, the United States EPA worked with the eight leading chemical companies to develop the 2010/2015 PFOA Stewardship Program [41]. The goal of this program was to reduce emission and product content of PFOA, PFOA precursors, and higher homologues by 95% by 2010, and to eliminate them completely by 2015. Participating companies provided baseline data in October 2006 and agreed to submit annual reports for years 2007 – 2015 (USEPA, 2014). This program was successful and all companies achieved the stated goals.

In January 2009, the EPA established a drinking water Provisional Health Advisory values for PFOA and PFOS. Provisional Health Advisory values are developed to provide information in response to an urgent

or rapidly developing situation. They reflect reasonable, health-based hazard concentrations above which action should be taken to reduce exposure to unregulated contaminants in drinking water. The Provisional Health Advisory level was established at 0.4 micrograms per liter (µg/L) for PFOA and 0.2 ug/L for PFOS for short-term exposures [42]. Although not thresholds for health effects, ATSDR has previously supported providing alternate water at sites with PFOA exceeding these levels.

In 2013, the EPA implemented reporting requirements for PFAS in public water systems via the Unregulated Contaminant Monitoring Rule 3 (UCMR3) [43-45]. The EPA has not established an action level for PFOA or PFOS in soil or sewage sludge.

In May 2016, the EPA established a lifetime health advisory (LTHA) for PFOA and PFOS (individually or combined) of 0.07 µg/L to replace the Provisional Health Advisory levels. When both PFOA and PFOS are found in drinking water, the combined concentrations of PFOA and PFOS should be compared with the LTHA [46]. The LTHA was developed to be protective of the most sensitive populations (fetuses and infants) using uncertainty factors to protect against short-term and long-term (lifetime) health effects. The LTHA concentrations do not represent fine lines between safe or unsafe conditions, but rather provide a margin of protection for individuals throughout their life from possible adverse health effects. At this time, the EPA also released chronic RfDs for PFOA and PFOS. The RfD for PFOA is 0.00002 mg/kg/day and the RfD for PFOS is 0.00002 mg/kg/day. RfDs are estimates of daily human exposure to that is likely to be without deleterious effects during a lifetime [37, 38].

In August 2015, ATSDR released proposed intermediate MRLs for PFOA and PFOS in the public comment draft of the Toxicological Profile for Perfluoroalkyl Compounds. The draft MRL for PFOA is 0.00002 mg/kg/day and the draft MRL for PFOS is 0.00003 mg/kg/day. MRLs are estimates of the daily human exposure to a hazardous substance that are likely to be without appreciable risk of adverse non-cancer health effects over a specified duration of exposure. These substance specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors and other responders to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean up or action levels for ATSDR or other agencies.

PFAS Contamination near Decatur, Alabama (AL)

In 2007, a PFAS manufacturer in Decatur, AL notified the EPA that it had unknowingly discharged PFAS into the Decatur Utilities wastewater treatment plant. Municipal sewage sludge from this facility was land applied to approximately 5,000 acres of privately owned agricultural fields in the region for approximately 12 years. To date, EPA has identified four direct sources of PFAS to the Decatur Utilities Plant: the 3M Company, Daikin America, Inc., Toray Fluorofibers America, Inc., and the Morgan County Landfill leachate [47].

Soil sampling

In 2007, the EPA conducted limited sampling of soil and sludge samples from two biosolid agricultural application sites and from the Decatur Utilities facility. Results indicated relatively high levels of PFOA and PFOS compared to other industrial and non-industrial sites in the United States. PFOS

concentrations in nine samples collected at biosolid application sites and the Decatur Utilities facility ranged from 589 to 1,296 µg/kg, while PFOA concentrations ranged from 55 to 2,531 µg/kg. The Decatur Utilities ceased land application of biosolids after learning of these PFAS levels in its biosolids [48].

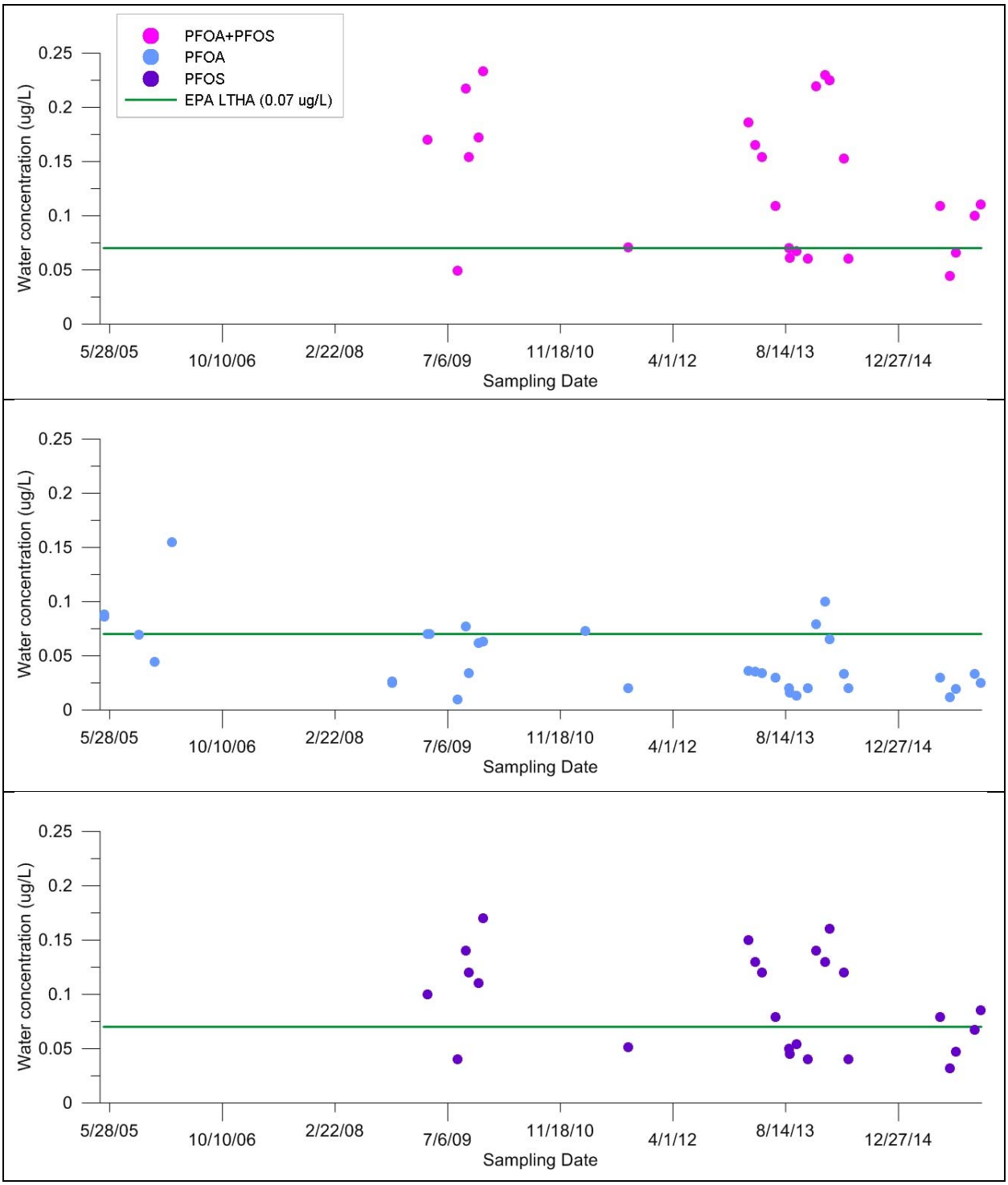
In March 2009, the EPA collected 30 soil samples in or near the fields with the highest applications of biosolids. The results indicated that the majority of the Decatur soils in the land application area have concentrations of PFAS above background levels. Concentrations of PFOA range from non-detect up to 312 µg/kg with most concentrations in the 100 to 200 µg/kg range. Concentrations of PFOS ranged from non-detect up to 325 µg/kg with most concentrations around 100 to 200 µg/kg [49].

Water sampling

Morgan, Lawrence, and Limestone counties are primarily served by three large municipal water systems – the West Morgan East Lawrence Municipal Water Authority, Decatur Utilities, and the City of Moulton.

Water samples of both raw and finished water from the West Morgan East Lawrence Municipal Water Authority have been analyzed for PFAS periodically since 2005 at the request of the Alabama Department of Environmental Management (ADEM) and the EPA. Concentrations of PFOA and PFOS in finished water from this water system can be seen in Figure 1. While PFAS have been detected in water samples from the West Morgan East Lawrence system, concentrations of PFOS and PFOA in finished water from this system have never exceeded the EPA's Provisional Health Advisory Levels (0.4 µg/L for PFOA; 0.2 µg/L for PFOS). Historically, EPA has concluded that these concentrations were not of concern and that residents could rely upon water from this system. However, in light of the evolving science and the recent availability of updated drinking water guidelines (EPA's LTHA) for PFOA and PFOS, this sampling data requires reevaluation. Finished water concentrations of PFOA and PFOS have exceeded the LTHA periodically, though not consistently, since 2005.

Figure 1: Water concentrations of PFOA and PFOS measured in finished water from the West Morgan East Lawrence Municipal Water Authority, 2005 - 2015. Source: Ed Poolos, Alabama Department of Environmental Management. Personal Communications. June 2016.



In November 2008, water samples from the City of Moulton and Decatur Utilities were collected for PFAS analysis. Neither of these systems had quantifiable levels of PFAS in the tested water samples. [50].

In February 2009, EPA collected 51 water samples from ground water wells, ponds, and a stream in or near the fields that received the highest applications of biosolids. The final EPA report identified the following results [51]:

- Six private drinking water wells were sampled.
    - Two had PFOA levels above EPA's provisional health advisory level. These two wells had PFOA levels of 2.2 µg/L and 0.6 µg/L respectively. Both of these residences were provided with bottled water and connected to the public water supply system by Decatur Utilities and a group of local industries.
- Thirteen water wells used as a supply for livestock, gardens, and lawns were sampled. Concentrations in these wells ranged from no detectable level to 6.41 µg/L PFOA and from no detectable levels to 0.15 µg/L PFOS. None of these wells are used for drinking water.
- Thirty-two ponds and one stream were sampled. Concentrations ranged from no detectable levels to 11.0 µg/L PFOA and from no detectable levels to 0.08 µg/L PFOS.

In response to these results, the EPA requested that local PFAS manufacturers identify additional private drinking water wells in the area and conduct quarterly sampling. Thirteen additional private drinking water wells were identified and sampled.

- One well had PFAS detections that exceeded the EPA's provisional health advisory level. This residence was connected to the public water supply.
- One well had PFAS detections that were below the EPA's provisional health advisory level but above the LTHA. This well was re-sampled in 2016. The measured concentrations of PFOA and PFOS remained above the LTHA and this residence was connected to a public water supply.

Previous Biomonitoring

In 2009, EPA contacted ATSDR and requested an Exposure Investigation (EI) in Morgan, Lawrence and Limestone Counties. A total of 153 people volunteered to have PFAS concentrations measured in their blood and samples were collected in April 2010. This investigation will henceforth be referred to as the 2010 EI. The 2010 EI targeted residents who may have higher non-occupational exposure to PFAS than the general population in the United States.

Each participant's blood was analyzed for eight PFAS [49]. At the time the 2010 EI report was released, the most current available data to which the results could be compared were the 2005-2006 National Health and Nutrition Examination Survey (NHANES) data. Since then, the 2009-2010 NHANES data have been made available.

Six PFAS measured (PFNA, PFHxS, PFDeA, Me-PFOSA-AcOH, Et-PFOSA-AcOH and PFOSA) were lower than or similar to the U.S. general population as defined by the 2009-2010 NHANES 95th percentile. The geometric mean levels of PFOA and PFOS were elevated in participants compared to the 95th percentile

measured in the U.S. general population, but were similar to or lower than levels found in other U.S. communities with known exposures to PFAS via drinking water or other environmental pathways.

Participants on the West Morgan East Lawrence public water supply system had elevated PFAS serum concentrations compared to participants with drinking water sources without detectable levels of PFAS.

In response to this investigation, ATSDR recommended:

- Continued efforts to reduce the levels of PFAS in the source water for the West Morgan East Lawrence public water supply system.
- Continued monitoring for PFAS in the affected public water supply and other potentially impacted public water supplies.
- Routine periodic monitoring of other local area public water supplies for potential contamination with PFAS.
- Additional biological PFAS testing in this community to verify that serum PFAS concentrations are declining over time and to identify whether additional public health actions may be needed.

2016 Exposure Investigation

Objectives

The 2016 EI follows through on the recommendation made in the 2010 EI report to conduct biological testing and included the following goals:

- **Provide a public health service to the community:** The investigation provided information to community members about their body burden of PFAS, including an assessment of how their PFAS-serum concentrations compare to national reference populations. Participants also learned how their current serum concentrations compare to those measured in 2010.
- **Generate hypotheses regarding pathways of exposures in the community:** Each individual participant received an interpretation of what their biomonitoring results suggest about how they are being exposed, and whether ATSDR believes that they might have non-drinking water exposures. ATSDR made recommendations to further reduce exposure as appropriate.
- **Advance the scientific understanding of the pharmacokinetics of PFAS in humans:** Very few estimates of biological half-life for PFAS exist in the scientific literature. This investigation generated the data necessary to calculate biological half-life for PFOA, PFOS, and PFHxS, thereby making a significant contribution to the body of scientific knowledge about these compounds. ATSDR will analyze this data and report the resulting estimates of biological half-life separately.

Agency Roles

ATSDR, the lead agency for the EI, collaborated with the National Center for Environmental Health (NCEH), ADEM, EPA Region 4, AXYS Analytical, Inc., and the University of Georgia. The roles of each organization are described in Table 1.

Table 1: Exposure Investigation Partner Organizations and Roles

Organization	Role
Agency for Toxic Substances and Disease Registry	Prepared the EI protocol which included fact sheets, questionnaire, consent and assent forms, and sampling and analysis plan. Conducted all recruitment activities, data analysis, and participant follow up. Coordinated all sample collection activities.
National Center for Environmental Health	Analyzed serum samples.
EPA Region 4	Assisted with collection of background information and sample collection.
Alabama Department of Environmental Management	Assisted with collection of background information, sample collection, and community outreach.
AXYS Analytical, Inc.	Analyzed urine samples.
University of Georgia	Consulted on pharmacokinetic modeling

Methods

Recruitment

The 2016 EI targeted a specific population in Morgan, Lawrence, and Limestone Counties in Alabama (Figure 2). The investigation specifically targeted participants in the 2010 EI (153 residents) for blood and urine testing. Participants had to meet the following inclusion criteria to participate in this investigation:

- Was 12 years of age and older
- Did not have a bleeding disorder and is not anemic
- Did not have current or past occupational (industrial) exposure to PFAS
- Provided written consent/assent/parental permission for blood and urine testing and responding to a questionnaire.

Children younger than 12 years old were excluded because the reference values to be used for comparison for serum concentrations in this investigation are only available for children 12 and older [52]. Participants with diagnosed conditions that impact kidney function (kidney disease, diabetes, hepatitis C, etc.) were asked to self-identify via the questionnaire, but were not excluded from the investigation.

No reimbursements or incentives were offered to participants and there were no costs to participants due to involvement in the study.

ATSDR contacted all 2010 EI participants by phone beginning in Summer/Fall 2015 to recruit them into the investigation. A maximum of three attempts to reach each participant by phone was made.

Recruited participants were sent a letter that confirmed their participation, gave information about the investigation and provided a 1-800 number for participants to call and make sampling appointments. Seventy-eight of the 153 people who participated in the 2010 EI agreed to be re-tested and 46 people completed all portions of the follow-up investigation. One participant was excluded from aggregate data analysis due to reported occupational exposure to PFAS.

Figure 2: Map of Investigation Area - Morgan, Lawrence, and Limestone Counties, AL

Informed Consent/Assent

Consent forms (Appendix A) were provided for participants to read and sign prior to any sample collection activities. Consent forms described the purpose of the investigation, the procedures for blood and urine collection, benefits and risks of participation, and provided contact information should participants have additional questions. ATSDR staff were available to answer any questions related to the informed consent forms.

Confidentiality

Confidentiality is protected to the fullest extent possible by law. All documents with personal identifying information (consent forms, assent forms, collection logs, etc.) are kept in locked cabinets at ATSDR. All electronic data is stored on a password-protected computer. De-identified samples were sent to the laboratories—no individual identifiers were included.

Records have been retained and will be disposed of in accordance with the CDC Records Control Schedule. Record copy of study reports will be maintained at ATSDR from two to three years in accordance with retention schedules. Digital records will be disposed of when no longer needed by program officials and will be kept no longer than five years following the study. Personal identifiers will be deleted from records when no longer needed and will be retained no longer than five years. Disposal methods will include erasing computer file, shredding paper materials, or transferring records to the Federal Records Center when no longer needed for evaluation and analysis. Records are retained for 20 years.

Questionnaire

Each participant was administered a short questionnaire (Appendix B) to gather information on risk factors for exposure. Participants were asked their current address, how long they have lived there, how long they have lived in the Morgan, Lawrence, or Limestone county area, and to identify their primary source of drinking water. Participants were also asked about their occupational history, and the frequency with which they work in the soil, consume locally grown vegetables, and eat locally caught fish. Participants were asked to identify any changes related to drinking water, consumption of locally caught fish and locally grown vegetables, or other changes that may impact their exposure to PFAS since the 2010 investigation.

Physical Measurements

Each participant had their height measured with a SECA 217 portable stadiometer with a measuring range of 20-205 cm and 1 mm graduations. Weight was measured with a SECA 869 scale with maximum capacity of 250 kilograms (kgs) (550 pounds (lbs.)), report graduations of 0.09 kg (0.2 lbs.), and greater than ±0.15% accuracy. Body fat percentage was measured with an Omron BF306 hand held body fat analyzer (accuracy standard estimate of error: 4.1%). All information was recorded by an ATSDR staff person. Body mass index was calculated using the following equation:

$$Body\ Mass\ Index = weight\ (kg)/height(m)^2$$

Serum Sampling

Five milliliter (ml) blood was collected by venipuncture by trained and licensed phlebotomists at a centralized sample collection location. Each sample tube was placed upright in a rack, allowed to clot for 30 minutes at room temperature, and then placed inside a storage box and kept at 40 °F. At the conclusion of the investigation the box was placed inside a plastic Saf-T-Pak™ biohazard bag, placed inside a Styrofoam shipping container with ice packs and hand delivered to the National Center for Environmental Health (NCEH) Laboratory in Atlanta, Georgia. ATSDR/NCEH staff maintained and managed proper chain of custody for all blood samples. Separation of serum was conducted by NCEH staff upon receipt at the NCEH laboratory.

Blood samples were analyzed for eleven PFAS: PFOSA, Et- PFOSA-AcOH, Me-PFOSA-AcOH, PFHxS, PFNA, PFDeA, linear perfluorooctanoate (n-PFOA), sum of branched PFOA isomers (Sb-PFOA), linear perfluorooctane sulfonic acid (n-PFOS), sum of isomers of perfluorodimethylheptane sulfonic acid (Sm-PFOS), and sum of isomers of perfluorodimethylhexane sulfonic acid (Sm2-PFOS). Total PFOA (PFOA) concentration was determined by adding the concentrations of n-PFOA and Sb-PFOA, and total PFOS (PFOS) concentration was determined by adding concentrations of n-PFOS, Sm-PFOS, and Sm2-PFOS. Limits of detection (LODs) for each analyte are reported in Table 3.

Serum samples were analyzed using an on-line solid phase extraction coupled to high performance liquid chromatography – isotope dilution tandem mass spectrometry method reported previously [53, 54]. Low-concentration quality control materials (QCs) and high-concentration QCs, prepared from a calf serum pool, were analyzed with the study samples and with reagent and serum blanks to ensure the accuracy and reliability of the data [53, 54]

Urine Sampling

When participants arrived at their first appointment, they were provided a high-density polyethylene (HDPE) urine collection container, a collection log, and instructions for urine collection. Participants were instructed to collect their entire first morning urine void the morning of their scheduled blood sample collection appointment. Participants were instructed to record the time of their collected first morning void and the time of their previous urine void in their collection log. Following sample collection, participants were instructed to cap the collection container, seal it in a plastic bag, and place it in a refrigerator or cooler until their scheduled blood collection appointment.

When participants arrived at their second appointment an ATSDR staff person recorded the total volume of urine collected, transferred a 50-ml aliquot of each urine sample into a cryovial and placed it in a cooler on dry ice. All samples were kept frozen and shipped overnight on dry ice to AXYS Analytical, Sidney, British Columbia, Canada. Samples were labeled with a coded identification number that matched the identification number on their blood sample in order to pair each participant's blood and urine samples. ATSDR personnel and contract laboratory staff maintained and managed chain of custody for all urine samples.

Urine samples were analyzed for five PFAS: PFOA, PFOS, PFHxS, PFNA, and PFDA. Test results were reported as picograms of the PFAS analyte per gram creatinine (pg/g creatinine) and as picograms per

milliliter of urine (pg/mL). All laboratory analysis were conducted using liquid chromatography – tandem mass spectrometry (LC-MS/MS) with established procedures for quality assurance and control according to the method of the contract laboratory, AXYS Method MLA-107 (Appendix C).

Data and Statistical Analysis

Geometric mean, minimum, maximum, and 95th percentile serum concentrations were determined for total PFOA, total PFOS, PFNA, PFHxS, PFDeA, Me-PFOSA-AcOH, Et-PFOSA-AcOH, and PFOSA. For PFAS concentrations below the limit of detection (LOD), an imputed value equal to the LOD divided by the square root of two was used [55].

Serum concentrations measured in 2016 were compared to serum concentrations reported in the 2011-2012 NHANES as this was the most current available NHANES data.

Individual serum PFAS concentrations measured in 2010 were compared to serum PFAS concentrations measured in 2016 for each individual. The Student's t-test for paired samples was used to evaluate the difference between concentrations in 2010 and 2016. Differences with a p-value greater than 0.05 were considered not statistically significant.

Given the high rate of non-detections in the urine, non-parametric statistical methods were used to calculate means and medians for urine concentrations. Kaplan-Meier methods were used to determine medians and means for PFAS with greater than 60% detection rates.

Pearson's correlation test was applied to test for linear co-occurrence of total PFOA in serum and urine samples collected in 2016. Correlation coefficients were calculated separately for men and women to account for potential variability in PFAS excretion in women due to excretion during pregnancy, lactation, and menstruation. Correlation coefficients could not be determined for other PFAS due to the high percentage of non-detects in urine.

Statistical analyses were performed with the freely available software R version 3.2.4 using the stats package and the NADA package (R Core Team, 2016).

Results

Participant Characteristics

Characteristics of 2016 EI participants are described in Table 2.

Table 2: Characteristics of Exposure Investigation Participants

Number of participants	45
Male:Female	22:23
Mean Age (years)	62.6
Mean Length of Residence Time (years)	29.4
Mean Body Weight (lbs)	196.0 (± 44.4)
Mean Body Mass Index	31.0 (± 7.6)
Body Fat %	35.9 (± 6.8)
Percent Participation by Drinking Water Source	

West Morgan East Lawrence	86.7%
Other Municipal Provider	11.1%
Private Well	0.0%
Bottled	2.2%

PFAS in Serum

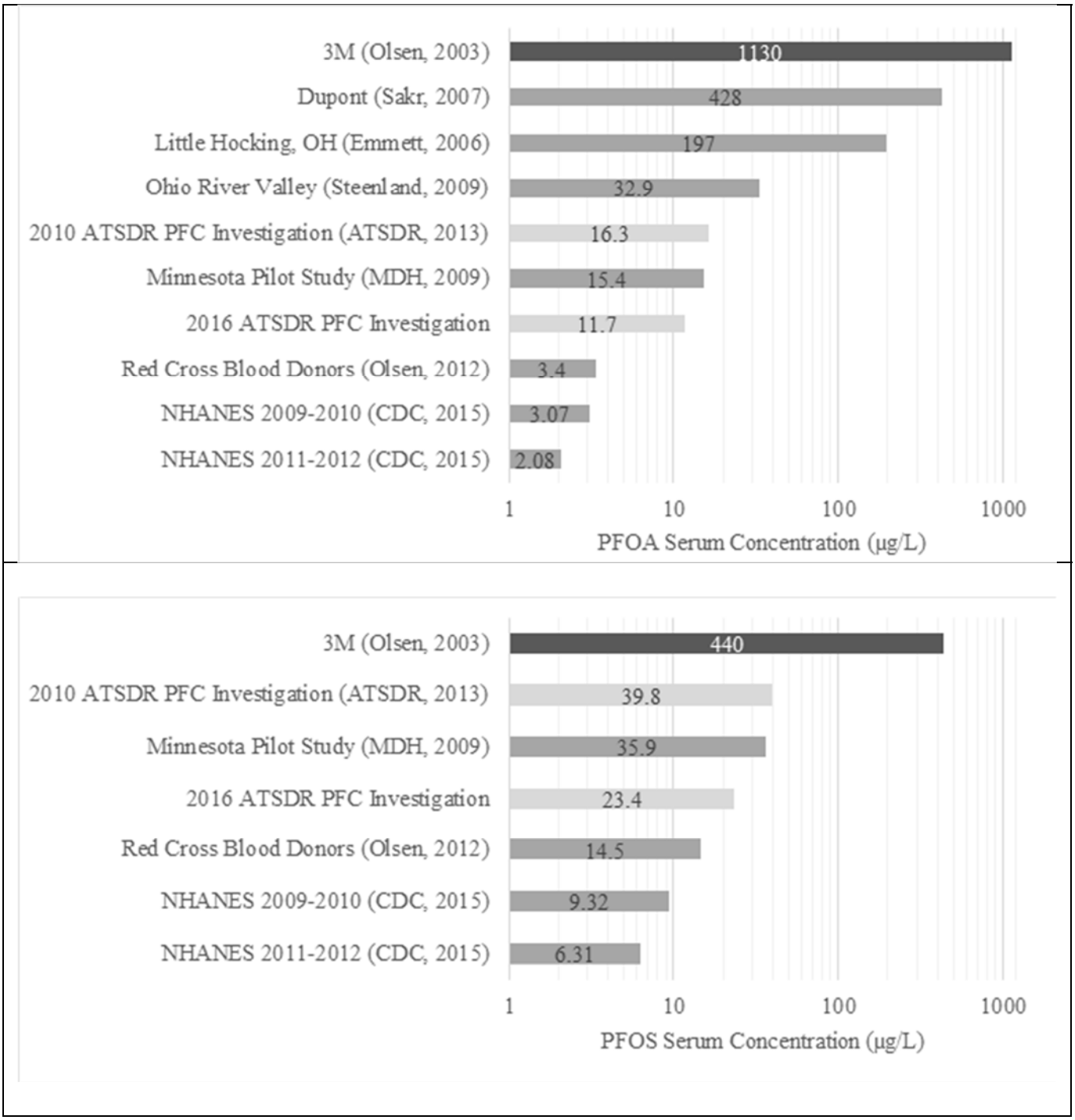
Aggregate results from the 2010 and 2016 blood sampling are reported in Table 3. In 2016, serum concentrations for five PFAS (PFNA, PFDeA, Me-PFOSA-AcOH, Et-PFOSA-AcOH, and PFOSA) were similar to or lower than the U.S. general population as defined by the NHANES 2011 – 2012 95th percentile. Geometric mean concentrations for total PFOS, PFHxS, and total PFOA were higher in participants than the 2011-2012 NHANES 95th percentile, but were lower than concentrations found in other U.S. communities with known exposures to PFAS (Figure 2).

Table 3: Summary of PFAS serum concentrations (µg/L) measured in the 2010 EI and 2016 EI and in NHANES 2009 – 2010 and 2011 – 2012.

	2010 EI (n = 155)	NHANES 2009 -2010	2016 EI (n = 45)	NHANES 2011 - 2012
Total PFOA				
Limit of Detection	0.1	0.1	0.1	0.1
Percent Detected	100	99.7	100	99.5
Geometric Mean	16.3	3.07	11.7	2.08
95th Percentile	61.1	7.5	39.1	5.68
Total PFOS				
Limit of Detection	0.2	0.2	0.1	0.2
Percent Detected	100	99.8	100	99.6
Geometric Mean	39.8	9.32	23.4	6.31
95th Percentile	149.0	32.0	70.6	21.7
PFHxS				
Limit of Detection	0.1	0.1	0.1	0.1
Percent Detected	100	99.4	100	98.4
Geometric Mean	6.4	1.66	7.7	1.28
95th Percentile	23.8	6.9	19.7	5.44
PFNA				
Limit of Detection	0.1	0.1	0.1	0.1
Percent Detected	100	99.8	100	99.3
Geometric Mean	1.7	1.26	0.8	0.881
95th Percentile	3.7	3.77	2.1	2.54
PFDeA				
Limit of Detection	0.2	0.1	0.1	0.1
Percent Detected	65	94.6	91	85.1
Geometric Mean	0.4	0.279	0.27	0.199
95th Percentile	1.4	0.9	0.97	0.69
Me-PFOSA-AcOH				
Limit of Detection	0.2	0.1	0.1	0.1
Percent Detected	63	75.9	59	53.9
Geometric Mean	0.4	0.198	0.15	*
95th Percentile	1.52	1.0	0.8	0.690
Et-PFOSA-AcOH				
Limit of Detection	0.2	0.1	0.1	0.1
Percent Detected	1	5.5	7	5.1
Geometric Mean	*	*	*	*
95th Percentile	*	0.1	*	0.11
PFOSA				
Limit of Detection	0.1	0.1	0.1	0.1
Percent Detected	0	0.1	2	0.8
Geometric Mean	*	*	*	*
95th Percentile	*	<LOD	*	<LOD

* Not calculated, proportion of results below limit of detection was too high to provide a valid result.

Figure 2: Comparison of Mean PFOA and PFOS Serum Concentrations in Occupational and Community Biomonitoring Studies. Occupational studies are shown in dark grey, community studies are shown in grey, and ATSDR investigations are shown in light grey. References: 3M Workers (Olsen et al. 2003); Dupont (Sakr et al. 2007); Little Hocking, OH (Emmett et al. 2006); Ohio River Valley (Steenland et al. 2009); Minnesota Pilot Study – Minnesota Department of Health 2009; Red Cross Blood Donors (Olsen et al. 2008); NHANES (CDC 2015)



Geometric mean serum concentrations of PFOA, PFOS, PFNA, PFDeA, and Me-PFOSA-AcOH were significantly lower (49%, 53%, 58%, 43%, and 60% respectively) in 2016 compared to 2010 (Table 4). Observed changes in the geometric mean serum concentrations of PFHxS were not statistically significant ($p > 0.05$). This data reflects the change in serum concentrations only amongst participants of both the 2010 and 2016 investigations (n = 45). Given that detectable levels of PFOA and PFOS in finished water samples, concentrations did not change significantly between 2005 and 2016 [56], this suggests that exposure from non-drinking water sources has likely decreased over time in this community.

Table 4: Change in Geometric Mean PFAS Serum Concentrations from 2010 to 2016

PFAS	Absolute Change (µg/L)	Percentage Change (%)	Two-tailed P-value, Student's T-test
PFOA	-11.2	-49%	0.00001
PFOS	-26.7	-53%	0.00001
PFHxS	-0.9	-11%	0.37
PFNA	-1.0	-58%	0.000000001
PFDeA	-0.2	-43%	0.0001
Me-PFOSA-AcOH	-0.2	-60%	0.0001
Et-PFOSA-AcOH	*	*	*
PFOSA	*	*	*

Changes calculated as $PFAS_{2016}$ - $PFAS_{2010}$. Time period is 2095 days.
* Not calculated, proportion of results below limit of detection was too high to provide a valid result.

PFAS in Urine

PFAS concentrations measured in urine samples collected in 2016 are reported in Table 5. Concentrations of PFDeA were below the analytical reporting limits in all samples.

Table 5: Urine concentrations of PFOA, PFOS, PFNA, and PFHxS - 2016 Decatur, AL Investigation

			Urine Concentration (µg/L)		Urine Concentration - Creatinine Adjusted (ug PFAS/g creatinine)	
PFAS	Limit of Detection ** (µg/L)	Percent Detected (%)	Mean	Median	Mean	Median
PFOA	0.01	95.6	0.027	0.022	0.031	0.024
PFOS	0.02	45.7	*	*	*	*
PFNA	0.01	30.4	*	*	*	*
PFHxS	0.02	52.2	*	*	*	*

* Not calculated, proportion of results below limit of detection was too high to provide a valid result.
** Detection limits vary for each individual sample as they are based on sample volume. The detection limit for a 50 mL sample is reported here. Additional information is available in Appendix C.

Pearson's correlation test suggested a weak linear relationship between serum PFOA and urine PFOA concentrations in women (Pearson's *r* = 0.35) and a strong linear relationship between serum PFOA and urine PFOA concentrations in men (Pearson's *r* = 0.75). The mean serum PFOA concentration was 14.1 µg/L amongst women and 15.2 µg/L amongst men, while the mean urine PFOA concentration was 25.2 pg/mL amongst women and 31.4 pg/mL amongst men. Correlation coefficients could not be determined for other PFAS due to the high percentage of non-detects in urine.

Assessment of Exposure to Drinking Water from the West Morgan East Lawrence Municipal Water Authority

ATSDR conducted a three step process to evaluate the public health implications of the PFAS contamination in drinking water supplies in this community. ATSDR evaluated ongoing and past PFAS drinking water exposures. First, ATSDR conducted an exposure pathway analysis. Second, ATSDR conducted a screening analysis by comparing the water sampling data to the EPA's LTHA. Third, ATSDR conducted a more detailed public health evaluation of contaminants of concern identified in the screening analysis [57].

Past PFAS Exposures

Greater than 85% of EI participants reported drinking water from the West Morgan East Lawrence Municipal Water Authority in both 2010 and 2016, a water supply that has detected PFOA and PFOS in finished water samples since testing began in 2005. Thus, a completed exposure pathway existed in this community in the past.

Following identification of the completed exposure pathway, ATSDR conducted a screening analysis of past PFOA and PFOS drinking water concentrations by comparing them to the EPA's LTHA. Drinking water concentrations of PFOA and PFOS in finished water samples from the West Morgan East Lawrence Water Authority collected between 2005 and 2015 exceeded the EPA's LTHA in 16 of 25 sampling events in which both PFOA and PFOS were measured, and in 3 of 8 additional sampling events in which only PFOA was measured (Figure 1). As a result, ATSDR identified PFOA and PFOS as contaminants of concern and conducted a more detailed public health evaluation.

For this more detailed evaluation, ATSDR applied EPA's RfDs for PFOS and PFOA and ATSDR's default exposure scenario assumptions. EPA's RfDs were selected for evaluation of estimated exposure doses in this community because these comparison values are protective of both short-term and long-term exposures and this community is believed to have been exposed to PFOA in drinking water for many years.

ATSDR's default exposure assumptions are defined by specific age ranges and exposure doses are estimated for each age group. ATSDR calculates a reasonable maximum exposure (RME) dose and central tendency of exposure (CTE) dose according to the following equation:

$$Dose = {Drinking\ Water\ Intake\ Rate\ \times Drinking\ Water\ Concentration}/{Body\ Weight}$$

The RME dose is the maximum estimated exposure dose that might occur in this community assuming water intake at the level of the 95th percentile reported in NHANES for each age group [58]. The CTE

dose is the average or mean exposure dose that can be estimated in this community assuming typical drinking water intake for each age group. Both the RME dose and CTE dose were calculated using the maximum PFOA and PFOS water concentrations reported in finished water samples from the West Morgan East Lawrence water system between 2005 and 2015. Body weights were selected based on data from NHANES 1999 – 2006, as reported in the USEPA Exposure Factors Handbook [58]. By calculating estimated exposure doses, ATSDR can better assess the possible public health implication for site-specific conditions among different age populations under different exposure durations.

The maximum reported concentrations of PFOA and PFOS in finished water from the West Morgan East Lawrence water system were 0.16 and 0.17 µg/L, respectively. EPA's RfD for PFOS is 2.0×10^{-5} (0.00002) mg/kg/day. EPA's RfD for PFOA is also 2.0×10^{-5} (0.00002) mg/kg/day. Estimated exposure doses using the maximum PFOA and PFOS water concentrations and the RME and CTE water intake scenarios were compared to these RfDs. Estimated CTE and RME doses were equal to or below the RfDs for PFOA and PFOS for every age group (Table 7).

In order to evaluate the potential risk of cumulative exposure to PFOA and PFOS, ATSDR calculated a hazard index. The hazard index approach uses the assumption of dose additivity to assess the non-cancer health effects of a mixture from the data of the components. The hazard index is the sum of the quotients of the estimated dose of a chemical divided by its RfD. If the hazard index is less than 1.0, it is highly unlikely that significant additive or toxic interactions would occur, so no further evaluation is necessary. If the hazard index is greater than 1.0, concern for the potential hazard of the mixture increases.

The hazard index for PFOA and PFOS was below 1.0 for every age group except for the birth to < 1 year and the 1 to < 2 year age group (Appendix F). Thus, ATSDR concludes that it is highly unlikely that additive interactions occurred for anyone over the age of two exposed to PFOA and PFOS at the maximum levels measured in finished water from the West Morgan East Lawrence Municipal Water Authority between 2005 and 2015.

The hazard index exceeds 1.0 for children under the age of one under both the RME and CTE scenario. The hazard index exceeds 1.0 for children between one and two only when the RME scenario is applied. While a hazard index greater than 1.0 increases the level of concern for the potential hazard of the mixture, there are no studies that quantitatively evaluate the cumulative risk of exposure to PFOA and PFOS. Given that the evidence demonstrates that people in this community were likely exposed to PFOA through non-drinking water sources in the past and that health effects have been associated with serum PFOA concentrations comparable to or lower than those observed in this population [18, 22, 59-64], ATSDR concludes that infants and young children whose primary drinking water source was the West Morgan East Lawrence Municipal Water Authority and who drank average or above average quantities of this water at the maximum concentrations detected may have an increased risk of harmful effects.

Current PFAS Exposures

ATSDR applied the same three step process to evaluate current exposures to PFAS. The majority of EI participants remain on the West Morgan East Lawrence water system, thus, a completed exposure pathway is still present.

In response to the release of the LTHA on May 19, 2016, the West Morgan East water system took steps to reduce levels of PFAS in their finished drinking water. On June 10, 2016 they announced a plan to purchase and blend water from Decatur Utilities (a nearby water systems with no detectable PFAS concentrations) with water from the West Morgan East Lawrence water system.

On June 13, 2016, ADEM collected a finished water sample from the West Morgan East Lawrence system in order to evaluate concentrations of PFAS in the blended water. The concentration of PFOA in this sample was below the detection limit. The concentration of PFOS in this sample was 0.028 µg/L.

ATSDR conducted a screening analysis of this data to determine if a detailed evaluation of current PFAS drinking water exposures is needed. Concentrations of PFOA and PFOS, both individually and combined, were below the LTHA. Thus, further evaluation is not needed.

Conclusions

1. Exposure to PFAS is decreasing over time in the people tested. Geometric mean serum concentrations of PFOA, PFOS, perfluorononanoic acid (PFNA), and 2-(N-methyl-Perfluorooctane sulfonamido) acetic acid (Me-PFOSA-AcOH) were significantly lower (28%, 41%, 54%, and 63% respectively) in 2016 than in 2010. Observed changes in the geometric mean serum concentrations of PFHxS and perfluorodecanoic acid (PFDeA) were not statistically significant.
2. Historical PFAS exposures amongst participants in the investigation were likely higher than exposures to the general U.S. population and were lower than or similar to exposures that occurred in other communities located near PFAS manufacturing or use. Geometric mean levels for three PFAS (PFOS, PFHxS, and PFOA) were elevated in EI participants compared to the U.S. general population as defined by the 2011 – 2012 National Health and Nutrition Examination Survey (NHANES) 95th percentile. However, geometric mean serum concentrations of PFOA and PFOS were lower than or similar to levels found in other U.S. communities with known exposures to PFAS.
3. Geometric mean serum concentrations for five PFAS (PFNA, PFDeA, Me-PFOSA-AcOH, 2-(N-ethyl-Perfluorooctane sulfonamido) acetic acid [Et-PFOSA-AcOH], and perfluorooctane sulfonamide [PFOSA]) were similar to or lower than the U.S. general population as defined by the 2011 – 2012 NHANES 95th percentile.
4. Exposure to PFAS in drinking water is not a current public health hazard for any age group. Concentrations of PFOA and PFOS measured in the West Morgan East Lawrence Municipal Water Authority are currently below the United States Environmental Protection Agency's (EPA's) lifetime health advisory (LTHA).
5. Drinking water from the West Morgan East Lawrence Municipal Water Authority in the past is not expected to be harmful for adolescents or adults (anyone over the age of two).

6. Infants and young children whose primary drinking water source was the West Morgan East Lawrence Municipal Water Authority and who drank average or above average quantities of this water at the maximum concentrations detected may have an increased risk of harmful effects resulting from additive exposure to PFOA and PFOS. ATSDR makes this conclusion based on the following:
    - Based on the assumptions used in our exposure dose calculations, the hazard index exceeds 1.0 for children under the age of one under both the Reasonable Maximum Exposure (RME) and Central Tendency Exposure (CTE) scenarios. The hazard index exceeds 1.0 for children between one and two only when the RME scenario is applied. While a hazard index greater than 1.0 increases the level of concern for the potential hazard of the mixture, there are no studies that quantitatively evaluate the cumulative risk of exposure to PFOA and PFOS.
    - Evidence suggests that people in this community, including infants and young children, were likely exposed to PFOA through non-drinking water sources in the past.
    - Health effects have been associated with serum PFAS concentrations comparable to or lower than those observed in this population, and young children have been identified as potentially sensitive to health effects resulting from exposure to PFOA and PFOS.

Recommendations

1. ATSDR recommends that community members concerned about exposures to PFAS consult with their physicians.
2. In light of the evidence that people living in the vicinity of Morgan, Lawrence, and Limestone Counties have blood levels of some PFAS that are elevated compared to national reference populations, ATSDR recommends that water systems downstream of PFAS facilities on the Tennessee River, including the West Morgan East Lawrence Municipal Water Authority, continue conducting routine monitoring of PFAS concentrations in finished drinking water and take steps to ensure that concentrations of PFAS in finished drinking water remain below the current EPA Lifetime Health Advisory for PFOA and PFOS (0.07 µg/L).

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Appendix A: Consent Forms

U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry
PFC Exposure Investigation, blood and urine sampling
Adult Consent Form (≥ 18 years of age)
Flesch-Kincaid Reading Level (without agency or chemical names): 8.0

Who are we and why are we doing this blood and urine testing?
We are from the Agency for Toxic Substances and Disease Registry (ATSDR), a federal public health agency based in Atlanta. We are inviting you to have a blood and urine test for a family of chemicals called Perfluoroalkyl Compounds (PFC). We are offering this test to find out how much of these chemicals is getting into your body and how quickly they are being removed from your body, and to do research on biological modeling of these chemicals. The data from your samples will be used to help us understand how you might be exposed to these chemicals.

The Environmental Protection Agency has found these chemicals in your community in soil fields treated with sludge from the local wastewater treatment plant. People that work or live near these fields may come into contact with these chemicals. Some private drinking water wells have been contaminated with this chemical. Recent tests in one public water system have found these PFC chemicals at levels below current guidelines. PFCs can be found in consumer products like non-stick cookware, paper coatings, stain-resistant carpets, nail polishes and fire-fighting foam. More research is needed to understand PFCs effect on human health.

What is involved in this testing?
In the blood test, a 5 milliliter (mL) sample of blood (about 1 teaspoon) will be collected from a vein in your arm. The blood sample will be tested for 12 different types of PFC chemicals. If you are anemic (low blood cells) or have a bleeding disorder then we will not be able to sample your blood.

In urine test, you will be provided a container in which to collect all of your urine the first time you urinate the day of your sample collection.

You will also be asked to report the time of the last time you urinate prior to collecting your urine sample. The urine sample will be tested for 5 different types of PFC chemicals.

You will also be asked to have your height, weight, and body fat percentage measured using a measuring stick, scale, and digital body fat analyzer and recorded. These characteristics impact how PFCs behave in your body and will allow ATSDR to better understand your exposures.

Your blood and urine will be sent to a lab for testing. We will mail you the test results along with what they mean approximately 6 months after testing, but some delays might occur. You may share these results with your doctor - it is your choice.

PFCs are beginning to generate increased interest across the United States. As a result, data from your samples (without any personal identifying information) will be kept for potential additional analysis in the future. Your blood sample may also be saved for future tests if you give consent. You will need to sign an additional consent form if you agree to allow your blood sample to be stored for future tests.

What are the benefits from being involved in this testing effort?

By being part of this testing effort, you will find out the amount of the PFC chemicals in your blood and how these levels have changed since 2010. We may also be able to tell you how quickly your kidneys remove some PFC chemicals from your body. If the tests show levels of PFC in your blood that are higher than most people or a rate of PFC removal slower than most people, you will get tips on how to avoid current and future exposure to PFC chemicals. We will give you written information about PFC chemicals.

Research to better understand the health effects associated with PFC exposure is ongoing, but scientists are not currently certain of how PFC levels in the blood can affect a person's health. More research is needed to clarify the risks posed by PFC exposure. Your participation in this study will help advance this research. We will **not** be able to tell you if the PFC levels in your blood will make you sick now or later in life.

We will **not** be able to tell you specifically from where or how the PFC chemicals entered your body. **No** medical diagnosis, treatment, or additional testing will be offered from this testing effort.

This testing is free for you.

What are the risks of being tested?
There may be some discomfort and minor bruising in area where the blood sample is collected. The entire collection (distributing consent forms, completion of questionnaire, blood and urine collection) will require approximately 35 minutes of your time.

What about my privacy?
We will protect your privacy as much as the law allows. We will give you an identification (ID) number. This number, not your name, will go on the blood and urine samples. We will not use your name in any report we write. We will keep a record of your name, address, and ID number so that we can send you the test results and an interpretation of what they mean. We keep all records with your name on them in a locked file cabinet or in a password-protected computer file. Your identifying information will also be protected should you choose to share your results with other federal or state agencies. Personal identifying information will not be shared with other agencies. Personal identifying information will be deleted from all records when it is no longer needed and will not be kept longer than five years. All collection logs and questionnaire forms with personal information will be shredded as soon as they are no longer needed and will not be kept longer than five years.

Who do I contact if I have questions?
If you have any questions about this testing, you can ask us now. If you have questions later, you can call Rachel Worley or Bruce Tierney, MD of ATSDR toll-free at 1-855-288-0242, or email them at RWorley@cdc.gov or BTierney@cdc.gov. If you have questions about your study rights you may contact the Centers for Disease Control and Prevention's Institutional Review Board at 1-800-584-8814.

Voluntary Consent
I agree to be tested. I have been given a chance to ask questions and feel that all questions have been answered. I know that being in this testing is my choice. I know that after choosing to be in this testing, I may stop at any time.

SIGNATURE

I have read this form or it has been read to me. I have had a chance to ask questions about this testing and my questions have been answered. I agree to be a part of this testing.

Place ID # label here

_____

Participant - Printed Name

_____ _____

Participant - Signature Date

May we share these test results with other Federal and State health and environmental agencies? Your identifying information will be protected should you choose to share your results with other federal or state agencies.

YES or NO (Circle One)

Address: _____

_____

Phone - Home #: _____

Phone - Cell #: _____

U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry
PFC Exposure Investigation, blood and urine sampling
Adult Consent for Storage of Blood Sample for Use in Future Research
Flesch-Kincaid Reading Level (without agency or chemical names): 7.0

What is this about?

Research to better understand the health effects associated with PFC exposure is ongoing, but scientists are not currently certain of how PFC levels in the blood can affect a person's health. More research is needed to clarify the risks posed by PFC exposure. It is possible that new tests will be developed in the future that will increase our understanding of how PFCs impact human health. We would like to keep your blood sample for five years so that scientists can test for more things if new tests are developed. To do this, we need your permission.

Your name will not be connected with any of the test results.

What are the risks?

Some people may feel uncomfortable about having their blood tested for other things.

Are there benefits for me?

There is not direct benefit to you if you let us keep your blood sample for future tests. But, helping carry out this research may increase our understanding of how PFCs impact human health.

Do I have to give permission?

If you do not want your blood to be used for other tests, it is okay. If you are okay with further testing, you must sign this form.

What about confidentiality?

If you allow us to save and use your blood, we will break the link between your name and your sample before any more tests are done. We don't believe it will be possible to connect the results of any new tests back to you.

Is there compensation?

You will not be paid.

Place ID # label here

Who do I contact if I have questions?

If you have any questions about this testing, you can ask us now. If you have questions later, or if you change your mind about having your sample stored, you can call Rachel Worley or Bruce Tierney, MD of ATSDR toll-free at 1-855-288-0242, or email them at RWorley@cdc.gov or BTierney@cdc.gov. If you have questions about your study rights you may contact the Centers for Disease Control and Prevention's Institutional Review Board at 1-800-584-8814.

VOLUNTARY CONSENT

I agree to allow my blood sample to be saved and used for other tests. I know allowing further testing is my choice. I know I can change my mind at any time before the link between my name and my specimen is broken. I will be given copy of this permission form to keep.

SIGNATURE

I give permission for my blood samples to be saved and used for other tests.

_____ _____/_____

Signature Date Time

_____

Printed Name

Appendix B: Questionnaire

U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry
PFC Exposure Investigation, blood and urine sampling Questionnaire
(ATSDR OMB Control No. 0923-0048)

Name: _____

Date of Birth: _____ (Month/Day/Year) **Sex:** Male Female

Address: _____

1. Are you Hispanic, Latino/a, or Spanish origin? One or more categories may be selected. You may skip this question.
   - o No, not Hispanic, Latino/a
   - o Yes, Hispanic, Latino/a

2. What is your race? One or more categories may be selected. You may skip this question.
   - o American Indian or Alaska Native
   - o Asian
   - o Black or African American
   - o Native Hawaiian or Other Pacific Islander
   - o White

3. How many years have you lived at your current address?

   _____ (years)

   Don't Know

   Refused to Answer

4. How many years have you lived in the Morgan/Lawrence/Limestone County area? _____ (years)

   Don't Know

   Refused to Answer

5. Has your doctor ever told you have:

Diabetes	Yes	No	Don't Know	Refused to Answer
Kidney Disease	Yes	No	Don't Know	Refused to Answer
Hepatitis C	Yes	No	Don't Know	Refused to Answer Know
Anemia	Yes	No	Don't Know	Refused to Answer Know

6. Are you currently undergoing dialysis treatment?

To be filled out by ATSDR Staff:

Height: _____

Weight: _____

Body Fat %: _____

Urine Volume: _____

Yes No Don't Know Refused to Answer

If participant is under the age of 17, skip to question #10.

7. To your knowledge, are you pregnant? If participant is male, skip to question #9.

   Yes No Don't Know Not Applicable Refused to Answer

8. Have you completed menopause? If participant is male, skip to question #9.

   Yes No Don't Know Not Applicable Refused to Answer

   If yes, how long ago did you complete menopause? _____ (years)

   Don't Know Refused to Answer

9. How frequently do you donate blood and/or plasma (circle one)?

Once per month	A few times per year	Once per year	Rarely	Never	Don't Know	Refused to Answer

10. Did you participate in the 2010 Exposure Investigation? If no, skip to question 13.

    Yes No Don't Know Refused to Answer

11. If yes, has your address changed?

    Yes No Don't Know Refused to Answer

12. If yes, please select any behaviors that have changed following the 2010 Exposure Investigation:

    - o My drinking water source changed from private well to public water system.
    - o My drinking water source changed from private well to bottled water.
    - o My drinking water source changed from public water system to bottled water.
    - o I have installed a filtration system on my private well.
    - o My drinking water source changed in some other way (please explain):

      _____

    - o My consumption of locally caught fish has increased.
    - o My consumption of locally caught dish has decreased.

- o My consumption of locally grown vegetables has increased.
- o My consumption of locally grown vegetables has decreased.
- o Other behaviors related to PFC exposure (please explain):

  _____

- o Refused to Answer

13. How frequently do you work or play in the soil (e.g. gardening, digging, farming, building, repairing, etc…) (circle one)?

Once per month	A few times per year	Once per year	Rarely	Never	Don't Know	Refused to Answer

If you work in the soil, at what address or place (e.g. daycare) does this occur (list all locations):

_____

Refused to Answer

14. How often do you eat "homegrown" or locally grown vegetables (circle one)?

Once per month	A few times per year	Once per year	Rarely	Never	Don't Know	Refused to Answer

15. How often do you eat fish caught from local ponds, lakes or rivers (circle one)?

Once per month	A few times per year	Once per year	Rarely	Never	Don't Know	Refused to Answer

16. What is the main source of drinking water in your home (circle one)?

Public – City or County

Name of water supplier:

Private Well

Spring

Pond

Cistern

Community Well

Bottled Water

Don’t Know

Refused to Answer

17. If you have a private well, has it been tested for PFCs?

    Yes No Don’t Know Refused to Answer

    If yes, do you know the date it was tested, who did the testing, and the results of the PFC testing?

Date (month/year)	Company/Government	PFC Results

18. Please list your job title and where you have worked for the past 20 years. If participant is under the age of 17, skip to end.

    Not Applicable

    Refused to Answer

Company Name	Job Title	Year Started	Year Ended

*** THANK YOU ***

Appendix C: Analytical Method for Urinalysis

1.1 Urine sample preparation

A 50 mL of portion of the urine sample was diluted to 500 mL using reagent water. When necessary the sample pH was adjusted to 6.5 ± 0.5 with 50% aqueous formic acid or ammonium hydroxide. The sample was spiked with the isotopically-labeled standards in Table C1. Oasis WAX cartridges (150 mg) were conditioned with 2 × 3.5 mL of 0.3% ammonium hydroxide in methanol followed by 5 mL of 0.1 M formic acid. The diluted urine samples were loaded at ~ 5 mL/min. After loading the SPE cartridges were washed with 10 mL of reagent water and 5 mL 1:1 methanol : 0.1 M formic acid. The cartridges were allowed to dry for ~ 15 seconds under vacuum. The analytes were eluted with 4 mL of 0.3% basic methanol. The final extract was spiked with recovery standard solution containing $^{13}C_2$-PFOUEA and $^{13}C_4$-PFOA and analyzed by LC-MS/MS.

1.2 LC-MS/MS analysis

Analysis was performed by liquid chromatography tandem mass spectrometry (LC–MS/MS) using a Waters 2795 HPLC connected via an electrospray interface to a Waters Quattro Ultima tandem mass spectrometer (Micromass, Manchester, UK) operated in negative ion electrospray multiple reaction monitoring (MRM) mode. Analyte separation was achieved on a Waters Xtera C18 MS column (10.0 cm, 2.1 mm i.d., 3.5 μm). The mobile phase and LC gradient are provided in Table C2. A series of eight solvent-based calibration solutions containing the native analytes, labeled surrogates, and labeled recovery standards were used to establish the initial calibration of the analytical instrument, Table C3. Quantification was achieved by isotope dilution using quadratic calibration equations weighted by the reciprocal of the standard concentration (1/x weighting) and excluding the origin.

1.3 Creatinine Adjustment

Prior to extraction a 500μL sub-sample was taken from each sample for creatinine analysis. Creatinine concentrations were used to determine the mass of creatinine per sample. Analyte concentrations were then re-quantified using the mass of creatinine, in grams, as the sample size, yielding an adjusted concentration with units expressed as analyte mass per gram of creatinine (ng/g(creatinine)).

Table C1. Analytes, parent and daughter mass ions, and quantification references.

Target Analyte	**Typical Retention Time (min.)**	**Parent Ion Mass**	**Daughter Ion Mass**	**Quantified Using**
Perfluorooctanoate (PFOA)	7.0	413	369 (169)[1]	$^{13}C_2$-PFOA
Perfluorononanoate (PFNA)	7.4	463	419	$^{13}C_5$-PFNA
Perfluorodecanoate (PFDA)	7.9	513	469	$^{13}C_2$-PFDA
Perfluorohexanesulfonate (PFHxS)	7.2	399	80 (99/119)[1]	$^{18}O_2$-PFHxS
Perfluorooctane sulfonate (PFOS)	8.2	499	80 (99)[1]	$^{13}C_4$-PFOS
Surrogate Standard				
$^{13}C_2$-Perfluorooctanoic acid ($^{13}C_2$-PFOA)	7.0	415	370	$^{13}C_4$-PFOA
$^{13}C_5$-Heptadecafluorononanoic acid ($^{13}C_5$-PFNA)	7.4	468	423	$^{13}C_2$-PFOUEA
$^{13}C_2$-Perfluorodecanoic acid ($^{13}C_2$-PFDA)	7.9	515	470	$^{13}C_2$-PFOUEA
$^{18}O_2$–Perfluorohexanesulfonate ($^{18}O_2$-PFHxS)	7.2	403	84 (103)[1]	$^{13}C_2$-PFOUEA
$^{13}C_4$–Perfluorooctanesulfonate ($^{13}C_4$-PFOS)	8.2	503	80 (99)[1]	$^{13}C_2$-PFOUEA
Recovery Standard				
$^{13}C_2$-2H-Perfluoro-2-decenoic acid ($^{13}C_2$-PFOUEA)	7.3	459	394	External
$^{13}C_4$-Perfluorooctanoic acid ($^{13}C_4$-PFOA)	6.9	417	372	External

[1] Alternate transition within brackets.

Table C2. Liquid chromatography gradient used in the present work.

Time (min)	Mobile Phase		LC flow (mL/min)	Gradient curve
	Aqueous %	Organic %		
0.0	85	15	0.2	1
1.0	85	15	0.2	6
5.0	70	30	0.2	6
8.5	100	0	0.2	6
11.3-14.5	85	15	0.2	4

Aqueous (solvent A) – 13mM ammonium acetate in 0.1% acetic acid (aqueous).
Organic (solvent B) – 10% aqueous acetonitrile.

Table C3. Nominal Concentrations of Calibration Solutions (ng/mL)

	CAL A	CAL B	CAL C	CAL D	CAL E	CAL F	CAL G	CAL H
PFOA	0.125	0.312	1.25	5.00	25.0	50.0	125	312
PFNA	0.125	0.312	1.25	5.00	25.0	50.0	125	312
PFDA	0.125	0.312	1.25	5.00	25.0	50.0	125	312
PFHxS	0.250	0.625	2.50	10.0	50.0	100	250	625
PFOS	0.250	0.625	2.50	10.0	50.0	100	250	625
$^{13}C_2$-PFOA	9.0	9.0	9.0	9.0	9.0	9.0	9.0	9.0
$^{13}C_5$-PFNA	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
$^{13}C_2$-PFDA	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
$^{18}O_2$-PFHxS	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
$^{13}C_4$-PFOS	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
$^{13}C_2$-PFOUEA	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
$^{13}C_4$-PFOA	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0

Appendix D: Estimated Exposure Doses for Community Members Drinking Water from the West Morgan East Lawrence Municipal Water Authority

Age Group	Exposure Assumptions			Estimated Exposure Dose (mg/kg/day)				Hazard Index for PFOA + PFOS	
	Drinking Water Intake (L/day)		Body Weight (kg)	maximum PFOA water concentration = 0.16 µg/L		maximum PFOS water concentration = 0.17 µg/L			
	Upper Percentile	Mean		RME	CTE	RME	CTE	RME	CTE
Birth to < 1 yr	1.113	0.504	7.8	0.00002	0.00001	0.00002	0.00001	**2.35**	**1.07**
1 to < 2 yr	0.893	0.308	11.4	0.00001	0.000004	0.00001	0.000005	**1.29**	0.45
2 to < 6 yr	0.977	0.376	17.4	0.00001	0.000003	0.00001	0.000004	0.93	0.36
6 to < 11 yr	1.404	0.511	31.8	0.00001	0.000003	0.00001	0.000003	0.73	0.27
11 to <16 yr	1.976	0.637	56.8	0.00001	0.000002	0.00001	0.000002	0.57	0.19
16 to <21 yr	2.444	0.77	71.6	0.00001	0.000002	0.00001	0.000002	0.56	0.18
Adults ≥ 21 yr	3.092	1.227	80	0.00001	0.000002	0.00001	0.000003	0.64	0.25
Lactating Women	3.588	1.665	73	0.00001	0.000004	0.00001	0.000004	0.81	0.38
Pregnant Women	2.589	0.872	73	0.00001	0.000002	0.00001	0.000002	0.59	0.20

Notes: CTE = central tendency of exposure, L = Liter, mg/kg/day = milligrams of chemical per kilogram of body weight per day, RME = reasonable maximum exposure concentration, µg/L = micrograms per liter, PFOA RfD = 0.00002 mg/kg/day, PFOS RfD = 0.00002 mg/kg/day.